

## Epidemiology and Prevention of CV Disease

### Increasing prevalence of metabolic syndrome in a Chinese elderly population: 2001–2010

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**Objective** The information on the changes of prevalence of metabolic syndrome (MetS) in China is limited. Our objective was to assess a 10-year change of the prevalence of MetS in a Chinese elderly population between 2001 and 2010.

**Methods** We conducted two cross-sectional surveys in a representative sample of elderly population aged 60 to 95 years in Beijing in 2001 and 2010 respectively. MetS was defined according to the 2009 harmonizing definition.

**Result** A total of 2 334 participants (943 male, 1 391 female) in 2001 and 2 102 participants (848 male, 1 254 female) in 2010 completed the survey. The prevalence of MetS was 50.4% (95% CI: 48.4%–52.4%) in 2001 and 58.1% (95% CI: 56.0%–60.2%) in 2010. The absolute change of prevalence of MetS was 7.7% over the 10-year period ( $P < 0.001$ ). The syndrome was more common in female than male in both survey years. Among the five components, hypertriglyceridemia and low HDL-C had increased most, with an increase of 14.8% (from 29.4% to 44.2%) and 9.9% (from 28.3% to 38.2%) respectively. The adjusted ORs of MetS for CHD, stroke and CVD were 1.67 (95% CI: 1.39–1.99), 1.50 (1.19–1.88) and 1.70 (95% CI: 1.43–2.01) in 2001, and were 1.74 (95% CI: 1.40–2.17), 1.25 (95% CI: 0.95–1.63) and 1.52 (95% CI: 1.25–1.86) respectively in 2010.

**Conclusion** The prevalence of MetS is high and increasing rapidly in this Chinese elderly population. Participants with MetS and its individual components are at significantly elevated ORs for CVD. Urgent public health actions are needed to control MetS and its components, especially for dyslipidemia.

### Effect of different body mass index and waist circumference on arterial elasticity in prehypertensive patients

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**Objective** To investigate the effect of different body mass index

(BMI) and waist circumference on arterial elasticity in prehypertensive patients.

**Methods** The basic information was collected in a total of 776 prehypertensive patients. According to BMI and waist circumference level, all subjects were divided into four groups, namely, normal BMI and normal waist circumference group (I group,  $n = 194$  cases), normal BMI and elevated waist circumference group (II group,  $n = 195$  cases), elevated BMI and normal waist circumference group (III group,  $n = 196$  cases), elevated BMI and elevated waist circumference group (IV group,  $n = 191$  cases). Brachial ankle pulse wave velocity (baPWV) and ankle-brachial blood pressure index (ABI) were observed in all patients. Arterial stiffness index (AI) was calculated using the blood lipid of all hypertension patients.

**Result** baPWV ( $2\ 120 \pm 263$ ) and AI ( $3.35 \pm 0.87$ ) in IV group were significantly higher than I group ( $P < 0.01$ ), II group and III group ( $P < 0.05$ ). ABI ( $0.72 \pm 0.15$ ) in IV group were significantly lower than I group ( $P < 0.01$ ), II group and III group ( $P < 0.05$ ). There were no statistical differences between II group and III group in ABI and AI ( $P > 0.05$ ). Result of  $2 \times 2$  factorial analysis showed that there was a distinctive and synergistic effect between excessive BMI and elevated waist circumference on arterial stiffness.

**Conclusion** Arterial elasticity function was apparent damaged in prehypertensive patients with abdominal obesity. Elevated BMI and elevated waist circumference had interaction and synergistic effect on the damage of arterial elasticity function.

### The study of association between PAI-1 gene and blood stasis syndrome in premature coronary heart disease of Hunan nation population.

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**Background** To investigate whether PAI-1 gene increased the risk of Heart Blood Stasis Syndrome (HBSS) in coronary heart disease (CHD) pedigrees, haplotype-based haplotype relative risk (HHRR) and transmission disequilibrium test (TDT) were used.

**Methods** Forty CHD pedigrees with at least one CHD patient in the first degree relatives of probands and ten pedigrees without CHD were collected during Oct. 2003 to Dec. 2012, of which premature CHD pedigrees with HBSS, parental genotype known of which were 25 and 18 respectively. PAI-1 genotype was measured by PCR-VNTR technique. HHRR and TDT were used with core pedigrees in base of the result that the polymorphism of PAI-1 was associated linked with premature CHD.

**Result** There were no significant difference in genotype distribution and allele frequencies between patients and parents in premature coronary heart disease pedigree groups (including pedigrees with HBSS and pedigrees without HBSS) ( $P > 0.05$ ), which illustrated that both of genotype and allele of PAI-1 gene did not deviate from Hardy-Weinberg equilibrium in premature coronary heart disease. But the cases' number of premature CHD pedigrees with HBSS whose CA repeat copy number  $N < 20$  was significantly higher than the number of non-BSS. In the method based on haplotype HHRR analysis method for 28 core pedigrees information to calculate the relevance between CHD and blood stasis PAI-1 allele CA18 and non-BSS PAI-1 allele CA20. In which 14 (W) CA18 gene transferred, 3 (Y) did not delivery among PAI-1 (2N) alleles of blood stasis pedigrees; 22 (X) transferred, 33 (Z) did not among

55 non-CA18 gene. Calculated by  $\chi^2$  formula:  $2N(WZ-XY) / (W+X)(W+Y)(X+Z)(Y+Z)$ , HHRR's  $\chi^2$  9.32,  $df = 1$ ,  $P < 0.05$ , which tipped that CHD with HBSS and CA18 of PAI-1 gene polymorphisms are associated. In PAI-1 (2N) alleles of the non-BSS pedigrees, 9 (W) CA20 gene transferred, 5 (Y) did not delivery; in 26 non-CA20 gene, 11 (X) transferred, 15 (Z) did not delivery, which suggesting that CHD without HBSS and CA20 of PAI-1 gene polymorphism are not associated ( $P > 0.05$ ); TDT test conducted for the 11 core pedigrees meet the requirements, which showed CA18 alleles from heterozygous parents to offspring passed 12 times, did not pass 3 times, the other alleles from heterozygous parents to offspring passed 3 times, did not pass 12 times. By  $\chi^2 = (bc) / (b+c) = 5.4$ ,  $P < 0.05$ , suggested that the susceptibility location of CHD with HBSS may be linked with CA18 of PAI-1 alleles; there were 6 non-BSS pedigrees meeting with TDT analysis, CA20 alleles from heterozygous parents to offspring passed 4 times, did not pass 2 times, the other alleles from heterozygous parents to offspring passed 2 times, not passed 4 times, which indicated that the susceptibility location of CHD with HBSS may be not linked with CA20 of PAI-1 allele ( $P > 0.05$ ).

**Conclusion** The CA18 alleles of PAI-1 Gene is associated with HBSS in CHD pedigrees. Indicating that the CA18 alleles of PAI-1 Gene may be linked with susceptibility location of HBSS in CHD of Hunan Han nation population.

### Validation and utility of the Framingham general cardiovascular disease risk score for predicting 10-year cardiovascular events in an inner Mongolian population: a prospective cohort study

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**Background** The Framingham general cardiovascular disease (CVD) risk score (FGCRS) is a widely-studied tool to identify individual with a high risk of global CVD, but the homogeneous nature of the Framingham population prevents simple extrapolation to other populations. We aimed to examine and recalibrate the FGCRS in an Inner Mongolian population, China.

**Methods** A randomly-derived, population-based, prospective cohort of 2 583 community participants free of CVD were followed up for new CVD events from 2002 to 2012. CVD events were defined as a composite of coronary heart disease (coronary death, myocardial infarction, coronary insufficiency, and angina), cerebrovascular events (including ischemic stroke, hemorrhagic stroke, and transient ischemic attack), peripheral artery disease (intermittent claudication), and heart failure. Information about CVD events on follow-up was obtained with the aid of medical histories, physical examinations at the study clinic, hospitalization records and communication with community physicians. According to the Framingham formulation, a 10-year risk of CVD was estimated for every participant. We compared the predicted and observed incidence of CVD events within each decile of calculated CVD risk scores based on the FGCRS. Recalibration was computed referring to the Result of comparison between observed and predicted risk of CVD. We assessed discrimination on the basis of C statistics and examined whether the prediction of incident CVD events on the basis of the FGCRS

improved after reclassification on the basis of recalibrated FGCRS using the net reclassification improvement and integrated discrimination improvement. Attributable risk proportion was calculated to estimate the effectiveness of use of the FGCRS by using COX proportional hazard model with 0–5 percent category as a reference.

**Result** After 22 821 person-years follow-up, 345 (13.36%) participants experienced CVD events. The FGCRS underestimated global CVD risk for Mongolian population (8.52% vs 13.36%). The relative excess observed risk for 10-year CVD events by 36% was similar in 7 of 10 deciles of calculated CVD risk scores based on the FGCRS. Recalibrated probabilities of CVD events were therefore obtained from the 10 year predictions by dividing the final score by 0.64 (1 minus 0.36), namely recalibrated CVD risk score of each participant was calculated by multiplying the result of the FGCRS by a correction factor of 1.56. The recalibrated FGCRS had significant improvement in prediction performance for Mongolians, as indicated by a marked integrated discrimination improvement (IDI = 0.069,  $P < 0.001$ ) and a net reclassification improvement (NRI = 0.150,  $P < 0.001$ ). After 10 years follow-up, cumulative incidences of CVD events in 0–5, 5–10, 10–20, 20–30, and  $\geq 30$  percent risk categories were 2.62%, 7.56%, 17.58%, 29.49% and 42.12%, respectively. Attributable risk proportion of CVD events for participants in 5–10, 10–20, 20–30, and  $\geq 30$  percent risk categories compared to 0–5 percent risk category were 65.21%, 85.50%, 91.87% and 94.13%, respectively.

**Conclusion** Validation and simple recalibration is needed when the FGCRS is applied in Mongolians. Our Result suggested that the FGCRS could be used in primary care practice to identify individuals at increased near-term risk of developing CVD.

### Is human urotensin II associated with essential hypertension independently of nitric oxide? A 1:1 matched case-control study

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**Background** Human urotensin II is the most potent vasoconstrictor identified to date. However, association between urotensin II and hypertension has been controversial and whether the association is independent of endothelial function is unclear. Here, we studied the association under adjustment for serum nitric oxide in hypertensive and normotensive human subjects.

**Methods** 197 newly diagnosed hypertensive patients without antihypertensive medication and 197 age- and sex-matched normotensive controls were recruited from the same community. Plasma urotensin II, serum nitric oxide and other traditional biomarkers including blood lipids, fasting plasma glucose and serum uric acid were examined for all participants. Correlations of urotensin II with blood pressure and nitric oxide were examined by using Pearson correlation analysis. Association between urotensin II and hypertension was evaluated by multivariate conditional logistic regression analysis. In addition to controlling for nitric oxide in multiple models, sub-group analysis was further performed in nitric oxide level-matched pairs of subjects to eliminate the

potential influence of nitric oxide on vassal action of urotensin II.

**Result** Hypertensive patients had higher plasma urotensin II [median (interquartile range): 9.32 (7.86 – 11.52) ng/mL vs 8.52 (7.07 – 10.41) ng/mL] and lower serum nitric oxide [19.19 (2.55 – 38.48)  $\mu$ mol/L vs 23.83 (11.97 – 43.40)  $\mu$ mol/L] than normotensive controls. Urotensin II positively correlated with systolic blood pressure ( $r = 0.169$ ,  $P < 0.001$ ), diastolic blood pressure ( $r = 0.113$ ,  $P = 0.024$ ) while negatively correlated with serum nitric oxide ( $r = -0.112$ ,  $P = 0.027$ ). Conditional logistic regression analysis showed that with per unit increment of urotensin II, risk of hypertension increased 8% (OR, 1.08; 95% CI, 1.02 – 1.15), and after adjustment for potential covariates, risk of hypertension was still increased despite the insignificance (OR, 1.05; 95% CI, 0.98 – 1.12). When participants were categorized into quartiles of urotensin II, ORs of hypertension for upper quartiles were calculated with the lowest quartile as a reference. In the univariate analysis, the OR of hypertension for subjects in the highest 25<sup>th</sup> percentile of the distribution of UII had 2.85 times the OR of hypertension than did individuals in the lowest 25<sup>th</sup> percentile (OR, 2.85; 95% CI, 1.52 – 5.34). In multivariate regression analysis, subjects in the highest quartile of urotensin II were more likely to have hypertension than those in the lowest quartile (OR, 2.33; 95% CI, 1.10 – 4.93). ORs of hypertension positively increased with UII level ( $P$  for trend = 0.046). Conditional logistic regression analysis in 106 pairs of serum nitric oxide level-matched cases and controls showed that both before and after adjustment for cigarette smoking, alcohol consumption, family history of hypertension, body mass index, total cholesterol, triglycerides, serum uric acid and FPG, OR of hypertension significantly and positively increased with UII level (all  $P$  values for trend  $< 0.05$ ). After multivariate adjustment, individuals in the highest 25<sup>th</sup> percentile of the distribution of UII were still more likely to have hypertension than those in the lowest 25<sup>th</sup> percentile (OR, 3.15; 95% CI, 1.13 – 8.78).

**Conclusion** Human urotensin II is markedly associated with essential hypertension and the association is independent of nitric oxide. Our Result suggest that urotensin II may have an etiological role in hypertension.

### Association of peroxisome proliferator-activated receptor gene – gene interactions and the lipoprotein

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**Objective** To examine the association between 10 single-nucleotide polymorphisms (SNPs) in the peroxisome proliferator-activated receptor (PPARs) and the level of lipoprotein-a [Lp (a)], as well as to investigate if there is gene – gene interaction among the SNPs on level of Lp (a).

**Methods** Subjects were sampled from cohort population of Prevention of Multiple Metabolic Disorders and Metabolic Syndrome Study, which was an urban community survey study conducted in Jiangsu Province, China. In total, 644 subjects (234 men and 410 women) were selected in random, and no individuals were consanguineous. Ten SNPs in PPARA (rs135539, rs4253778, rs1800206). PPARG (rs2016520, rs9794) and PPARG (rs10865710, rs1805192, rs709158, rs3856806, rs4684847) were genotyped and analyzed. SNPstats program was used to examine the association between the SNPs and Lp (a). Gene-gene interactions were explored with generalized multifactor dimensionality

reduction (GMDR) method.

**Result** The frequencies of all genotypes obeyed the law of Hardy-Weinberg equilibrium. It was showed that there was association of genotypes of variants in rs1800206 with the level of Lp (a), after adjustment for gender, age, smoking, alcohol, waist circumference, blood glucose, total cholesterol, triglycerides, and physical activity: Lp (a) was significantly higher in the individuals with mutant (LV+VV) comparing to those with wildtype (LL) ( $P = 0.0009$ ). Mean difference was 44.26 mg/l, and 95% CI was 18.23 – 70.30. The associations of other 9 SNPs in PPARs with Lp (a) were not significantly whether the covariates were adjusted or not. Pairwise LD analysis among SNPs was conducted, and all  $D'$  was less than 0.75. After gender, age, smoking, alcohol, waist circumference, blood glucose, total cholesterol, triglycerides, and physical activity were adjusted, gene-gene interaction among rs1800206, rs135539 in PPARA and rs10865710, rs1805192, rs4684847 in PPARG on Lp (a) level were significant ( $P = 0.001$ ), in which prediction accuracy was 0.6848 and cross-validation consistency was 10/10.

**Conclusion** It was suggested that rs1800206 was associated with a higher level of Lp (a). In addition, a gene-gene interaction on Lp (a) level was identified among rs1800206, rs135539, rs10865710, rs1805192, rs4684847.

### Prediabetes and short term outcomes in nondiabetic patients after acute ST-elevation myocardial infarction

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**Objective** Prediabetes state is defined as the time period before the development of symptomatic diabetes. Limited evidence is available for evaluating the correlation between prediabetes and short term outcomes in nondiabetic patients with ST segment elevation myocardial infarction (STEMI).

**Methods** 4 787 nondiabetic patients after STEMI with typical chest pain onset within 12 hours were enrolled. 7 and 30 day follow-ups from admission to hospitals were performed. According to new ADA criteria, the study population was stratified into three groups: normal (HbA1c  $\leq 5.6\%$ ,  $n = 2 378$ ), prediabetes (HbA1c: 5.7 – 6.4%,  $n = 1490$ ) and newly diagnosed diabetes (HbA1c  $\geq 6.5\%$ ,  $n = 919$ ). The primary outcomes of our study were all-cause mortality and Major Adverse Cardiac Events (MACE) at 7 day and 30 day.

**Result** The proportions of prediabetes and newly diagnosed were 31.1% and 19.2%. Rates of 7-day and 30-day mortality and MACE were similar among different HbA1c groups. Multivariable Cox regression analysis showed that compared with patients with normal glucose metabolism, prediabetes (HR, 1.003; 95% CI, 0.865 – 1.165) and newly diagnosed diabetes (HR, 0.887; 95% CI, 0.739 – 1.064) did not correlate with 30 day MACE. However, base glucose was the independent predictor for short term MACE (HR, 1.031; 95% CI, 1.017 – 1.046).

**Conclusion** Nondiabetic patients after STEMI had higher incidence of latent DM. Newly diagnosed DM and prediabetes were not correlated with short term outcomes in nondiabetic patients with STEMI, yet admission glucose level was the independent predictor for short term MACE. To reduce the incidence of short term MACE after STEMI, more attention should be paid to control high level of glucose



and intrinsic stress state.

### An integrated solution for employee cardiovascular disease management program in social community

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Lifestyle of employees in urban China has changed thoroughly along with the social and economic development. As a result, employees are more exposed to health risk factors. In May 2011, the National Center of Cardiovascular Diseases (NCCD) of China launched an employee cardiovascular disease management program at some corporations in Beijing. Through adopting up-to-date technologies and developing self-owned patent management information system and technology tools, this program, named “Healthy Heart, New Life”, piloted an integrated solution for employee cardiovascular disease management in social community. The Result proved that puzzled difficulties in health management among employees, such as individualized health education, knowing blood pressure for all, knowing cardiovascular risks for all, and monitoring blood pressures through self-aids practice, etc, were well resolved in this pilot program and good effects were gained.

### Detection rate of overweight and obesity in Han, uygur and Kazakh children and adolescents of Xinjiang

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**Objective** To investigate the detection rate of overweight and obesity in Han, Uygur and Kazakh Children and adolescents of Xinjiang.

**Methods** Random samples were used to analyze the detection rate of overweight and obesity based on data from Han, Uygur and Kazakh Children and adolescents aged 7 – 14 years from 3 regions in Xinjiang Uygur autonomous region, including Hetian locality, Kashi locality and Fuhai locality. All subjects were investigated by family and personal general situation and the physical examination.

**Result** The present study was performed in 13 809 Han, Uygur and Kazakh Children and adolescents aged 0 – 18 and eligible data of 11 903 subjects were actually analyzed aged 7 – 14 years of Xinjiang Uygur autonomous region. The detection rate of obesity were significantly higher in female than in male, the detection rate of overweight were significantly higher in male than in female ( $\chi^2=9.072$ ,  $P < 0.05$ ). Different nationality students of overweight and obesity rate of different, kazakh students are overweight detection rate is highest, the han nationality students the highest detection rate of obesity, difference have statistical significance ( $\chi^2=390.50$ ,  $P < 0.05$ ).

**Conclusion** The detection rate of obesity was significantly higher than the national average level of the Xinjiang Uygur autonomous region. There are different gender and ethnic students of differences. Counter-measures must be taken immediately so as to prevent the development of obesity. Most importantly, we must make people realize the harm of obesity to our Children.

### Types of atrial fibrillation and one year outcomes in patients with nonvalvular atrial fibrillation

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**Objective** Atrial Fibrillation (AF) increases the risk of incident stroke and systemic embolism. But different types of AF and one year outcomes in patients with nonvalvular AF were not validated.

**Methods** 1 697 patients with nonvalvular AF were enrolled. One year follow-up from admission to hospitals were performed. According to types of AF, the study population was stratified into three groups: group I (Persistent AF), group II (Paroxysmal AF) and group III (Permanent AF). The primary outcome of our study was stroke or Non-CNS systemic embolism. The primary safety outcome was major hemorrhage. Secondary outcome was all cause of death.

**Result** Our Result indicated that rates of the primary outcome were consistent ( $P = 0.08$ ) among group I (9.1%), group II (6.2%) and group III (9.4%); The rates of all cause of death were different ( $P < 0.001$ ) among group I (12.2%), group II (9.1%) and group III (20.9%). The rates of major hemorrhage were consistent ( $P = 0.41$ ) among group I (1.5%), group II (1.1%) and group III (0.7%). After adjusting the baseline characteristics, logistic regression analysis indicated that compared with persistent AF, paroxysmal AF (Odds Ratio: 0.658; 95% CI: 0.402 – 1.076,  $P = 0.096$ ) and permanent AF (Odds Ratio: 0.851; 95% CI: 0.550 – 1.317,  $P = 0.469$ ) were not associated with one year stroke or Non-CNS systemic embolism. However, compared with persistent AF, permanent AF (Odds Ratio: 1.913; 95% CI: 1.260 – 2.904,  $P = 0.002$ ) was associated with all cause of death.

**Conclusion** AF, whatever the types, confers the similar risk of incident stroke and Non-CNS systemic embolism to patients with nonvalvular AF. However, patients with permanent AF confront higher incidence of all cause of death.

### Haplotypic analyses of Pro12Ala and C1431T variants associated with essential hypertension

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**Objective** The peroxisome proliferator-activated receptor gamma (PPARG) is one of the ligand-activated transcription factors in the nuclear hormone receptor superfamily which have metabolic effects but also exert anti-inflammatory action. In addition, the potential use of PPARG activators for cardiovascular protection associated with anti-hypertensive treatment for high blood pressure will be proposed. Some

researchers have even considered PPARG a new target for the treatment of hypertension. The objective of this study was to investigate the association of Pro12Ala and C1431T polymorphisms of PPARG2 and their haplotypes with susceptibility to essential hypertension (EH).

**Method** Participants were recruited within the framework of the Prevention of Multiple Metabolic Disorders and MS in Jiangsu Province cohort population survey conducted from 1999 to 2007 in the urban community of Jiangsu province of China. 820 subjects (270 males, 550 females) were selected by simple stochastic sampling method and no individuals were related. The PPARG Pro12Ala and C1431T polymorphisms were genotyped by TaqMan probes method and analyzed by single-nucleotide polymorphism haplotype analysis. The Logistic regression model was used to examine the association of Pro12Ala and C1431T polymorphisms with EH and the SNPStats software was used to analysis haplotypes.

**Result** The polymorphism allele frequencies of Pro12Ala and C1431T in this study were 26.5% and 29.2%, respectively. After adjustment for sex, age, smoking status and BMI as covariates, carriers of the 12Ala allele (PA + AA) of Pro12Ala (dominant model) was at a decreased risk of EH (OR = 0.70, 95% CI: 0.52 – 0.89, P = 0.02). Carriers of Ala/Ala homozygous or Pro/Ala heterozygous (codominant model) were also reduced the EH risk, but did not reach the statistically significant (OR = 0.58, 95% CI: 0.33 – 1.02, P = 0.05 and OR = 0.74, 95% CI: 0.54 – 1.01, P = 0.05, respectively). There was no difference noted related to the 1431T allele of C1431T under the dominant model or codominant model (P = 0.59, P = 0.67, respectively). Compared to the most common haplotype Pro-C, we found that haplotype 4 (Ala-T) was associated with a statistically significantly decreased risk of EH after adjustment for sex, age, smoking status and BMI (OR = 0.62, 95% CI: 0.41 – 0.85, P = 0.02). The estimated frequency of haplotype composed of the 12Ala and 1431T (haplotype 4) was 9.54%.

**Conclusion** This study suggested that the Pro12Ala polymorphism was associated with EH and haplotype analysis showed for the first time that the Ala-T haplotype may be a genetic marker of EH.

### Evidence on association between peroxisome proliferator-activated receptor delta and essential hypertension in Chinese-Han population

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**Objective** PPAR $\delta$  (Peroxisome proliferator-activated receptor delta), is expressed in many tissues and stimulates fatty acid oxidation. Beyond these major roles, PPAR $\delta$  also have been shown to play a role in other biological processes, including the regulation of inflammatory and oxidative pathways. The aim of this study was to investigate the association between the PPAR $\delta$  gene variants and essential hypertension (EH) in an Chinese-Han population.

**Methods** Two polymorphisms were detected: +294T/C in exon 4, and C2806G in exon 9. The frequencies of the rare alleles were 30.4% and 22.1% in a population-based group of 820 subjects (270 males, 550 females). Individual polymorphism and haplotype data were available for analysis.

**Result** Carriers of the C allele of +294T > C and the G allele of C2806G were at a decreased risk of essential hypertension (OR: 0.77, 95% CI: 0.63 – 0.95, P < 0.01 and OR: 0.66, 95% CI: 0.53 – 0.82, P < 0.0001, respectively). In comparison with the most common haplotype, haplotype 2 (C-C) which consist of the +294C and 2806C alleles and

haplotype 3 (T-G) which consist of the +294T and 2806G alleles, were associated with a statistically significantly decreased risk of essential hypertension (OR: 0.77, 95% CI: 0.63 – 0.93, P = 0.0065 and OR: 0.66, 95% CI: 0.53 – 0.83, P = 0.0004, respectively). In addition, haplotype 2 and 3 were also associated with lower SBP and DBP values than the common haplotype, with a decrease of 1.82 mm Hg for haplotype 2 (95% CI: -3.56 – -0.08, P = 0.04) and 2.93 mm Hg for haplotype 3 (95% CI: -4.81 – -1.05, P = 0.0023) being recorded for SBP, while decreases of 1.25 mm Hg for haplotype 2 (95% CI: -2.14 – -0.35, P = 0.0066) and 1.34 mm Hg for haplotype 3 (95% CI: -2.35 – -0.33, P = 0.0092) were recorded for DBP.

**Conclusion** These Result may help to clarify the role of the PPAR $\delta$  gene variants in EH, and this evaluation of the polymorphisms and haplotypes of this gene furthers their characterization as genetic factors indicating a decreased risk for EH. Detection of these haplotypes may be useful for predicting genetic risk of EH.

### Goal attainments and their discrepancies for LDL cholesterol and apolipoprotein B in over 2 000 Chinese hospitalized patients with known coronary artery disease or type 2 diabetes mellitus

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**Background** LDL-C is primary treatment target for patients with dyslipidemia. The apo B, an emerging biomarker for cardiovascular risk prediction, appears to be superior to the LDL-C. However, little is known about goal attainments and their discrepancies for LDL-C and apo B in Chinese patients with known coronary artery disease or type 2 diabetes mellitus.

**Methods** 2 172 hospitalized patients with known coronary artery disease or DM, aged > 27 years of old, were enrolled. The success rates for apo B and LDL-C goal attainments were evaluated and compared by categorization and by sex.

**Result** When the success rates for apo B were compared with the ones for LDL-C, the apo B goal attainment rates were all higher than the LDL-Cs across all categorizations, with the statistically significant differences seen in all patients, CAD alone and DM alone (P = 0.000), but not in coexistence of CAD and DM (P = 0.190). The trend toward to higher success rates for LDL-C and apo B goal attainments in men than in women are noteworthy across all categorizations although only in all patients and in DM alone patients were the statistically significant differences found (P < 0.01).

**Conclusion** The LDL-C lags behind the apo B in goal attainments in Chinese patients. Whether these discrepancies are associated with the occurrence differences for CAD and for stroke between the East Asia and the Western countries warrants further study.

## Relation between hypertension and heavy drinking on the risk of stroke in Mongolian adults of Inner Mongolia, China

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**Background** Hypertension is a big challenge in public health and one of the most important risk factors of cardiovascular diseases. No study has specifically evaluated the combined effects of hypertension and heavy drinking on the risk of stroke in a minority of China.

**Methods** A prospective cohort study from 2003 to 2012 was conducted among 2 530 people aged 20 years and older from Inner Mongolia, China. We categorized the participants into four subgroups according to blood pressure and drinking status (non-hypertension/nondrinkers, non-hypertension drinkers, hypertension/nondrinkers and hypertension drinkers). Age-gender adjusted and multivariate-adjusted hazard ratios (HRs) for the incidence of stroke due to the combination of hypertension and alcohol consumption were calculated and compared with non-hypertension/nondrinkers.

**Result** The cumulative incidence rate of stroke among four subgroups were 1.5%, 2.8%, 7.4% and 12.5%, respectively ( $P < 0.001$ ). The multivariate-adjusted HRs (95% confidential intervals) of groups with non-hypertension drinkers, hypertension/nondrinkers and hypertension drinkers were 1.030 (0.476 – 2.229), 2.644 (1.452 – 4.816) and 2.901 (1.556 – 5.410), respectively.

**Conclusion** These findings suggest that hypertension is an independent risk factor of stroke in Inner Mongolians. Hypertensives with heavy drinking were at the highest risk of stroke in the population, suggesting that hypertension and heavy drinking have a synergistic effect on stroke incidence.

## Alcohol consumption and risk of stroke and coronary heart disease in Eastern Asian men: a meta-analysis of prospective cohort studies

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**Objective** To assess the dose-response relationship between alcohol consumption and risk of stroke, coronary heart disease (CHD) morbidity, mortality and all-cause mortality among Eastern Asian men.

**Methods** Potential prospective cohort studies were retrieved by searching Pubmed (1966 – 2012), OVID (1980 – 2012), Embase (1980 – 2012) and ISI Web of knowledge (1986 – 2012) using Medical Subject Headings alcohol drinking, ethanol, stroke, cerebrovascular disease, coronary heart (or artery) disease, myocardial infarction, mortality, etc., and Koreans, Japanese or Chinese. From the relevant retrieved reports, 21 prospective cohort studies met the criteria and were included in the study. Information on study design, participant characteristics, level of alcohol consumption, CHD outcome, control for potential confounding factors and risk estimates was abstracted using a standardised protocol. For each study, relative risks (RR) and 95% CI were extracted and pooled with either a fixed effect model or random effect model according

to the result of the test of heterogeneity.

**Result** The study focused on male subjects, ranging from 1 322 to 108 461 people among the 21 cohort studies. Compared with non-drinkers, the RRs on ischemic stroke for those who drank alcohol  $\leq 20$ , 21 – 40, 41 – 60,  $> 60$  g/d, were 0.85 (0.78 – 0.93,  $P = 0.0002$ ), 0.94 (0.79 – 1.11,  $P = 0.46$ ), 1.08 (0.86 – 1.37,  $P = 0.50$ ), and 1.24 (0.96 – 1.59,  $P = 0.10$ ), respectively. Similarly, the RRs on haemorrhagic stroke were 0.92 (0.75 – 1.12,  $P = 0.46$ ), 1.11 (0.96 – 1.28,  $P = 0.17$ ), 1.20 (0.92 – 1.56,  $P = 0.18$ ), 1.74 (1.32 – 2.28,  $P < 0.0001$ ); the RRs on CHD morbidity were 0.65 (0.34 – 1.23;  $P = 0.18$ ), 0.48 (0.26 – 0.87;  $P = 0.02$ ), 0.46 (0.32 – 0.67;  $P < 0.01$ ) and 0.48 (0.29 – 0.78;  $P < 0.01$ ), respectively. RRs on CHD mortality were 0.98 (0.73 – 1.31;  $P = 0.87$ ), 0.68 (0.58 – 0.79;  $P < 0.01$ ), 0.64 (0.43 – 0.96;  $P = 0.03$ ), 0.75 (0.54 – 1.03;  $P = 0.08$ ); and on all-cause mortality, were 0.83 (0.75 – 0.91,  $P = 0.0001$ ), 0.93 (0.87 – 0.99,  $P = 0.03$ ), 1.01 (0.95 – 1.07,  $P = 0.86$ ), 1.32 (1.29 – 1.36,  $P < 0.01$ ).

**Conclusion** In Eastern Asian men, light alcohol consumption ( $\leq 20$  g/d) was associated with decreased risk of ischemic stroke; whereas, heavy alcohol intake was associated with increased risk of stroke, particularly haemorrhagic stroke and all-cause mortality; and moderate alcohol consumption (21 – 60 g/d) was associated with decreased risk of CHD morbidity and mortality.

## One-year cardiovascular event rates in Chinese patients with atherothrombotic disease

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**Objective** We sought to assess the risk profile, management and subsequent 1-year cardiovascular (CV) event rates in Chinese patients with coronary artery disease (CAD), stroke, peripheral artery disease (PAD), or with two or more cardiovascular risk factors.

**Method** From Oct. 2004 to Jan. 2005, 3 732 Chinese patients with either atherosclerotic arterial disease ( $n = 2 689$ ) or at least 2 risk factors for atherothrombosis ( $n = 734$ ) were sequentially enrolled. Outcomes of interest included CV death, myocardial infarction (MI), stroke and hospitalization for atherothrombotic events. Event rates were adjusted for age and sex using the corrected group prognosis method in the Cox proportional hazards mode.

**Result** During a mean follow-up time of  $13.6 \pm 1.5$  months, 309 participants (8.3%) were lost. Overall, the all cause death rate was 8.6% (294 deaths), with CV deaths accounting for 41.2% (121 deaths; 3.5% overall). CV death was 1.2% for patients with multiple risk factors only, and 3.7% for patients with CAD, 4.1% for patients with stroke, and 5.1% for patients with PAD. For the end point of CV death/MI/stroke/hospitalization for atherothrombotic events, the highest event rate occurred among patients with 3 vascular disease locations (31.8%), followed by those with 2 (25.9%), 1 location (20.8%) and those with risk factors only (13.2%,  $P < 0.001$ ). Medication was more intense in CAD patients compared with other patients. The lowest levels of statin and anti-thrombotic treatment occurred within the PAD-only group. A large percentage of patients did not reach the therapeutic target values specified in current guidelines.

**Conclusion** In Chinese patients with established atherosclerotic arterial disease, those with PAD (6.3%) had higher CV mortality than



those with CAD (4.2%) and stroke (5.0%), and a substantial increase in cardiovascular event rates with increasing numbers of affected arterial beds. Our study suggests a need to improve detection and consequent management of multi-site atherosclerotic arterial disease.

### Evaluation of arterial stiffness and related risk factors in healthy examination subjects

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**Objective** To investigate the possible risk factors involving pulse wave velocity (PWV) in healthy people.

**Methods** 323 subjects from Shougang Corporation examination center were enrolled into our study. They were divided into two groups: PWV < 9 (n = 37) group and PWV ≥ 9 (n = 286) group. Carotid-femoral pulse wave velocity (CFPWV) was detected by the Complior apparatus.

**Result** The incidence of hypertension was significantly higher in PWV ≥ 9 group. The levels of systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP), triglycerides (TG) were significantly higher in PWV ≥ 9 group than in control group (141.2 ± 19.9 vs 129.0 ± 18.8 mm Hg, P < 0.001; 88.4 ± 11.1 vs 82.1 ± 10.8 mm Hg, P = 0.001; 52.8 ± 12.9 vs 46.8 ± 10.6 mm Hg, P = 0.007; 2.13 ± 1.64 vs 1.19 ± 0.73 mmol/L, P < 0.001). High-density lipoprotein cholesterol (HDL-C) was higher in PWV < 9 group. PWV was positively correlated with age, SBP, DBP, PP, glucose, HbA1c, uric acid, TG in the entire study group (r = 0.124, 0.307, 0.259, 0.255, 0.187, 0.340, 0.169, 0.278, respectively, all P < 0.05). There was negative correlation between PWV and HDL-C in the entire group (r = -0.283, P < 0.001). Multivariate analysis showed that SBP, HbA1c were significant independent associating factors of PWV in all subjects (β = 0.314, P = 0.003; β = 0.307, P = 0.003).

**Conclusion** The levels of SBP, DBP, PP, TG were significantly higher in PWV ≥ 9 group than in control group. HDL-C might play an important role in the development of arterial stiffness. More studies should be investigated in future.

### Prevalence of difficult-to-control hypertension among hospital and community treated hypertensive patients in China

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**Objective** The prevalence of difficult-to-control hypertension (DCH) in China is unknown. Uncover the burden and basic characteristics of DCH may help improving blood pressure control.

**Methods** Treated hypertensive patients were analyzed. Using data from an institutional based retrospective medical records collection (N = 6 597, from year 2006 to 2008) and two community based prospective studies in Xinyang County from 2005 to 2006 (N = 2 629) in the middle region of China and Hongxionglong Reclamation Region in 2009 (N =

574) in the southeast part of China, treated hypertension patients were classified DCH if their blood pressure still above goal (≥ 140/90 mm Hg in common or ≥ 130/80 mm Hg for those with diabetes and chronic kidney disease) after prescribed 3 antihypertensive drugs (including a diuretic) or ≥ 4 drugs regardless of blood pressure.

**Result** Among in-hospital treated hypertension patients, 13.4% met the criteria of DCH, the corresponding rates were 23.7% in Xinyang community and 38.7% in Hongxinlong community, respectively. As age increased from 40 – 50 years to ≥ 70 years, rates of DCH increased from 9.1% to 17.8% in hospital, 18.8% to 28.8% in Xinyang and 32.3% to 46.7% in Hongxinlong. Body mass index was significantly higher in DCH patients (26.9 kg/m<sup>2</sup> in Xinyang and 27.8 kg/m<sup>2</sup> in Hongxinlong) vs in non-DCH treated patients (26.1 kg/m<sup>2</sup> in Xinyang and 26.4 kg/m<sup>2</sup> in Hongxinlong, both P < 0.001, not analyzed in hospital data). Association of other characteristics (uric acid, blood lipid, smoke, drink) and comorbidities with DCH varied in different regions. In-hospital DCH patients were more likely to have chronic kidney disease, coronary artery disease, diabetes mellitus and heart failure. Orthostatic hypotension (only detected in Xinyang) was more common in DCH patients compared with in controlled hypertension (≤ 3 drugs) patients.

**Conclusion** DCH was not rare in China, and the rates and characteristics varied in different region. Rising body mass index was a relatively consistent and adjustable risk factor of DCH. Causing of DCH and its diversity could be further studied.

### The effect of homocysteine level on the control rate of blood pressure in hypertensive cases

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**Objective** To explore the effects of homocysteine (Hcy) level on the control rate of blood pressure in hypertension cases, and to provide theoretical evidences for formulation the measure about the hypertension prevention, and to elevate the control rate of blood pressure in hypertension cases.

**Methods** According to geographic location and population distribution, 6 villages in 3 towns were randomly selected from 11 towns, which were the provincial standardized management areas for hypertension cases in Peixian County, Xuzhou City, Jiangsu Province, used stratified random sampling method. High blood pressure was screened in the residents over 18 years old, and the target investigative subjects were recruited according to the screening Result. 1 802 hypertension subjects were selected according to the recruited standard after screening. At last, 1 798 eligible hypertension cases which had integrated information after questionnaire investigation, medical examination, and some relative biochemistry test (included Hcy test) were analyzed in our study. Then, community doctors, who accepted the training of hypertension standardized management and get the certification, managed these hypertension patients according to unified management scheme. One year later, the control rate of blood pressure was calculated by the last time measured Result of blood pressure level (SBP ≥ 10 μmol/L group (higher Hcy group) and < 10 μmol/L group (lower Hcy group), and the control rate of blood pressure was compared

between these two group. Meanwhile, hypertension cases were also divided into four groups according to Hcy interquartile range, the control rates of blood pressure were compared among these four groups. Other related risk factors were explored with logistic regression analysis.

**Result** Averaged age of 1798 hypertension cases was  $58.15 \pm 7.97$  years, including 789 men and 1009 women, account for 43.91% (778/1772) and 56.09% (994/1772) respectively. After one year followed up, 26 subjects were lost because of emigration, migrant for work, death and other reasons, accounting for 1.45% (26/1798) dropout rate. Therefore, data of 1772 eligible subjects were analyzed after 1 year follow-up, averaged age was  $58.16 \pm 7.94$  years, including 778 men and 994 women, account for 43.91% (778/1772) and 56.09% (994/1772) respectively. Total control rate of blood pressure was 50.56% (896/1772), 50.00% (389/778) in male, 51.01% (507/994) in female, and there was no significant difference between gender in the control rate ( $\chi^2 = 0.177$ ,  $P = 0.674$ ). The control rate of blood pressure in lower Hcy group (61.54%) was significant higher than that in higher Hcy group (49.41%) ( $\chi^2 = 7.335$ ,  $P = 0.007$ ). The control rate of blood pressure were 55.97%, 51.99%, 47.53%, and 46.98% respectively according to the groups of Hcy interquartile range, and the Result of trend chi-square test showed that there was significant difference ( $\chi^2 = 8.602$ ,  $P = 0.003$ ), which indicated that the control rate of blood pressure was decreased with Hcy level increasing. Result of multi-factors logistic regression analysis showed that the control rate of blood pressure in non-hyperhomocysteinemia group exceeded 71.6% than that in hyperhomocysteinemia group (OR = 1.716, 95% CI 1.223 – 2.408), when the age, sex, smoking, drinking, and relative biochemical test Result were adjusted.

**Conclusion** As an important risk factors of cardiovascular prognosis in hypertension cases, higher level of Hcy could significantly affect the control rate of blood pressure, hyperhomocysteinemia might be an important risk factor which affect the control rate of blood pressure in our country.

### The cut-off value of waist-to-height ratio for detecting the level of central obesity in Chinese adult population

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**Objective** To explore the cut-off value of waist-to-height ratio (WHtR) for detecting the level of central obesity and predicting cardiovascular disease risks in Chinese adult population.

**Methods** A total of 30 630 participants aged 35 – 59 years in China were surveyed for cardiovascular diseases risk factors in two independent cross-sectional studies that carried out in 1992 – 1994 and 1998, respectively. Sensitivity, specificity and Youden's index for hypertension, abnormal glucose, high serum TC, low serum HDL-C and clustering of risk factors ( $\geq 2$  risks above individually) were calculated to evaluate the efficacy population cut-off point of WHtR. The cut-off point value for central obesity was depended on the point of WHtR with the highest Youden's index. The cut-off point value for sever central obesity was fixed on the point whose specificity of the point was gathered more than 90%. And the cut-off point value to indicate low weight was determined by the percentile distribution of WHtR, at which the 5<sup>th</sup> percentile (P5) of point, both in male and female population. Based on the principle of convenient and practical for use, the cut-off values of WHtR for the level of central obesity were determined.

**Result** The cut-off values of WHtR for central obesity were 0.49 in males and 0.50 in females, and for severe central obesity were 0.54 and 0.57 for men and women, respectively. Additionally, the cut-off points of WHtR for each of the 4 cardiovascular risk factors to evaluate the severity separately ranged from 0.54 to 0.55 in male, and ranged from 0.57 to 0.58 in female. The P5 of WHtR, which was the point values of WHtR to indicate low body weight, was 0.40 in both male and female population.

**Conclusion** The optimal cut-off value of WHtR for defining central obesity, low body weight and severe central obesity should be recommended as 0.50, 0.40 and 0.57, respectively. For Chinese adults, WHtR at 0.40 – 0.49 as 'normal', 0.50 – 0.57 as 'central obesity',  $\geq 0.57$  as 'sever central obesity' and  $< 0.40$  as 'Low body weight'.

### Survival of Chinese patients with pulmonary arterial hypertension in the modern management era

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**Background** In a previous study of Chinese patients with idiopathic pulmonary arterial hypertension (IPAH) in the non-targeted therapy era, we reported 1- and 3-year survival estimates of only 68% and 39%, respectively. However, it is not yet known whether the survival of patients with PAH is improved in the modern management era.

**Method** A retrospective cohort study was undertaken in 276 consecutive newly diagnosed "incident" patients with IPAH and connective tissue disease-associated pulmonary arterial hypertension (CTDPAH) referred between 2007 and 2009. Baseline characteristics and survival in two groups were compared.

**Result** 1- and 3-year survival estimates were 92.1% and 75.1%, respectively, in patients with IPAH, and 85.4% and 53.6%, respectively, in patients with CTDPAH. Patients with CTDPAH had a significantly lower mean pulmonary artery pressure, more pericardial effusion, and more severe impairment of the diffusion capacity of the lung for carbon monoxide (DLCO) than patients with IPAH. A diagnosis of CTDPAH, WHO functional class III or IV, DLCO  $< 80\%$  of predicted, and the presence of pericardial effusion were independent predictors of mortality. The 1- and 3-year survivals of male patients were 93.5% and 77.5%, respectively, in those with IPAH, and 71.1% and 47.4%, respectively, in those with CTDPAH.

**Conclusion** The survival of patients with PAH has been improved in Chinain the modern management era, despite the high costs of treatment and financial constraints. However, the survival of patients with CTDPAH is inferior to that of patients with IPAH. Our study also indicates poorer survival in male CTDPAH patients.



### Risk factors associated with mortality in the surgical treatment of 563 patients with the simple total anomalous pulmonary venous connection

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**Objective** To analyse the surgical Result and the risk factors of mortality of patients with total anomalous pulmonary venous connection.

**Methods** A total of 563 patients with surgically corrected TAPVC from Oct. 1996 to Sep. 2012 admitted to our hospital were enrolled in this study. Patients only with VSD, ASD and PDA were included. Data reviewed include age, weight, anatomic type, operative data et al.

**Result** The median age and weight at reparaire was 4.45 years old and 12.3 kg. The TAPVC anatomy was supcardiac in 277 (49.2%), cardiac in 231 (41%), infracardiac in 17 (3%), and mixed in 38 patients (6.8%). Overall in-hospital surgical mortality for simple TAPVC was 6% (34/563). Mortality was 11.1% (30/270) from 1996 to 2007, and 1.4% (4/293) from 2008 to 2012. The number of in-hospital deaths was 34, consisting of supcardiac in 15, cardiac in 12, infracardiac in 1, and mixed in 6 patients. The causes of death were respiratory failure (18 patients), serious low cardiac output syndrome (9 patients), sudden cardiac arrest (3 patients), toxic shock syndrome (1 patient) and MODS (3 patients). There was a significant decrease in mortality when comparing 1996 to 2007 with 2007 to 2012 ( $P < 0.01$ ). Significant risk factors for mortality were young age ( $P < 0.01$ ), low weight ( $P < 0.01$ ), long CPB time ( $P = 0.002$ ), long OCCLD time ( $P = 0.002$ ) and cardiac connectin type ( $P < 0.01$ ).

**Conclusion** Operative Result of TAPVC have dramatically improved in the past 16 years. However patients having young age, low weight, long CPB time, long OCCLD time increased operative mortality. Specific subtypes still experience significant mortality.

### Efficacy of folic acid supplementation alone on endothelial function and plasma homocysteine concentration in coronary artery disease: a meta-analysis of randomized controlled trials

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**Background** Experimental and epidemiological evidences have shown that combined therapy of folic acid is an effective agent for improving endothelial function and lowering plasma homocysteine concentration in cardiovascular disease. However, the efficacy of folic acid supplementation alone on endothelial function and plasma homocysteine concentration in coronary artery disease (CAD) has not been well established.

**Objective** Our purpose is to conduct an updated meta-analysis of relevant randomized controlled trials (RCTs) to estimate the effect of folic acid supplementation alone on endothelial function and plasma homocysteine concentration in patients with CAD.

**Methods** An extensive search of PubMed was used to identify RCTs comparing folic acid and placebo therapy. Mean difference (MD) with 95% confidence interval (CI) was performed as a measure of the association between folic acid supplementation and endothelial function/

plasma homocysteine concentration.

**Result** Of 377 patients included, 191 underwent folic acid supplementation and 186 underwent placebo treatment. Compared with placebo group, folic acid supplementation alone had a significant efficacy on increasing flow-mediated dilation (FMD) (MD 57.72  $\mu\text{m}$ , 95% CI, 50.14 – 65.31); plasma homocysteine concentration (MD -3.66  $\mu\text{mol/l}$ , 95% CI -5.44 – -1.87;  $P < 0.05$ ;  $I^2 = 87\%$ ). There was no significant change in the response to end diastolic diameter (EDD), glyceryl-trinitrate (GTN) diameter change, heart rate, baseline and peak hyperaemic flow, systolic and diastolic blood pressure between folic acid and placebo group ( $P > 0.05$ ).

**Conclusion** This meta-analysis suggests that folic acid supplementation 5 mg daily for greater than 4 weeks significantly improve FMD and lower plasma homocysteine concentration in patients with CAD. However, RCTs are still needed to confirm current findings.

### Acute effect of air pollution on cardiovascular and cerebrovascular disease mortality in Tianjin, 2001–2009: a time-series study

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**Objective** To explore quantitatively the effect of air pollution on cardiovascular and cerebrovascular disease mortality and provide basis for prevention and control of cardiovascular and cerebrovascular disease in Tianjin.

**Methods** Mortality data in 2001 – 2009 were from Tianjin mortality surveillance system maintained by the Tianjin Centers for Disease Control and Prevention (CDC), meteorological data and air pollution data were from Tianjin Meteorological Bureau and Tianjin Environmental Monitoring Station, respectively. Generalized Additive Model (GAM) extended Poisson regression was used to examine the relationship between air pollution and mortality in Tianjin, and controlling with time trends, weather, the day of week and population.

**Result** Cardiovascular and cerebrovascular diseases mortality in Tianjin increased from year 2001 to 2009 with the crude mortality rate of 295.31/100 000 to 345.55/100 000, and with the standardized mortality rate of 268.30/100 000 to 218.78/100 000. Air pollutants were more strongly associated with cardiovascular and cerebrovascular disease mortality: by single GAM analysis, a 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{SO}_2$ ,  $\text{NO}_2$  and  $\text{PM}_{10}$  accounted for average 0.70% (95% CI, 0.47 – 0.94%), 0.51% (95% CI, 0.27 – 0.74%) and 0.16% (95% CI, 0.06 – 0.27%) increase in daily mortality in 0 – 5 lag days, and for 1.13% [95% CI (0.76 – 1.51%)], 0.78% (95% CI, 0.41 – 1.15%), 0.61% (95% CI, 0.51 – 0.71%) increase in daily mortality in exposure days. By multiple GAM analysis, a 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{SO}_2$ ,  $\text{NO}_2$  and  $\text{PM}_{10}$  accounted for 0.77% (95% CI, 0.58 – 0.97%), 0.41% (95% CI, 0.05 – 0.78%) and 0.38% (95% CI, 0.12 – 0.64%) increase in daily mortality. Low temperature, low wind speed and population size were all significantly associated with cardiovascular and cerebrovascular disease mortality ( $P < 0.05$ ).

**Conclusion** The paper showed that air pollution was a risk factor for cardiovascular and cerebrovascular disease mortality in Tianjin. Our study supported the possibility that acute pathogenetic processes in the cardiovascular and cerebrovascular disease could be induced by the air pollution. Our study also provided important information to develop air pollution control for cardiovascular and cerebrovascular disease mortality prevention, in order to decrease the burden of it.

### Red cell distribution width as a prognostic marker in Eisenmenger syndrome

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**Objective** Previous studies have found independent relationship between red cell distribution width (RDW) and prognosis in patients with pulmonary hypertension of mixed aetiologies and idiopathic pulmonary arterial hypertension (PAH). We designed this study to investigate the significance of RDW in predicting survival in patients with Eisenmenger Syndrome (ES).

**Method** We retrospectively reviewed the clinic records and collected the baseline data of patients newly diagnosed as ES in our hospital during the period from January 2005 to October 2009. The follow-up data were collected periodically by a specifically designed network database until December 31<sup>st</sup>, 2012. The end point was all-cause death.

**Result** A total of 109 patients with ES were included. During a median follow-up time of 4.2 (IQR 3.7–5.0) years, 21 patients (19.3%) died. Baseline RDW of non-survivals were higher than survivals ( $16.9\% \pm 4.4\%$  vs  $14.3\% \pm 2.3\%$ ,  $P = 0.015$ ), and RDW had significant correlations with arterial oxygen saturation ( $r = -0.408$ ,  $P = -0.399$ ,  $P = 0.224$ ,  $P = 0.019$ ) and total pulmonary pressure (TPR) ( $r = 0.438$ ,  $P = 0.019$ ). Kaplan-Meier analysis showed that patients with RDW  $\geq 14.4\%$  had a lower survival rate ( $P = 0.001$ ) than patients with RDW  $< 14.4\%$ , and multivariate Cox regression analysis showed that WHO-function class, RDW, TPR and PAH targeted therapy were independent prognosis markers of ES. When RDW of patients with ES increased 1%, risk of all-cause death increased 16.2% (95% CI, 3.6%–30.2%).

**Conclusion** Baseline RDW correlates with hemodynamics of patients with ES and is an independent prognostic marker in ES.

### Pre-hospital delay in acute myocardial infarction: an clinical characteristics analysis of 1 004 patients in 3 years in an emergency center in Beijing

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**Objective** To explore the clinical characteristics, the pre-hospital

delay, the treatment and prognosis of patients with acute myocardial infarction (AMI) in 3 years in an emergency center in Beijing.

**Methods** 1 004 patients with AMI in Emergency Ward and Emergency Intensive Care Unit (EICU) of Beijing Anzhen Hospital from Mar. 2004 to Mar. 2007 were collected by retrospective analysis method. All the cases were diagnosed with clinical symptom, electrocardiogram, dynamic myocardial enzyme monitor and percutaneous coronary angiography. The information of all patients were collected by a self-designed clinical report form, including age, gender, occupation, education, height, body weight; symptom, onset-time, visiting-time, transportation mode, smoking history, disease history (hypertension, diabetes, stroke, coronary artery disease), heart rate and blood pressure in-hospital, onset place and treatment. Per-hospital delay time (PDT) was defined as the difference between the onset-time and visiting-time of the AMI patient and was measured in hours. All cases were divided into 3 groups by their visiting date, according to the date documented from the hospital, those were group A (Mar. 2004 to Mar. 2005), group B (Mar. 2005 to Mar. 2006) and group C (Mar. 2006 to Mar. 2007). Then, clinical characteristics, pre-hospital delay, treatment and prognosis were all compared by groups.

**Result** Totally 1 004 AMI patients (761 males, 75.8% and 243 females, 24.2%, with average age  $60.9 \pm 12.8$  years old) were presented to the hospital. There were significant differences in history of stroke, coronary artery disease and smoking among 3 groups ( $P > 0.05$ ). PCI treatment indicated an increased trend year by year (group A 32.3%, group B 63.4%, group C 64.5%,  $P > 0.05$ ).

**Conclusion** More and more AMI patients were benefited from reperfusion therapy recently, but shorten pre-hospital delay still should be the important strategy to get better prognosis from early reperfusion therapy.

### Variability of self-measured blood pressure at home associated with carotid artery stiffness and microalbuminuria in masked hypertensives

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**Objective** To explore the association between variability of self-measured blood pressure at home and carotid artery stiffness and microalbuminuria in masked hypertensive patients.

**Methods** One hundred and thirteen participants, who took part in the health examination in health examination center, were divided into three groups, namely, normotension group, masked hypertension group, and hypertension group base on office blood pressure measurement and self-measured blood pressure at home. All of the subjects were performed carotid intima-media thickness, stiffness index  $\beta$ , and microalbuminuria detection.

**Result** Official systolic blood pressure, self-measured systolic blood pressure at home, self-measured diastolic blood pressure at home, variability of self-measured systolic blood pressure at home, and variability of self-measured diastolic blood pressure at home in masked hypertension group were significantly higher compared with normotension group ( $P < 0.05$ ). Carotid intima-media thickness was ( $1.41 \pm 0.26$ ) mm, stiffness index  $\beta$  was  $1.58 \pm 0.10$ , and microalbuminuria was ( $11.88 \pm 3.62$ ) mg/L in masked hypertension group, respectively. They were significantly higher than in normotension group ( $P < 0.05$ ). Result of Pearson correlation and multiple linear regression analysis

shown, that carotid intima-media thickness, stiffness index  $\beta$ , and microalbuminuria were significant positively correlated with variability of self-measured systolic blood pressure at home ( $r = 0.761, 0.587$ , and  $0.554$ , all  $P < 0.05$ , respectively) and variability of self-measured diastolic blood pressure at home ( $r = 0.609, 0.329$ , and  $0.368$ , all  $P < 0.05$ , respectively). And variability of self-measured systolic blood pressure at home was a independent risk factor of carotid intima-media thickness, stiffness index  $\beta$ , and microalbuminuria.

**Conclusion** Variability of self-measured blood pressure at home was elevated, and correlated with carotid artery stiffness and microalbuminuria in masked hypertensive patients.

### Relation of C-reactive protein and white blood cell count with in-hospital death among patients with acute myocardial infarction

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**Objective** To explore the association between C-reactive protein (CRP), white blood cell (WBC) count and in-hospital death among patients with acute myocardial infarction (AMI).

**Methods** A total of 843 AMI patients consecutively admitted to hospital in the Second Affiliated Hospital of Soochow University from Jan. 1998 to Oct. 2010 were selected as study subjects. Data of demographic characteristics, lifestyle, admission blood pressure, clinical laboratory tests and medical history were collected from all subjects. Multivariate logistic regression analysis and Kaplan-Meier survival curve were used to estimate the association between CRP and WBC count and in-hospital death among AMI patients.

**Result** In the logistic regression analysis, after adjustment for multiple factors, the risk of in-hospital death was significantly increased ( $P < 0.05$ ) with increased CRP level and WBC count. Compared to lowest quartile of CRP and WBC, odds ratio (95% CI) of death associated with highest quartiles of CRP and WBC were 1.821 (0.923 – 3.594) and 4.489 (2.140 – 9.419), respectively. The Result of Kaplan-Meier survival curve analysis, survival probabilities of normal CRP and normal WBC groups were significantly higher compared to those of abnormal CRP and abnormal WBC groups ( $P < 0.05$ ).

**Conclusion** These findings suggested that increased CRP and WBC count were associated with the risk of in-hospital death among AMI patients. CRP and WBC was valuable in predicting the prognosis of AMI.

### 2-year follow-up study in patients with acute myocardial infarction: an analysis of 424 cases

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**Objective** We sought to investigate in-hospital, 1-year and 2-year mortality in AMI patients and analysis the association of risk factors and mortality.

**Methods** 424 AMI patients were selected. Mortality was obtained by means of case inquiry, phone call and Hospital Information System.

**Result** In-hospital, 1-year and 2-year mortality were 4.2%, 14.4% and 17.5% individually. After Logistic regression analysis, heart dysfunction was related to in-hospital, 1-year and 2-year mortality of AMI. The OR (95% CI) were 7.66 (2.35 – 25.00), 5.94 (3.32 – 15.21),

4.83 (1.94 – 12.01) individually. Age was related to 1-year and 2-year mortality. Respiratory failure and gastrointestinal bleeding were related to in-hospital mortality in AMI patients.

**Conclusion** Heart dysfunction may be the independent risk factor of in-hospital, 1-year and 2-year mortality in AMI patients. Pneumonia, respiratory failure, gastrointestinal bleeding, tumor and renal dysfunction maybe increase the risk of mortality in AMI patients.

### Perpetual impact of pregnancy-induced hypertension on high sensitivity C-reactive protein

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**Objective** To investigate the perpetual impact of pregnancy-induced hypertension (PIH) on high sensitivity C-reactive protein (hsCRP).

**Methods** 512 cases of PIH were identified and matched with 512 controls. The hsCRP levels at the time of the healthy examination were compared between two groups.

**Result** Levels of hsCRP during healthy examination were significantly higher in PIH group than in control group. The concentration of hsCRP in PIH group and control group were 0.70 (0.23 – 2.06) mg/L, 0.60 (0.201.28) mg/L, respectively. After adjustment for the index before delivery and, the risk of high hsCRP in PIH group was 2.46 fold (95% CI 1.43 – 4.24), and after further adjustment for index during healthy examination, the risk of high hsCRP in PIH group was 2.03 fold (95% CI 1.30 – 3.15).

**Conclusion** PIH is an independent risk factor for perpetual high hsCRP.

### A common NOS1AP genetic polymorphism is associated with QTc interval and mortality in chronic heart failure in a Chinese Han case-control population

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**Backgrounds** Several independent population-based studies have demonstrated that variants in NOS1AP are associated with cardiac repolarization and sudden cardiac death (SCD). The objective of the current study was to investigate whether SNPs previously reported in NOS1AP are related to both QTc interval and 4-year mortality in chronic heart failure (CHF) in a Chinese Han case-control study.

**Methods** A total of 1428 patients with CHF and 480 control subjects were genotyped and the correlations between these SNPs and both QTc interval and endpoint were analyzed. Multiple linear models and Cox proportional hazards regression models were used.

**Result** During a median follow-up period of 52 months, 467



(32.70%) patients died, of whom 169 (36.19%) were SCD. No significant associations between SNPs and either QT interval or SCD except rs12567209 were observed. The A allele of rs12567209 was associated with a prolongation of the QT interval by 4.03 ms in the entire cohort ( $P = 0.026$ ), as well as in prolonged QTc interval-stratified of the entire cohort and CHF group (+3.27 ms,  $P = 0.043$  and +3.43 ms,  $P = 0.033$ , respectively). The association of variant with QTc interval was seen only in male, regardless in different stratifications (+5.05 ms,  $P = 0.021$  in the entire cohort, +4.10 ms,  $P = 0.021$  and +4.80 ms,  $P = 0.013$  in prolonged QTc interval-stratified of the entire cohort and CHF group). After adjustment for age, gender and QTc interval, patients carrying the A allele of rs12567209 had an increased risk of all-cause death and SCD [HR 1.30 (95% CI 1.05 – 1.61);  $P = 0.013$  and HR 1.42 (95% CI 1.01 – 2.00),  $P = 0.042$ , respectively]. This effect described here was modest after adjustment for other suspected risk factors.

**Conclusion** The A allele of rs12567209 in NOS1AP were associated with prolonged QTc interval and increased risk of all-cause death and SCD in patients with CHF in the Chinese Han population, and functional analysis is warranted.

### Genetic variation in the ATP2B1 gene is associated with arterial stiffness in Chinese hypertensive population

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**Objective** Recent progress in GWAS has increased the number of known genetic susceptibility loci for arterial stiffness and hypertension. It remains unclear, however, whether the new single nucleotide polymorphisms (SNPs) that confer susceptibility to high blood pressure were also associated with arterial stiffness. The study investigated whether the eight new single nucleotide polymorphisms (SNPs) that confer susceptibility to high blood pressure were also associated with arterial stiffness through evaluation of brachial-ankle pulse wave velocity (ba-PWV) and ankle-brachial index (ABI).

**Methods** Patients ( $n = 121$ ) with essential hypertension from Jiangyin of China were enrolled in this study. We genotyped at the following SNPs: ATP2B1 rs2681472, ATP2B1 rs2681492, PLCD3 rs12946454, CYP2J2 rs11105354, c10orf107 rs1530440, ZNF652 rs16948048, FGF5 rs16998073, PLEKHA7 rs381815. The SNPs were genotyped using the Multiplex SNaPshot technique. Arterial stiffness was evaluated by measuring brachial-ankle pulse wave velocity (ba-PWV) and ankle-brachial index (ABI).

**Result** The frequencies of genotypes were in accordance with the Hardy-Weinberg equilibrium. In our study, ATP2B1 rs2681472 showed significant association with arterial stiffness. There was no evidence for an association with arterial stiffness for the other seven genetic loci. We found that ba-PWV and ABI differed significantly by genotype in ATP2B1 rs2681472 (all  $P < 0.05$ ). The patients with the T allele compared with the CC genotype, showed greater ba-PWV and ABI ( $P < 0.05$ ). The other SNPs were not significantly associated with ba-PWV and ABI. Stepwise multiple regression analysis was performed to investigate the major factors that influenced the ba-PWV. The independent variables were age, gender, WHR, BMI, heart rate, systolic blood pressure and genotype. The dependent variable was ba-PWV and ABI respectively. Multiple regression analysis showed that rs2681472 in ATP2B1 gene was a significant predictor of ba-PWV and ABI.

**Conclusion** This study indicates that hypertensive individuals

carrying the T allele of ATP2B1 rs2681472 are predisposed to stiffer arteries. The hypertensive individuals with the T allele should be considered at high risk for cardiovascular disease.

### Prevalence of microalbuminuria among middle-aged population of China: a multiple-center cardiovascular epidemiological study

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**Objective** Few studies have examined microalbuminuria (MAU) in Chinese populations. We assessed the prevalence of MAU and the relationships with other cardiovascular risk factors among middle-aged Chinese population.

**Methods** Data from a cross-sectional survey on risk factors of cardiovascular disease, which were conducted in 2009 – 2010. There were about 1 000 participants each from 12 different research populations including southern and northern, urban and rural in different parts of China, with international standardized examination and measurement. Half the subjects were men and half were women; their ages ranged from 35 to 64 years. Out of them, there were 10 315 participants were eligible for analysis in our study. MAU was defined as the urine albumin to creatinine ratio at 30 to 300 mg/g from a single-spot morning urine sample.

**Result** The overall prevalence of MAU is 12.76% in total population, which was higher in female than in male (15.04% vs 10.09%,  $P < 0.0001$ ). The prevalence of MAU increased across categories of age (respectively 9.48% vs 12.73% vs 15.57% at age 35 – 44 years, 45 – 54 years and 55 – 64 years,  $P < 0.0001$ ), increased largely across categories of blood pressure (BP) (respectively 8.53% vs 15.92% vs 23.42% vs 43.73% in persons with normal BP, hypertension stage 1, hypertension stage 2, hypertension stage 3,  $P < 0.0001$ ), and was higher in people with obesity than those of overweight and normal weight (19.17% vs 12.06% vs 10.33%,  $P < 0.0001$ ), and in people with diabetes than those of non-diabetes (25.10% vs 11.47%,  $P < 0.0001$ ). Logistic regression analysis showed that female (OR = 1.95, 95% CI: 1.67 – 2.24), triglyceride (OR = 1.40, CI: 1.21 – 1.63), alcohol drinking (OR = 1.22, 95% CI: 1.02 – 1.46), high sensitivity C reactive protein (OR = 1.01, CI: 1.00 – 1.02), southerner (OR = 0.78, CI: 0.69 – 0.89), obesity (OR = 1.32, CI: 1.12 – 1.55), diabetes (OR = 2.01, CI: 1.67 – 2.38), hypertension stage 1 (OR = 1.80, CI: 1.55 – 2.08), hypertension stage 2 (OR = 2.86, CI: 2.37 – 3.45) and hypertension stage 3 (OR = 7.50, CI: 5.91 – 9.53) were independently associated with MAU.

**Conclusion** Microalbuminuria was found to be common in middle-aged population of China, especially those with obesity, hypertension and diabetes. Microalbuminuria is associated with gender, region, hypertension, diabetes, alcohol drinking, body mass index, triglyceride and high sensitivity creatine protein.

## An 11-year analysis of bibliographical trends at the circulation, 2000–2010

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**Objective** Bibliometric analysis acting as an efficient way to measure the quality by using of mathematical techniques to investigate journals is accepted universally. The Circulation is the top-ranked journals in cardiovascular diseases and plays an important role in representation of the hottest topics and research trends in this field. The current study was conducted as the definitive bibliometric analysis of the journal at a length of 11 years from 2000 to 2010.

**Methods** Articles data for the current study was obtained from the official website of Circulation journal affiliated to the American Heart Association (<http://circ.ahajournals.org>). Historical data on journal performance, such as the impact factors, citable items, total citations received, was extracted from the JCR® and MedSCI®. All articles were classified according to their categories or subjects by scanning the title, abstract, and keywords artificially. All statistical calculations in current study were performed using the EXCEL® 2010 package (©Microsoft Corporation) and SPSS® version 19.0 (©IBM company).

**Result** A total of 11 645 articles were published in the 11-year period from 2000 to 2010, of which research articles comprised the vast majority (56.07%). The Clinical Investigations and Reports is twice the number than Basic Science Reports, counting 39.3% vs 16.77%. Correspondence (9.6%) was the next common type. And this followed by Editorials (8.45%), Images in Cardiovascular Medicine (8.39%), Brief Rapid Communications (3.24%), Corrections (2.65%), Cardiovascular News (2.23%), European Perspectives in Cardiology (1.89%), Circulation Electronic Pages (1.42%), Issue Highlights (1.33%), Clinical Summaries (1.12%), AHA Scientific Statement (1.10%), etc. In the research articles, the proportion of the clinic investigate and basic research maintained stably compared to the total items. Focused on the research articles, the rank of subjects followed Coronary Heart Disease (12.58%), Arrhythmia/Electrophysiology (11.97%), Heart Failure (11.40%), Molecular Cardiology (9.89%), Vascular Biology (9.87%), Epidemiology (7.10%), Imaging (6.90%), Interventional Cardiology (6.13%), Hypertension (3.38%), Valvular Heart Disease (2.62%), etc. The impact factor enjoyed a gradually increase during the 11 years and rose to 14.429 by the year of 2010.

**Conclusion** This journal prefer the newly founds which derived from or would have application to clinic practice than laboratory experiments. The doubling of items quantity of Correspondence and Editorials demonstrated that editors were apt to introduce present concept and propose for broadly discussion on one hand; and readers took part in the interaction enthusiastically on the other hand. The Coronary Heart Disease, Arrhythmia/Electrophysiology and Heart Failure, all of which might have high prevalence and mortality ranked first three amounts of articles yearly and overall in that period.

## Effect of serum albumin on the functional outcome among acute ischemic stroke patients

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**Objective** To investigate the effect of serum albumin, measured within 24 h after admission, on the functional outcome among acute ischemic stroke patients.

**Methods** In a non-concurrent cohort study from Jun. 1 2009 to May 31 2011, we continuously included 8 778 patients aged  $\geq 40$  years with acute ischemic stroke. Serum albumin, fasting glucose, blood pressure, lipid profiles, serum creatinine, blood urea nitrogen and fibrinogen were measured and demographic characteristics such as smoking, alcohol consumption, history of hypertension and diabetes, etc. were investigated at the time of admission. Functional outcome was measured when patient was discharged using modified Rankin Scale (mRS). Poor outcome was defined as mRS  $\geq 3$  or death. Serum albumin decreased was defined as serum albumin.

**Result** In total of 8 778 patients with acute ischemic stroke, 1 411 (16.07%) subjects had poor outcome and 1 118 (12.74%) subjects had serum albumin decreased. Subjects with poor outcome had significantly lower serum albumin level and higher rate of serum albumin decreased than subjects without poor outcome ( $38.20 \pm 5.83$  vs  $39.93 \pm 4.67$  g/L, 21.97% vs 10.97%, all  $P < 0.05$ ). The risks of poor outcome with serum albumin in the third and the fourth quartile were higher than that in the first quartile, HR and 95% CI were 0.687 (0.587 – 0.804), 0.747 (0.638 – 0.874) respectively, after adjusting for age, gender, history of diabetes, history of atrial fibrillation, hypertension, hyperglycemia, recurrence, smoking, alcohol consumption, triglycerides, blood urea nitrogen, fibrinogen and serum globulin. The trend P value changed little after controlling the potential confounding factors and the dose-response relationship between serum albumin and the risk of poor outcome remained significant ( $P$  value for trend  $< 0.0001$ ).

**Conclusion** The current study indicated that lower serum albumin was associated with a higher rate of poor outcome in acute ischemic stroke patients. Higher serum albumin may be neuroprotective in ischemic stroke in humans.

## Prevalence and associated risk factors for stroke among middle-aged population of China: a multiple-center cardiovascular epidemiological study

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**Objective** To evaluate the prevalence of and risk factors for stroke

among middle-aged populations in China.

**Methods** Data was collected from a cross-sectional survey on risk factors of cardiovascular diseases conducted in 2009–2010. There were about 1000 participants each from 12 different research populations including southern and northern, urban and rural in different parts of China, with international standardized examination and measurement. Half of the subjects were men and half were women, aged from 35 to 64 years old. Descriptive statistics and logistic regression models were used in the analysis.

**Result** After excluding those participants with missing values for age, 11 623 subjects were eventually included in the study. The overall prevalence of stroke in the study population was 1.5%. Among the stroke patients, 68.8% were male, 66.3% had ischemic stroke, and 21.9% were hemorrhagic ones. Significant risk factors for all strokes were: age, male, hypertension, diabetes, sedentary behavior, cigarette smoking and hypercholesterolemia ( $P < 0.05$  for all). These risk factors were all significant for ischemic stroke, whereas male, hypertension, sedentary behavior, hypercholesterolemia were significant risk factors for hemorrhagic stroke. Tea drinking (OR 0.629,  $P = 0.011$ ), moderate alcohol drinking (OR 0.355,  $P = 0.0002$ ) might provide protection against stroke. In those patients with high blood pressure, 33.1% took anti-hypertensive medications regularly, only 9.3% had their blood pressure controlled at 140/90 mm Hg. 29.5% of diabetic patients took hypoglycemic drugs or insulin therapy regularly. 18.8% of patients with hypercholesterolemia took lipid-lowering drugs within two weeks of the study.

**Conclusion** Targeted interventions that reduce blood pressure, serum cholesterol and promote physical activity, could considerably lighten the stroke burden.

### Prevalence, awareness, treatment, control and associated risk factors of hypertension among middle-aged population of China: a multiple-center cardiovascular epidemiological study, 2009–2010

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**Objective** This study aimed to estimate the current hypertension prevalence, awareness, treatment, control and associated risk factors among middle-aged populations in China.

**Methods** Data was collected from a cross-sectional survey on risk factors of cardiovascular diseases conducted in 2009–2010. There were about 1 000 participants each from 12 different research populations including southern and northern, urban and rural in different parts of China, with international standardized examination and measurement. Half the subjects were men and half were women, aged from 35 to 64 years old. Out of them, there were 11 619 participants were analyzed. Abdominal obesity was defined as waist circumference  $> 85$  cm in men and  $> 80$  cm in women.

**Result** The crude prevalence of hypertension in the study population was 37.6% (41.1% in male, 34.6% in female), and the prevalence showed a rising trend with increasing age ( $P$  for trend  $< 0.001$ ). Overall, hypertension prevalence was higher in northerners than southerners (40.8% vs 33.2%,  $P < 0.001$ ), and lower in successive Educational attainment groups. Among all the hypertensive patients recognized in

the study, 46.6% were aware of their high blood pressure, 33.1% took anti-hypertensive drugs regularly, but only 9.3% of hypertensive patients had their blood pressure controlled at 140/90 mm Hg. For those who received treatment, only 28.0% were adequately controlled. Compared with male patients, female patients had a higher treatment rate (38.3% vs 27.9%,  $P < 0.001$ ), and controlled their blood pressure more effectively (11.2% vs 7.3%,  $P < 0.001$ ). Logistic regression analysis showed that age, residential region, educational attainment, physical activity, alcohol drinking, tea drinking, abdominal obesity, diabetes, apoB/apoAI ratio, serum UA (Uric Acid) levels were independently associated with hypertension.

**Conclusion** Hypertension is highly prevalent and poorly aware and controlled in the study population. It is urgent to take effective actions to change this status.

### Characteristics of coronary lesions in hypertensive patients with coronary artery disease

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**Objective** The main purpose is to compare the degree of coronary artery changes in CHD patients with or without hypertension, and analyze bifurcation lesion in CHD patients with hypertension.

**Methods** 1 015 CHD patients were enrolled. SYNTAX score system was used to assess the severity of coronary artery disease status. The incidence of bifurcation disease, total number of bifurcation lesion, Bifurcation Score and Bifurcation Ratio were compared.

**Result** An increase in SYNTAX score, the total number of bifurcation lesions, Bifurcation Score and Bifurcation ratio was observed in hypertension group. Age, history of DM, TC, history of smoking and history of hypertension were independent predictors of the SYNTAX score. A positive correlation was found between bifurcation ratio and history of hypertension.

**Conclusion** The patients with hypertension have more severity of coronary artery lesion and higher ratio of coronary bifurcation lesions.

### The optimal intervals for long-term blood pressure screening and the associated risk factors of intervals in a Chinese population

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**Objective** To estimate the optimal intervals for long-term BP monitoring and the related risk factors.

**Methods** A retrospective cohort study was conducted on 7 894 participants without antihypertensive medication at baseline from Jan. 2005 to Dec. 2010. Participants underwent annual health check-



up at Qingdao-Fuwai hospital. Data on cardiovascular disease related risk factors were collected. The true long-term changes in BP were determined by the signal-noise-ratio (SNR) - the Ratios between long-term ('Signal') variances and short-term variances ('Noise') of systolic blood pressure (SBP) given the number years of check-up. The optimal intervals for long-term BP check-up were detected by the minimal years of SNR > 1.0 or its 95% confidence interval (CI) including 1.0. The validity of optimal intervals was evaluated by the true positive measurement and the associated risk factors of optimal intervals were evaluated in stratified analysis.

**Result** A total group of 7 894 adults (aged 18 years older) were recruited in this study. The mean age was  $44 \pm 10$  years for men,  $46 \pm 9$  years for women. The mean of SBP increased from 117.5 mm Hg in 2005 to 122.4 mm Hg in 2010. The estimated short-term variance of SBP was 58.3 mm Hg<sup>2</sup>. The long-term variance of SBP increased from 11.2 mm Hg<sup>2</sup> in 2006 to 67.4 mm Hg<sup>2</sup> in 2010. The optimal interval for blood pressure check-up interval was three years on the whole, when the 95% CI of SNR of SBP at the third year included 1.0 (SNR 0.8, 95% CI 0.7 - 1.0). The BP screening interval was highly associated with cardiovascular risk factors, such as age, dislipidemia, diabetes and overweight. Participants with any of those risk factors, the optimal interval would get shortened 1 to 2 years.

**Conclusion** The optimal blood pressure screening intervals are 4 years for men and 3 years for women without previous CVD risk factors and the intervals are shortened in persons with aging and other CVD risk factors in the Chinese population.

### The 12-year trend of cardiovascular disease risk factors prevalence, awareness, treatment and control in a China urban community population

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**Objective** To examine the long-term trend of prevalence and control statuses of five CVD risk factors, which includes hypertension, hypercholesterolemia, diabetes, obesity and smoking in a China community population.

**Methods** A retrospective study was conducted by using a 12-year (2000 - 2011) health checkup data from a large community-based Chinese population in Qingdao city of China. A total of 159 027 annually health checkup records of adults aged 25 - 64 years were included in this study. The study subjects attended health checkup for chronic diseases and an epidemiological survey for disease Related risk factors. The rates of each year were age-adjusted using the China 2000 Population Survey Data. The locally weighted polynomial regression Methods (LOESS) was used for fitting trend curves and Cochran-Armitage Methods was used for trend test.

**Result** From 2000 to 2011, there was an increase in body mass index of 0.03 kg/m<sup>2</sup> per year, whereas the smoking decreased. For blood

pressure, the mean systolic blood pressure decrease was 1.4 mm Hg per year; the mean diastolic blood pressure decrease was 0.6 mm Hg. For total cholesterol level, the mean decrease was 0.02 mmol/L per year. For the fasting glucose level, the mean increase was 0.02 mmol/L. On the whole, the prevalence of CVD risk factors were still high, the rates of risk factors awareness, treatment and control showed a significantly increase over the 12-year period, however, the control rate of risk factors, especially in hypercholesterolemia, glucose is still far from being satisfactory.

**Conclusion** The age-adjusted prevalence of five CVD risk factors had a non-linear trend of slowly decreasing, though the speed was not promising. However the decreasing trend could be reversed by the population is aging, which still lead the problem of CVDs out of control in the coming decade in China.

### Investigation of the cardiovascular risk factors by 10-year risk estimation of ischemic cardiovascular disease (ICVD) in Kazak population in Xinjiang province of China

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**Objective** To investigate into the status of primary risk factors of cardiovascular disease in Kazak population in Ili of Xinjiang Province.

**Methods** In total, the participants aged  $\geq 35$  years and living for more than five years in Ili were selected with Stratified Random Sampling and investigated with epidemiological Methods. All the participants were interviewed by trained and certified observers under a structured questionnaire. FPG, blood lipids, BMI, and BP of all sampled population were measured. The risk of CVD in people aged from 35 to 59 was evaluated by the Methods and tools of 10-Year Risk Estimation of Ischemic Cardiovascular Disease in Chinese.

**Result** A total of 1 126 Kazak subjects (443 males and 683 females) from Ili of Xinjiang Province were enrolled. The mean values of SBP, BMI, triglycerides, TC, HDL and LDL cholesterol in male group were significantly higher than those of female group ( $P < 0.01$ ), but there were no significant differences between the two groups in the level of age ( $45.54 \pm 6.93$  vs  $44.75 \pm 6.67$ ,  $P = 0.056$ ). The mean value (%) of 10-year morbid risk of each age group in men group was higher than that of corresponding age group in women group ( $P < 0.05$ ) in younger than 50 years groups but no difference in over 50 years old groups ( $P > 0.05$ ). There were 94.8% males and 95.6% females whose 10-year absolute risk of ICVD was less than 10% ( $P = 0.536$ ) and 5.19% males and 4.39% females higher than 10% ( $P = 0.536$ ). The relationship between cardiovascular risk factors and mean levels of 10-year morbid risk are listed as follows. There are significant difference in levels of SBP, TC, and BMI between low-risk and high-risk, moderate-risk groups ( $P < 0.05$ ), with the exception of FBG ( $P = 0.354$ ). The detection rate of smoking is higher in high-risk group ( $P < 0.05$ ). The cardiovascular risk factors are more common in moderate-risk and high-risk populations than low-risk groups.

**Conclusion** The prediction models and simplified tools for estimating 10-year-risk of ICVD in Chinese can predict satisfactorily the occurrence of cardiovascular disease in Kazak population in Ili of Xinjiang Province.

## Epidemiological survey of smoking in Han, Uyghur, and Kazakh population in adults of Xinjiang province

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**Objective** An epidemiological survey of smoking in Han, Uyghur, and Kazakh populations in adults of Xinjiang Province of China.

**Methods** Four-stage selected random samples aged 35 and over were used to analyze the status of smoking in different nationalities, ages, and sexes in Xinjiang Province. The selection was done from six localities (i.e., Urumqi, Kelamayi, Fukang, Turfan Basin, He Tian, and Yi Li), twenty-three municipalities, and five autonomous counties of Xinjiang Province from 2007 to 2010. A total of 13 375 people were surveyed.

**Result** We investigated gender, age, height, weight, education level, occupation, smoking history, and drinking history among Han, Uyghur, and Kazakh populations and found they were statistically different ( $\chi^2 = 46.122, P < 0.05$ ;  $\chi^2 = 113.133, P < 0.05$ ;  $\chi^2 = 225.727, P < 0.05$ ;  $\chi^2 = 136.254, P < 0.05$ ;  $\chi^2 = 2681.0, P < 0.05$ ;  $\chi^2 = 6340.0, P < 0.05$ ;  $\chi^2 = 342.3, P < 0.05$ ;  $\chi^2 = 180.2, P < 0.05$ ). In general, the smoking prevalence was 28.6%, with male and female prevalence of 54.9% and 5.8% respectively ( $\chi^2 = 4251, P < 0.05$ ). Likewise, the prevalence was 31.3% in Han, 18.8% in Uyghur, and 35.1% in Kazakh populations respectively. The rates were different among different nationalities ( $\chi^2 = 342.3, P < 0.05$ ) with the highest being in the Kazakh population. The smoking prevalence in 35–44 age-grouped population reached its peak values ( $\chi^2 = 29.714, P < 0.05$ ). With increase in the level of education, smoking prevalence showed a rising trend. The bachelor's degree and above reached its peak value ( $\chi^2 = 361.0, P < 0.05$ ). Smoking rates among Uyghur, Han, and Kazakh populations in different education levels were statistically different ( $\chi^2 = 80.953, P > 0.05$ ;  $\chi^2 = 214.4, P < 0.05$ ;  $\chi^2 = 21.638, P < 0.05$ ). Smoking prevalence of different marital status was distinct and that of unmarried was the highest ( $\chi^2 = 119.3, P < 0.05$ ). The differences among Uyghur, Han, and Kazakh populations had statistical significance ( $\chi^2 = 53.902, P > 0.05$ ;  $\chi^2 = 68.265, P < 0.05$ ;  $\chi^2 = 14.793, P < 0.05$ ).

**Conclusion** Smoking prevalence status is pretty serious in Xinjiang Province.

## The impact on direct medical economic burden from nosocomial infection in congenital heart disease patients

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**Objective** To explore the impact of nosocomial infection on the direct medical economic burden (DMEB) in the operated patients with congenital heart diseases (CHDs), including the atrial septal defect (ASD) and ventricular septal defect (VSD) patients.

**Methods** With a retrospective study, the 10 014 (mean age was  $11.38 \pm 13.22$  years, male 5 437, female 4 577) CHD cases hospitalized by cardio-surgery or interventional therapy in the year 1998–2008

were investigated on the DMEB (including what had expended on examination cost, medicine cost, operation cost, nursing cost, and so on). Of them the 6 880 ventricular septal defect (VSD) cases and 3134 atrial septal defect (ASD) cases were investigated. The data management was finished with Epidata (3.2). All the statistical procedures were finished with SAS 9.2, with the mean  $\pm$  standard deviation (mean  $\pm$  SD) for the data central tendency estimation, t-test (satisfied with equal variance and normal distribution) and t'-test (not satisfied with equal variance or normal distribution) for the two means significant difference test, the covariance analysis and stratified analysis were applied for the controlling of confounding factors (age, sex).

**Result** General nosocomial infection rate was 4.24%. The DMEB mean in nosocomial infection group was significantly higher than that in non-nosocomial infection group ( $52\,499 \pm 27\,744$  vs  $32\,864 \pm 14\,655, t = 14.50, P < 0.0001$ ), the relative increase rate in the DMEB mean was 59.75%. With the covariance analysis for age adjusted, the DMEB adjusted mean in nosocomial infection group was still significantly higher than that in non-nosocomial infection group ( $53\,137 \pm 754$  vs  $32\,841 \pm 157, t' = 26.32, P < 0.0001$ ), the relative increase rate in the DMEB adjusted mean was 61.80%. With the sex stratified analysis and age covariance analysis for the sex and age adjusted, the DMEB adjusted mean in male nosocomial infection group was still significantly higher than that in male non-nosocomial infection group ( $54\,085 \pm 959$  vs  $32\,853 \pm 221, t' = 21.55, P < 0.0001$ ), the relative increase rate in the DMEB adjusted mean was 64.63%. The DMEB adjusted mean in female nosocomial infection group was still significantly higher than that in female non-nosocomial infection group ( $51\,377 \pm 1\,237$  vs  $32\,831 \pm 222, t' = 14.74, P < 0.0001$ ), the relative increase rate in the DMEB adjusted mean was 56.49%.

**Conclusion** The nosocomial infection is still a great risk factor in the increase of CHD patients DMEB. So controlling nosocomial infection is the important guarantee for the DMEB reduction.

## Factors associated with smoking cessation among middle-aged male smokers of China: a multiple center cardiovascular epidemiological study

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**Objective** To examine the factors associated with smoking cessation among middle-aged Chinese.

**Methods** Data from a cross-sectional survey on risk factors of cardiovascular disease, which were conducted in 2009–2010, with international standardized examination, measurement and interviewer-administered questionnaires. There were about 1000 participants each from 12 different research populations including southern and northern, urban and rural in different parts of China. Half of the subjects were men and half were women; their ages ranged from 35 to 64 years. Out of them, there were 2683 male smokers were analyzed. Current smokers were defined as persons who reported smoking at least 400 cigarettes in their lifetime and smoked cigarettes in recent one month. Former smokers were defined as persons who had smoked before but did not smoke in recent one month.

**Result** A total of 5 344 men participated in the study. The mean

age of the respondents was  $50 \pm 8$  years. Of the respondents, 36.1% were never smokers, 7.9% were former smokers and 56.0% were current smokers. Of the smokers, 79.4% had never tried to quit smoking. Univariate analysis shows that race, education, levels of physical activity, number of cigarettes per day, lifetime smoking period, drinking, individual history and family history (including hypertension, coronary heart disease or stroke) were significantly associated with smoking cessation ( $P < 0.05$ ). Multivariate logistic regression modeling showed that those who were older (for 45–54 year, OR = 2.15, 95% CI: 1.58–2.93; for 55–64, OR = 2.40, (95% CI: 1.65–3.48, compared with those who aged 35–44); those who were residents of Han (OR = 1.43, 95% CI: 1.14–1.79, compared with those who were minority) and attained education to high school or above (OR = 1.60, 95% CI: 1.27–2.02, compared with those who attained education less than high school); those who smoked  $\leq 10$  cigarettes per day (OR = 1.30, 95% CI: 1.06–1.60, compared with those who smoked 1–10 cigarettes) and smoked 15–24 years (OR = 2.86, 95% CI: 2.10–3.90) or 5–14 years (OR = 2.72, 95% CI: 1.64–4.52), compared with those who smoked  $\geq 25$  years; those whose family members had ever suffered hypertension, coronary heart disease or stroke (OR = 1.28, 95% CI: 1.05–1.57); those who were nondrinkers (OR = 1.33, 95% CI: 1.09–1.61); and those who had ever suffered chronic respiratory disease (OR = 1.95, 95% CI: 1.28–3.05), were more likely to attempt to quit.

**Conclusion** Several predictors were identified that could provide a scientific basis for establishing smoking cessation strategies in China. The findings also have implications for future surveys on the quitting process among Chinese.

### The effect of habitual tea consumption on hypertension among middle-aged men of China: a multiple center cardiovascular epidemiological study

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**Objective** To assess the effect of habitual tea consumption on hypertension in the middle-aged men in China.

**Methods** Data were collected from a cross-sectional survey on risk factors of cardiovascular disease, which was conducted in 2009–2010. There were about 1 000 participants each from 12 different research populations including southern and northern, urban and rural in different parts of China, with international standardized examination and measurement. Half of the subjects were men and half were women; their ages ranged from 35 to 64 years. This study was to assess the effect of habitual tea consumption on hypertension in men among the participants. Tea drinking was defined by the frequency of consumption at least 3 times each week.

**Result** Out of all, 2868 participants (61.6%) were habitual tea drinkers. There was a strong inverse correlation between tea drinking and hypertension after adjusting other risk factors of hypertension ( $P < 0.001$ ). The odds ratio (OR) of hypertension was 0.76 [95% confidence interval (CI): 0.67–0.87] for subjects who drank tea compared to those who did not. Compared with non-habitual tea drinkers, the association for tea consumption between 1–10 gram per day and hypertension was statistically significant with an OR value of 0.69 (CI: 0.60–0.81).

However, when the amount of tea consumption was more than 20 gram per day, tea drinkers were at higher risk of hypertension than non-habitual tea drinkers (OR = 1.48, CI: 1.14–1.91). The risk of developing hypertension decreased by 44% for those who drank flower tea compared with those who drank other tea. Subjects who drank tea for 1–9 years had a lower risk of hypertension (OR = 0.67, CI: 0.50–0.90) compared to those who did not.

**Conclusion** Tea drinking was independently associated with prevalence of hypertension, which might play a role in the prevention of the disease. But the amount of tea consumption was not the more the better. It is worthy to further study.

### 2-year clinical outcomes of everolimus-eluting stent as compared to paclitaxel stent in patients undergoing percutaneous coronary interventions. A meta-analysis of randomized clinical trials

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**Objective** Our purpose was to perform a meta-analysis of randomized controlled trials evaluating safety and efficacy in 2-year of everolimus-eluting stents (EES) compared with paclitaxel-eluting stents (PES), in patients undergoing percutaneous coronary intervention (PCI).

**Methods** We undertook a literature search using Medline, EMBASE, the Cochrane Central Register of Controlled Trials, proceedings of international conference, scientific session abstracts and relevant websites, until May 2013. Information about study design, inclusion and exclusion criteria, baseline characteristics, sample size and 2 year follow up clinical events were extracted from final literatures. Included studies comprised randomized trials evaluating EES vs PES, with patients undergoing PCI, at 2-year follow up.

**Result** We identified 4 randomized controlled trials comparing EES vs PES in 6 722 patients with 2-year follow up clinical events. At 2-year follow up, patients receiving EES, as compared to PES, experienced significantly lower myocardial infarction events (OR = 0.56; 95% CI, 0.43–0.72,  $P < 0.0001$ ) and ischemia driven target lesion revascularization (OR = 0.57; 95% CI: 0.45–0.71,  $P < 0.0001$ ), but without difference in mortality (OR = 0.85; 95% CI: 0.63–1.16,  $P = 0.32$ ) and cardiac mortality (OR = 0.91; 95% CI: 0.59–1.41,  $P = 0.68$ ). A trend towards lower 2-year target lesion failure event rates in favor of EES compared to PES was found (OR = 0.63; 95% CI: 0.53–0.75,  $P < 0.0001$ ).

**Conclusion** At 2-year follow up, patients treated with EES have lower rates of myocardial infarction, ischemia driven target lesion revascularization and target lesion failure events comparing to PES. However, there are no significant differences in rates of mortality and cardiac mortality. Our study suggested that EES can reduce more clinical events at 2-year follow up with respect to PES.



### Accuracy of the automated oscillography electronic device in measuring blood pressure in children

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**Objective** Mercury sphygmomanometer auscultation method (MSA) was common instrument to measure blood pressure (BP), while the automated oscillography electronic measurement (OSC) devices become common for home BP monitoring. The objective of this study was to assess the accuracy of OSC in Chinese children and adolescents compared with the BP readings by using the standard MSA.

**Methods** A total of 679 adolescents aged between 7 and 17 years participated in the study. The participants were from Shanghai city, a field of 2013 national annual student fitness and health survey, evenly composed of boys and girls. The automated Omron HEM-7012 monitor and MSA, were used to measure three times respectively on the same subject and two instruments were used in turns. BP of two devices were recorded and compared. Z-score of BP value by OSC were derived for systolic blood pressure (SBP) and diastolic blood pressure (DBP) separately for boys and girls by age and height percentiles using the GAMLSS of LMS equations method. Diagnosis value of OSC was analyzed by using receiver operating characteristic (ROC) compared with hypertension status diagnosed based on MSA according to the current national recommendation.

**Result** A total of 667 subjects aged between 7 and 18 years participated in the study. The proportion of male was 54.5%, Gender distribution was not balanced in each age group. The mean SBP by MSA were higher than one by OSC. DBP was just the opposite. There was statistically significant difference with regard to BP values between the two devices (for SBP,  $t = 12.56$ ,  $P < 0.001$ ; for DBP,  $t = 7.89$ ,  $P < 0.0001$ ). In total, 90% students had difference of SBP and DBP within 15 mm Hg, 75% had difference within 10 mm Hg. Only 44% and 45.5% subjects with difference within 5 mm Hg measured by two devices. After the adjustment of gender and age, the partial correlation coefficients between OSC and MSA were 0.773 for SBP and 0.407 for DBP ( $P < 0.01$ ). ROC analysis showed that AUCs of SBP and DBP were 0.628 (95% CI: 0.586 – 0.669) and 0.691 (95% CI: 0.651 – 0.731), respectively.

**Conclusion** The measurement Result of comparing OSC and MSA are consistent with other researches. From the result of ROC analysis, diagnosis value of OSC is less satisfying and can not take place of MSA for diagnosis hypertension. Future studies are expected to explore how to efficiently use the two devices in combination for screen and diagnose hypertension.

### Physical activity levels, sport activities and risk of acute myocardial infarction in China population: Result of the interheart study

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**Background** Physical activity (PA) during leisure time has been inversely associated with cardiovascular disease (CVD) risk in Western populations; however, few studies have evaluated the different aspects of PA both at work and during leisure time in relation to CVD, and this association has not been examined in China. The present study aimed to address the relation between PA and risk of acute myocardial infarction (AMI) in China population.

**Methods** We conducted a hospital-based case-control study. Cases were first AMI ( $n = 2\ 909$ ). Controls were matched to cases on age and sex. 2 947 controls who did not report previous angina or physical disability completed a questionnaire on work and leisure-time PA. We used logistic regression to control for other risk factors.

**Result** We observed an inverse association between strenuous leisure-time PA and AMI risk. The OR of leisure-time PA adjusted for age and sex for strenuous exercise group compared with mainly sedentary group was 0.74 (95% CI: 0.61 – 0.90), and for mild and moderate exercise group 0.96 (95% CI: 0.85 – 1.08). Multivariate adjustment for other risk factors did not substantially alter the association. After adjustment for age and sex, the OR of work-related PA for heavy work-related PA, compared with mainly sedentary was 1.44 (95% CI: 1.06 – 1.94), for walking, climbing, and lifting 1.00 (95% CI: 0.77 – 1.30) and for walking at one level 0.90 (95% CI: 0.75 – 1.07). The model adjusted for all variables, the ORs were 1.37 (95% CI: 0.95 – 1.99), 0.94 (95% CI: 0.70 – 1.27) and 0.85 (95% CI: 0.70 – 1.05).

**Conclusion** Leisure-time physical activity, including as much as 4 – 6 hour/week and  $\geq 7$  hour/week sports, was protective for AMI risk and sedentary lifestyles were positively associated with risk of AMI. Heavy work-related PA could increase AMI risk in China population.

### Impact of arterial stiffness on cerebrocardiac vascular prognosis

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**Objective** To assess the impact of multiple noninvasive arterial stiffness indexes on cerebrocardiac vascular prognosis.

**Methods** 198 patients with risk factors of CAD underwent four noninvasive tests of arterial stiffness at least two times and were divided into increased arterial stiffness group and control group, by augmentation index (Aix@75) increased or not during follow-up. Major adverse cardiac and cerebral events were compared between two groups.

**Result** During follow-up, the rate of primary and all end point events were significantly higher in increased arterial stiffness group.

Multivariate Cox regression analysis revealed that increasing Aix@75, common carotid atherosclerotic plaque, multivessel CAD and cerebral vascular disease history were independent predictors of prognosis of vascular diseases. Kaplan-Meier curve revealed the greater the increase in Aix, the worse prognosis.

**Conclusion** The Result indicated a high value of noninvasive arterial stiffness tests in evaluating prognosis.

### The atrial fibrillation registry in China: baseline characteristics and patient management

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**Background** To describe patient characteristics, risk factors, comorbidities, management strategy, and control of Chinese atrial fibrillation (AF) patients in the emergency department (ED) daily practice.

**Methods** We conducted a prospective, observational registry of patients with AF/flutter in China. Participants were enrolled in the ED. Baseline characteristics were collected and follow-up was planned at 1 year.

**Result** Of the 2 016 Chinese patients from 19 sites, 54.8% were women. 618 (30.7%) had paroxysmal, 452 (22.4%) had persistent, and 945 (46.9%) had permanent AF. The most common comorbidity was hypertension (55.5%), followed by coronary artery disease (41.8%), heart failure (37.4%) and current smoking (21.5%). The prevalence of comorbidities, such as heart failure valvular heart disease, and history of stroke or transient ischemic attack, increased as AF progressed, as well as the mean CHADS<sub>2</sub> score. In patients with non-valvular AF, 110 (12.7%) of those with CHADS<sub>2</sub> ≥ 2 were prescribed with oral anticoagulants (OACs), while 119 (15.6%) of those with CHADS<sub>2</sub> < 2 received. In 324 patients with valvular AF qualified for OACs, 134 (41.4%) actually used. INR value was within the target INR range (2.0 – 3.0) only in 96 patients (26.4%). About one sixth of patients received ≥ 1 antiarrhythmic agents (AADs), while rate-control agents were used more frequently (68.4%). 78.3% of persistent and 97.7% of permanent AF patients were still in AF/flutter when left ED.

**Conclusion** The risk profile of Chinese patients was different from previous studies in other countries, and the use of oral anticoagulants was inadequately deviate from current guidelines.

### Sugar sweetened beverages consumption and risk of coronary heart disease and stroke: a meta-analysis of prospective studies

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**Objective** We performed a meta-analysis to summarize the evidence with respect to the associations between Sugar sweetened beverages (SSBs) consumption and the risk of CHD and stroke.

**Methods** We searched for articles published up to Feb. 2013 through PubMed, EMBASE and Cochrane Library Database and

reviewed reference list of the retrieved articles. Prospective studies with reported relative risks (RRs) with 95% confidence intervals (CIs) of CHD or stroke for different categories of SSBs consumption were included. Fixed- and random-effects models were used to evaluate the associations by comparing the highest and lowest categories of SSBs consumption in relation to risk of CHD and stroke.

**Result** Five prospective studies with 7 396 CHD cases and 6 501 stroke cases (3 403 ischemic stroke cases and 1 595 hemorrhagic stroke cases, explicitly) among 301 209 participants were included in the meta-analysis. The pooled RRs (95% CI) in the highest category of SSBs consumption in comparison with the lowest category of SSBs were 1.17 (1.07 – 1.28) for CHD and 1.04 (0.93 – 1.17) for total stroke. Additionally, a one-serving per day increase in SSB consumption was associated with a 15% increased risk of CHD. For stroke subtype, a modest but significant inverse association between SSBs consumption and hemorrhagic stroke was observed with pooled RR (95% CI) of 0.78 (0.63 – 0.98). No statistically significant association was observed for ischemic stroke (RR: 1.15, 95% CI: 0.82 – 1.61).

**Conclusion** Result from our meta-analysis indicate that higher consumption of SSBs is associated with increased risk of CHD and decreased risk of hemorrhagic stroke, but not for total stroke or ischemic stroke. The suggestive not conclusive findings warrant future researches.

### Cardiovascular diseases risk profiles among hypertensive patients with obstructive sleep apnea-hypopnea syndrome from Xinjiang, China

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**Objective** Obstructive sleep apnea hypopnea syndrome (OSAHS) is a risk factor for several cardiovascular conditions. It is essential to know the major cardiovascular risk factors (CRFs) of OSAHS during a clinical evaluation.

**Methods** This is a retrospective study enrolling 1 666 in-patients with hypertension that underwent polysomnogram. The anthropometric data, the early onset CVD family history, cigarette smoking, the blood pressure, the fasting serum glucose, lipid profiles and hs-CRP levels were evaluated and compared between OSAHS group and non-OSAHS group.

**Result** Of 1 666 patients with hypertension, 1 307 were detected to be combined with OSAHS. The percentage of smoking, dyslipidemia, hyperglycemia, elevated hs-CRP level and obesity indicated increasing trend with severity of OSAHS. With the severity of OSAHS, the number of CRFs in one individual increased greatly (Trend  $\chi^2 = 117.36$ ,  $P < 0.001$ ). Multivariate logistic regression analysis showed that the BMI (OR = 1.21; 95% CI: 1.16 – 1.26), systolic blood pressure (OR = 1.01; 95% CI: 1.00 – 1.02), total cholesterol (OR = 1.15; 95% CI: 1.02 – 1.36), age (OR = 1.07; 95% CI: 1.05 – 1.09) were significantly risk factors to OSAHS, while being female may be a protective factor with OR = 0.41.

**Conclusion** In the present study, the mostly found cardiovascular profile of hypertensive patients with OSAHS was obesity and plasma total cholesterol, as well as the unmodifiable factors of age and sex, the severer of OSAHS, the more CRFs clustered.

## A novel statistical method for comparing effectiveness of two treatments—simulated randomized controlled trials

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**Objective** To develop a new statistical method for comparing effectiveness of two treatments based on regularly collected treatment data.

**Methods** The rationale of the method is described as following: subjects with same health condition but received 2 different treatments respectively were performed simulated randomization into two arms for 100 times, the outcome variables were compared by using student-t tests for continuous variables and chi-square tests for categorical variables. Crossovers that were defined as subjects with contradictory assigned treatment by the simulated randomization with the actually received treatments were excluded from comparisons of means. The ratio of the frequency of rejected- $H_0$  hypothesis tests to the frequency of not-reject- $H_0$  hypothesis tests, called ODDs, and 95% CI were used to judge the overall hypothesis testing, and effect size estimations were computed based on the mean of 100 mean differences and 95% CI. The theoretical distribution of ODDs and its 95% CI, and the confounding effect were analyzed in simulated datasets with various between-group mean differences and statistical power (ranging from 0.5 to 0.85) with varied sample sizes ( $n = 50, 100, 500, \text{ and } 1000$ ). STATA 11.0 was used for programming. The performance of RCTs was compared with bootstrap based on a real RCT dataset with 3 outcome variables.

**Result** The ODDs and 95% CI were perfectly and linearly correlated with the between-group mean differences and statistical power, by difference sample size. The probability of loss of balance of confounding was below 5% for equal and unequal sample size of two arms after excluding misclassified subjects. The sRCT has good consistence in hypothesis testing and performance in effect size estimation compared with true RCT and bootstrap for outcome variable with normal distribution.

**Conclusion** The proposed novel analytical method, simulated RCTs based on real clinical treatment data, can be used to compare effectiveness of two treatments as preliminary evidence to RCTs.

## Association between homocysteine level and T lymphocyte subsets in patients with H type hypertension

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**Objective** The aim of this study was to assess the relationship between homocysteine level and T lymphocyte subsets in patients with H type hypertension.

**Methods** The study included 242 consecutive H type hypertension patients. All patients were divided according to homocysteine level tertiles, group 1: the lowest tertile [11.76 (10.91, 12.55)] ( $n = 80$ ), group 2: the midcan tertile [15.01 (14.04, 16.08)] ( $n = 82$ ), group 3: the highest tertile [20.44 (18.01, 26.37)] ( $n = 80$ ). Records all parameters. Analyzing all above difference and their relationship with homocysteine in every group.

**Result** Multivariable linear regression analysis showed that CD4 and serum creatinine was significantly associated with serum

homocysteine.

**Conclusion** Serum homocysteine levels in H type hypertension patients were independently related to CD<sub>4</sub> and serum creatinine level which indicates that cellular immunity (CD<sub>4</sub>) involved in the development of H type hypertension.

## Gender-Specific relationship between carotid intema-media thickness and cardiac diastolic function in a healthy Chinese population

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**Background** It has been suggested the existence of ventricular-arterial coupling effect which could be a key determinant of cardiovascular performance. However, little is known about the gender differences in ventricular-arterial interaction in healthy Chinese population.

**Objective** To identify gender difference in the associations between carotid intema-media thickness (CIMT) and cardiac diastolic function in healthy Chinese individuals.

**Methods** We examined 852 healthy participants (aged 30 – 98 years, 46% men) in three north China cities by M-mode ultrasonography to analyze CIMT and cardiac structure and function. Cardiac function was measured by determining the ratio of early diastolic peak flow velocity (E) and late diastolic peak flow velocity (A) (E/A), as well as the deceleration time of the early mitral velocity (MV-DT). Cardiac dysfunction was defined as E/A values < 25<sup>th</sup> percentile (E/A < 0.778 for males and LAV values > 75<sup>th</sup> percentile (LAV > 34.86 ml for males and > 32.16 ml for females), and MV-DT values > 75<sup>th</sup> percentile (MV-DT > 210 ms for males and > 195 ms for females).

**Result** CIMT, E/A, LAV, and MV-DT significantly correlated with age in both males (CIMT:  $r = 0.418, P < 0.01$ ; E/A:  $r = -0.325, P < 0.01$ , LAV:  $r = 0.123, P < 0.05$ ; MV-DT:  $r = 0.175, P < 0.01$ ) and females (CIMT:  $r = 0.429, P < 0.01$ ; E/A:  $r = -0.423, P < 0.01$ ; LAV:  $r = 0.180, P < 0.01$ ; MV-DT:  $r = 0.174, P < 0.01$ ). Interestingly, left ventricular ejection fraction (LVEF) was not significantly correlated with age in both genders. CIMT was significantly associated with lower E/A in an unadjusted model in tertile II and III. The odds ratio (95% CI) for males was 2.428 (1.36 – 4.335) and 3.017 (1.674 – 5.437), respectively. However, this association disappeared upon age adjustment. The odds ratio (95% CI) for females was 3.298 (1.742 – 6.246) and 6.002 (3.202 – 11.251), respectively, and were still significant after adjustments for all other variables, including age, blood pressure, blood lipid and inflammatory markers (tertile II: 3.031, 95% CI: 1.228 – 7.48; tertile III: 3.224, 95% CI: 1.308 – 7.946). A higher MV-DT significantly correlated with higher CIMT only in an unadjusted model for females, and this association was lost upon age adjustment. There were no significant association between CIMT and higher values of LAV.

**Conclusion** Aging related increases in CIMT correlated with the decline in cardiac diastolic function only in females, which may contribute to the higher incidence of heart failure with preserved ejection fraction.



## Educational level, obesity and incident diabetes among Chinese adult men and women aged 18–59 years old: an 11–Year follow-up Study

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**Objective** To determine whether educational level and overweight/obesity was associated with the development of diabetes among Chinese adult men and women, when mediating factors were measured repeatedly and when long term exposure is accounted for.

**Methods** A retrospective cohort (2000 – 2011) of 10 704 participants aged 18 – 59 years (8 238 men, 2 466 women) in Qingdao Port Health Study (QPHS) were recruited in this study. The annual health checkup records included personal lifestyle, height, weight, waist circumference, resting heart rate, blood pressure, fasting plasma glucose, total cholesterol, triglycerides and plasma uric acid. Factors associated with incidence of diabetes was estimated by using hazard ratios (HR), 95% confidence interval (CI) and P-trend value, generated from Cox proportional hazards regression models.

**Result** During 110 825 person-years of follow-up, 1 056 new onset cases (9.5 per 1 000 person-years) of diabetes were identified. Compared with the participants of high educational level, those with low educational level had a higher risk of diabetes [HR (95% CI)] after adjustment for long term exposure to risk factors: [1.43 (1.11 – 1.86)] among men. The association was not found among women and the adjusted HR (95% CI) of diabetes was 1.15 (0.60 – 2.21). With normal weight as reference, the HR (95% CI) of diabetes after adjustment for long term exposure to risk factors, was 1.69 (1.38 – 2.09) for overweight and 2.24 (1.66 – 3.02) for obesity among men, which was 1.81 (1.12 – 2.92) and 2.58 (1.37 – 4.86) among women, respectively. The increased risks of low educational level were independent of mediators among men, through normal weight (P trend = 0.0313) and overweight (P trend = 0.0212) group but not obesity group (P trend = 0.0957). The association was not found among women.

**Conclusion** Baseline overweight/obesity was an independent risk factor of diabetes for both men and women. Low educational level was adversely associated with incident diabetes through normal weight, overweight and obesity groups, with the association being substantially attenuated by mediating factors only in the obesity group among men. The association was not found among women.

## Association between kidney function and Framingham global cardiovascular risk score

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**Background** Renal function is considered a predictor for cardiovascular disease (CVD) risk. Estimated glomerular filtration rate (eGFR) is a feasible clinical measure of kidney function. Framingham global CVD risk score (FRS) equation is the most widely accepted tool for predicting CVD risk in the general population. Most studies confirm that chronic kidney disease is an independent risk factor for CVD, but conclusion in individuals with eGFR  $\geq 60$  ml/min/1.73 m<sup>2</sup> is uncertain. This study examined the association between FRS and eGFR in a Chinese population with eGFR  $\geq 60$  ml/min/1.73 m<sup>2</sup>.

**Methods** Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation and CKD-EPI equation for Asians (CKD-EPI-ASIA) were used to measure eGFR and individuals with eGFR  $< 60$  ml/min/1.73 m<sup>2</sup> were excluded. Pearson correlation coefficient was used to evaluate the association between FRS and eGFR after adjustment for traditional cardiovascular risk factors.

**Result** Significantly inverse association between FRS and eGFR was confirmed in our two analyses, with Pearson correlation coefficients of -0.669, -0.698 (eGFRCKD-EPI,  $P < 0.001$ ,  $P < 0.001$ ), and -0.658, -0.690 (eGFRCKD-EPI-ASIA,  $P < 0.001$ ,  $P < 0.001$ ). FRS was not significantly associated with eGFR after adjustment for traditional cardiovascular risk factors in 2008 ( $P > 0.05$ ). However, with increasing FRS and decreasing eGFR, eGFR was independently associated with FRS in 2011 ( $P < 0.05$ ).

**Conclusion** Renal function is a risk factor for CVD, even in individuals with eGFR  $\geq 60$  ml/min/1.73 m<sup>2</sup>. With increasing FRS and decreasing eGFR, renal function was independently associated with CVD risk.

## Hypertension control in community health centers across China: analysis of antihypertensive drug treatment patterns

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**Objective** To assess the pattern of antihypertensive drug treatment in community health centers (CHCs) across China.

**Methods** 1 000 CHCs were selected, based on geographical location, previous cooperative experience, and accepting the invitation to implement a protocol of community-based standardized blood pressure management. Baseline information for each hypertensive patient under the care of CHCs was collected and the present pattern of hypertensive drug treatment was analyzed.

**Result** 92 325 hypertensive patients were recruited. The most frequently prescribed drug class was single pill combinations (SPCs)

(48.9%), followed by calcium channel blockers (CCBs) (36.8%), angiotensin converting enzyme inhibitors (ACEIs) (18.3%), beta blockers (BBs) (10.4%), diuretics (7.9%), and AT1 receptor blockers (ARBs) (4.0%). Most of the SPCs (86.7%) consisted of centrally active drugs (reserpine, clonidine) and/or vasodilators (dihydralazine, dibazole, pargyline). The most preferred drug class on mono therapy remained SPC (52.8%), followed by CCB (25.8%). ACEI+CCB was the most used combination for two-drug therapy (25.0%), ACEI+CCB+BB for three drug therapy (17.6%). ACEI and BB combination was used by 3.6% of patients, while ACEI+BB+diuretic and ARB+BB+diuretic were used by 4.6% and 2.4% of patients, respectively. The proportion of patients on mono-, SPC-, and 2+ therapies was 36.3%, 40.6%, and 23.1%, respectively; the corresponding control rates were 27.7%, 25.0%, and 22.5%.

**Conclusion** Our study ascertained major shortcomings in the present status of antihypertensive pharmacotherapy in routine medical practice in China. SPCs, mostly composed of less-used drugs, were the most preferred medication. Intensive professional education of primary care physicians in CHCs is warranted.

### Survey on prevalence of cardiovascular diseases and its risk factors in China (China CVD study): background, aim, and method and design

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**Objective** Survey on Prevalence of Cardiovascular Diseases and its Risk Factors in China are to obtain data on prevalence and distribution of following conditions in the general population of China: 1) high blood pressure, obesity, smoking, alcohol consumption, physical inactivity; 2) impaired fasting glucose, dyslipidemia, atrial fibrillation, chronic heart failure, valvular heart disease, cardiomyopathy, abdominal aortic aneurysm, peripheral arterial disease; 3) congenital heart disease among neonates; and 4) coronary heart disease events and stroke events.

**Method and Result** Using a stratified multistage random sampling method, a representative sample of 500 000 participants aged  $\geq 15$  years old will be selected in 22 provinces, 5 autonomous regions and 4 municipalities across China to survey for Aim I and IV; a sub-sample of 70 000 participants aged  $\geq 35$  years old will be recruited for Aim II. 40 000 neonates will be screened for Aim III in random-selected hospitals. All of the investigators will be trained before the survey in site. Data on demographic and other factors, including education, occupation, and lifestyle will be recorded. For each participant, self reported history of CVD will also be recorded. Blood pressure, height, weight, and waist circumferences will be measured using standard Methods. ECG, ABI, UCG, as well as total cholesterol, high density lipoprotein cholesterol, triglycerides, glucose, and creatinine, will be collected. All of the neonates will be tested using UCG.

**Conclusion** This study will provide fully evidence-based scientific information about the prevalence and distribution of CVD and its risk factors. It is useful for the development of CVD prevention and control strategies in China.

### Features of complementary and alternative medicine use by patients with coronary artery disease in Beijing: a cross-sectional study.

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**Objective** Few studies have been conducted to investigate the prevalence, types, attitudes, reasons, as well as associated factors of complementary and alternative medicine (CAM) use in patients diagnosed with coronary artery disease (CAD) in China. Therefore, the aims of the present study were to: (1) determine the prevalence, types, perceived effectiveness, and reasons of CAM use in CAD patients in Beijing; (2) investigate the differences between CAM users and non-CAM users; (3) explore possible different CAM use features between CM and WM hospitals.

**Method** From May to Jul. 2009, 546 out of 600 distributed questionnaires resulted in valid values were included in the present study.

**Result** CAM was used by 69% of the patients with CAD. "Few side effects" (49.6%) was the main reason of CAM use; whereas "doubt of effect" (61.5%) was the main reason for non-use. Patent herbal medicine (90.7%) was the most commonly used type. Compared with the non-CAM use group, CAM users tended to be older, have a longer disease duration and better current health status. In addition, CAM users had significant lower odds for emergency admission and hospitalization within the past one year.

**Conclusion** Patients with CAD from Chinese medicine and Western medicine hospitals differ in CAM use frequency, types, perceived effectiveness, as well as reasons for CAM use or non-CAM use. For a better understanding of features and the prevalence of CAM use, large scale randomized studies are warranted.

### Risk factors for morning blood pressure surge: fasting blood glucose and blood lipid

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**Objective** To investigate risk factors for morning blood pressure surge (MBPS) in outpatients and provide evidences for targeted prevention and treatment.

**Methods** Two hundred and eighty subjects (male, 161; female, 119) aged from 19 to 79 were recruited from persons attending 24-hour ambulatory blood pressure monitoring (ABPM) in Fuwai Hospital (Beijing) from Jan. to Jun. in 2011. They have not been treated by antihypertensive agents. Subjects were divided into morning surge group (MS group) and non-morning surge group (non-MS group) by the highest quartile of morning systolic blood pressure surge (28.4 mm Hg) for further analysis on the relation between hypertension, fasting blood glucose (FBG), blood lipid and exaggerated morning blood pressure surge.

**Result** The baseline characteristics, such as age, body mass index and percentage of gender, were almost similar in both MS group and non-MS group. Systolic blood pressure (SBP), diastolic blood pressure

(DBP) and mean arterial pressure (MAP) and FBG in MS group was respectively  $140.0 \pm 16.4$  mm Hg,  $90.1 \pm 13.7$  mm Hg,  $106.4 \pm 13.0$  mm Hg and  $5.59 \pm 0.85$  mmol/L which were all significantly higher than those in non-MS group (P value was 0.004, 0.049, 0.005 and 0.009, respectively). In addition, the percentage of patients with hypertension was significantly higher in MS group when compared to that in non-MS group (73.9% vs 52.1%,  $P = 0.002$ ). Day-time SBP and MAP in MS group were higher than those in non-MS group while night-time SBP, DBP and MAP were lower in MS group ( $P < 0.05$ ). After adjusting for age, gender, body mass index, hypertension, impaired fasting glucose and higher cholesterol level were independent risk factors for exaggerated morning blood pressure surge and odds ratios were 2.596 (95% CI: 1.392 – 4.841), 2.381 (95% CI: 1.304 – 4.347) and 1.904 (95% CI: 0.866 – 4.190), respectively. After adjusting for age, gender, body mass index, hypertension, impaired fasting glucose and higher low-density lipid-cholesterol level were also independent risk factors for exaggerated morning blood pressure surge and odds ratios were 2.491 (95% CI: 1.332 – 4.661), 2.340 (95% CI: 1.284 – 4.265) and 1.610 (95% CI: 0.874 – 2.963), respectively.

**Conclusion** Impaired fasting glucose and higher blood lipid levels were independent risk factors for exaggerated morning blood pressure surge in outpatients. Therefore, controlling blood pressure, FBG and blood lipid by lifestyle modification and treatment are all beneficial for lowering morning blood pressure surge.

### Effects of home-based exercise programs at the intensity of anaerobic threshold in aged patients with acute myocardial infarction after primary percutaneous coronary intervention

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**Objective** Cardiac rehabilitation program is an essential part of the contemporary care of the patient with cardiovascular disease (CVD). Guidelines for prescribing aerobic exercise for patients with CVD is available elsewhere, except China. The major cause is the safety and the adherence. By the mid-1980s, it was established that post-MI patients could undertake prescribed home aerobic exercise safely and achieve a level of functional improvement similar to that resulting from supervised exercise in traditional CR. To investigate the effects of home-based exercise maintenance programs at the intensity of anaerobic threshold (AT: anaerobic threshold) for exercise tolerance in aged patients with acute myocardial infarction after primary percutaneous coronary intervention.

**Methods** Ninety-seven patients with aged AMI ( $\geq 65$  years of age) who had undergone successful PCI were assigned to either a rehabilitation ( $n = 50$ ) or a control group ( $n = 47$ ), who finished twice cardiopulmonary exercise test (CPET). Patients in rehabilitation group finished their home-based exercise programs at AT intensity for 3 months. The intensity of training was prescribed to obtain their heart rate of AT intensity. Patients monitored their heart rates during exercise and adjusted their exertion levels to achieve the intensity goals. Their every training was written in their exercise list.

**Result** It was feasible and safe to precede sub-maximal CPET in aged patients with AMI after PCI. Their heart rate at AT intensity ( $92 \pm 6$  beat·min<sup>-1</sup>) was lower than their traditional minimal target heart rate ( $103 \pm 8$  beat·min<sup>-1</sup>) and lower than heart rate ( $101 \pm 9$  beat·min<sup>-1</sup>) at ischemic threshold following CPET. Patients in rehabilitation group safely finished

their home-based exercise maintenance programs at AT intensity. The O<sub>2</sub> consumption ( $8.2 \pm 3.9$  to  $12.9 \pm 4.7$  ml·min<sup>-1</sup>·kg<sup>-1</sup>) ( $P = 0.039$ ) and workload ( $25.1 \pm 5.9$  to  $33.7 \pm 6.1$  J·s<sup>-1</sup>) ( $P = 0.027$ ) at AT level and the O<sub>2</sub> consumption ( $13.2 \pm 3.6$  to  $15.1 \pm 2.8$  ml·min<sup>-1</sup>·kg<sup>-1</sup>) ( $P = 0.003$ ) and workload ( $51.7 \pm 11.9$  to  $60.3 \pm 11.8$  J·s<sup>-1</sup>) ( $P = 0.046$ ) at peak level increased after 3 months in rehabilitation group, and the O<sub>2</sub> consumption ( $8.3 \pm 4.7$  to  $9.0 \pm 3.1$  ml·min<sup>-1</sup>·kg<sup>-1</sup>) and workload ( $26.1 \pm 5.7$  to  $26.9 \pm 7.2$  J·s<sup>-1</sup>) at AT level and the O<sub>2</sub> consumption ( $12.6 \pm 4.9$  to  $12.8 \pm 3.7$  ml·min<sup>-1</sup>·kg<sup>-1</sup>) and workload ( $49.1 \pm 14.5$  to  $53.4 \pm 12.6$  J·s<sup>-1</sup>) at peak level had not obvious change after 3 months in control group.

**Conclusion** It was feasible and safe to proceed sub-maximal CPET in aged patients with AMI after PCI. Individually exercise programs at AT intensity in aged AMI patients after successful PCI may be safely finished in home and can improve their exercise cardiopulmonary function.

### Patients with atrial fibrillation and other primary diagnosis in the emergency department: baseline characteristics and outcomes

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**Background** Atrial fibrillation (AF) is common in the emergency department (ED), however, patients with AF sometimes visit ED because of other primary reason. There are no data on the characteristics and outcomes of ED patients with atrial fibrillation who have other primary ED diagnoses.

**Methods** In this prospective observational multicentre registry study, all AF cases were confirmed by the electrocardiograms (ECGs) in the ED from Nov. 2008 to Oct. 2011 in China. Repeat ED visits were excluded. By pulling all patient charts, we separated patients with a primary diagnosis of atrial fibrillation from those with other primary ED diagnoses, using the EPs' first diagnosis written on the ED chart. Patient's demographics, medical history, type of AF, treatment, and outcome of emergency room visit were collected at baseline by the treating physicians using a standardized questionnaire. The main outcome measure was all-cause mortality at 1 year post-ED visit. As a secondary analysis, logistic regression was used to compare 1 year mortality of these patients to those with primary ED diagnoses of atrial fibrillation seen during the same time period.

**Result** During the study period, 2 016 Chinese patients visited the ED, AF was the primary reason only in 825 patients (40.9%), while AF was the secondary diagnosis in the remaining patients. Patients with secondary AF diagnosis were older ( $69.8 \pm 13.1$  vs  $66.6 \pm 13.3$  years) and thinner (BMI,  $23.2 \pm 3.6$  vs  $24.0 \pm 3.5$ ), while systolic blood pressure (SBP) was higher ( $133.8 \pm 24.7$  vs  $129.0 \pm 21.3$ ) and heart rate was lower ( $97.4 \pm 27.1$  vs  $107.9 \pm 31.3$ ). Permanent AF was more frequent (61.2% vs 26.3%) in patients with secondary AF diagnosis and they were less likely to be paroxysmal AF (21.1% vs 44.5%). Meanwhile, the prevalence of risk factors and comorbidities, such as heart failure (49.1% vs 20.5%), coronary artery disease (46.6% vs 35.0%), stroke/TIA (11.7% vs 17.6%), valvular heart disease (19.6% vs 12.5%), and diabetes mellitus (17.2% vs 13.0%) was higher. Similarly, there was an increase in CHADS<sub>2</sub> [cardiac failure, hypertension, age, diabetes, stroke (doubled)] score ( $2.1 \pm 1.4$  vs  $1.4 \pm 1.3$ ), but there was no difference in antithrombotic therapy between two groups. The most common primary



ED diagnoses were congestive heart failure (30.3%), respiratory diseases (7.7%), stroke/TIA (7.6%), dyspnea (7.1%), fever (7.0%), palpitation (6.0%), coronary artery disease (6.0%), dizzy (5.7%), and chest pain not yet diagnosed (5.0%). 1-year mortality were 7.8% and 18.3%, respectively. In the adjusted analysis, an alternative primary ED diagnosis was associated with an increased risk of death (HR = 1.84; 95% CI, 1.38 – 2.46,  $P < 0.001$ ).

**Conclusion** Patients seen in the ED with AF and different primary ED diagnoses are older and have more comorbidities higher than patients with primary ED diagnoses of AF. 1-year mortality was also higher in patients with secondary AF diagnosis. Future studies of AF in the ED should distinguish between these two populations and the potential contribution of AF to mortality in the setting of other primary ED diagnoses.

### Is the CHADS<sub>2</sub> score predicts prognosis in atrial fibrillation patients concomitant with valvular atrial fibrillation

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**Background** We sought to evaluate the prognostic performance of the CHADS<sub>2</sub> score for prediction of death and major adverse events (MAEs) in patients with atrial fibrillation (AF) and valve heart disease (VHD).

**Methods** In China AF registry, we enrolled 2 016 patients with AF, 336 of whom were concomitant with VHD. We calculated the CHADS<sub>2</sub> scores (congestive heart failure, hypertension, age  $\geq 75$ , diabetes mellitus (1 point each), and prior stroke or transient ischemic attack (TIA) (2 points). All patients were followed by 1 year. The primary outcome was death from any reason. The second outcome was the composite adverse events of death, stroke, and non-CNS systemic embolism.

**Result** Of 336 patients with valvular atrial fibrillation (VAF), the mean CHADS<sub>2</sub> score was  $1.5 \pm 1.2$ , which was lower than that in patients with non-valvular atrial fibrillation (NVAF). Compared to patients with low (0-1) CHADS<sub>2</sub> scores, those with intermediate (2 – 3) and high (4, 5 and 6) CHADS<sub>2</sub> scores had an increased rate of death (14.1%, 13.1%, and 23.8%, respectively;  $P = 0.375$ ), but not of MAEs (18.8%, 17.2%, and 33.3%, respectively;  $P = 0.247$ ). The Kaplan-Meier analysis did not reveal a tendency of higher CHADS<sub>2</sub> score toward death (log-rank test,  $P = 0.459$ ), or MAEs (log-rank test,  $P = 0.356$ ). However, after adjustment for reason for Emergency Department (ED) visit, type of AF, tobacco use, and antithrombotic therapy, the CHADS<sub>2</sub> score was not an independent risk factor of death ( $P = 0.692$ ) or MAEs ( $P = 0.507$ ) in VAF patients.

**Conclusion** In patients with VAF, the CHADS<sub>2</sub> score is not related to death or MAEs.

### Body mass index and mortality in patients with atrial fibrillation

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**Background** Obesity is associated with the development of atrial fibrillation (AF) and may impact atrial fibrillation-related outcomes. To date, it's unclear whether body mass index (BMI) predicts death and major adverse events (MAEs) in atrial fibrillation patients.

**Methods** We conducted a prospective, observational registry of patients with AF/atrial flutter in China. Participants were enrolled in the ED. Baseline characteristics were collected and follow-up was planned at 1 year. The primary outcome was death from any cause, and the secondary outcome was major adverse events (MAEs, a composite endpoint of death, stroke, non-CNS system embolism, and major bleeding).

**Result** Of the 2 016 subjects with AF, 162 (9.0%) had a body mass index (BMI) in the underweight category (BMI  $< 18.5 \text{ kg/m}^2$ ), 1 224 (60.7%) were categorized as normal weight (BMI  $18.5$  to  $25.0 \text{ kg/m}^2$ ), 524 (25.7%) patients in overweight group (BMI  $25.0$  to  $30 \text{ kg/m}^2$ ), and 105 (4.6%) subjects met the BMI criteria for obesity ( $\geq 30.0 \text{ kg/m}^2$ ). The rate of death and MAEs were higher in underweight (23.9% and 27.7%) and normal (15.7% and 22.7%) weight patients than overweight (8.1% and 16.1%) and obesity patients (8.6% and 20.0%). On multivariate analysis, BMI stratification was associated with 1-year all-cause mortality ( $P = 0.008$ ). Using underweight patients as reference, the risk of death was significantly lower in overweight (HR = 0.52; 95% CI: 0.33 – 0.84,  $P = 0.007$ ), but not in normal weight (HR = 0.91; 95% CI: 0.62 – 1.32,  $P = 0.616$ ) and obesity patients (HR = 0.57; 95% CI: 0.26 – 1.21,  $P = 0.141$ ). Continuous analyses of BMI also revealed BMI predicted 1-year mortality in patients with AF (HR = 0.94; 95% CI: 0.90 – 0.97,  $P = 0.69$ ) for normal weight, 0.86 (95% CI: 0.58 – 1.27,  $P = 0.438$ ) for overweight, and 1.09 (95% CI 0.63 – 1.89,  $P = 0.753$ ) for obese. As a continuous variate, BMI was also not associated with MAEs (HR = 0.98; 95% CI: 0.95 – 1.01,  $P = 0.139$ ).

**Conclusion** In patients with AF, lower BMI appears to be a risk factor of 1-year mortality.

### Characteristics and antithrombotic treatment of patients with valvular and non-valvular atrial fibrillation in China: data from a multicenter hospital E.R. based prospective registry

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**Background** The real-life clinical characteristics and clinical management of patients with atrial fibrillation (AF) in China is not well established. Studies focusing on this topic relied mainly on foreign samples of patients, scarcely representative of Chinese population group. We aimed at evaluating baseline clinical characteristics and antithrombotic treatment of patients with AF in a large Chinese sample.

**Methods** This prospective registry enrolled patients presenting

to emergency departments with AF or atrial flutter, either as the primary reason for their visit or as a secondary diagnosis on the basis of consecutive fashion at 19 sites in China. Data collected at baseline included demographics, medical history, nature of atrial fibrillation, and treatments initiated at diagnosis. The characteristics and their treatment (whether on anti-platelet treatment or on oral anticoagulation) of patients with valvular AF were compared with those with non-valvular AF.

**Findings** Of 2 016 patients enrolled between Nov. 2008 and Oct. 2011, 336 (16.7%) were patients with valvular AF while 1 678 (83.2%) with non-valvular AF. 618 (30.7%) were patients with paroxysmal AF, 452 (22.4%) with persistent AF, and 452 (22.4%) with permanent AF. Patients with valvular AF were significantly younger and constituted of more females, more likely to have heart failure and permanent pacemaker implanted than those with non-valvular AF. They also had lower BMI and less likely to have coronary heart disease, prior myocardial infarction, hypertension, diabetes mellitus, prior stroke, cognitive deficits, prior COPD. A less frequent use of anti-platelet agents, mainly aspirin, in the valvular AF group was observed compared with non-valvular AF group (43.4% vs 59.5%), on the contrary, a more frequent use of oral anticoagulants in the valvular AF group was observed (41.9% vs 14.0%). 14.7% of patients with valvular AF did not receive either antithrombotic treatment. Further analysis divided 1678 patients with non-valvular AF into CHADS<sub>2</sub> score  $\geq 2$  (n = 903) group and CHADS<sub>2</sub> score  $< 2$  (n = 775) group. 63.1% of patients with CHADS<sub>2</sub> score  $\geq 2$  were on anti-platelet treatment. They were significantly older, more likely to have coronary heart disease, prior myocardial infarction and hypertension compared with those on oral anticoagulant. 14.1% of patients with CHADS<sub>2</sub> score  $\geq 2$  were receiving oral anticoagulant, who were more likely to have prior stroke. The rest 22.8% patients were not treated with either antithrombotic treatment. 53.4% of patients with CHADS<sub>2</sub> score.

**Interpretation** These contemporary registry data on valvular and non-valvular atrial fibrillation in Chinese population indicate that anti-platelet medication or oral anticoagulation remains underutilized according to stroke risk scores. The fact that anti-platelet agents were used more frequently than oral anticoagulant in non-valvular AF may be attributed to the comorbidities of coronary heart disease, hypertension, diabetes mellitus or prior stroke, which are the absolute indications for anti-platelet agents. The reason of insufficient prescription of oral anticoagulation may be concern of bleeding risk when combined with anti-platelet agents.

### Blood pressure reference percentile curves in 2–6 year old children in Shanghai

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**Objective** Children over the age of 3 years who were seen in medical care settings should have their blood pressure (BP) measured at least once during every health care episode according to The US fourth report diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatricians and other health professionals need the criterion of hypertension for age and sex when evaluating children's BP. Although, The criterion of blood pressure has existed in china, few reference of the automated BP recorder can be consult in

preschool children. The aim of this study therefore was to develop blood pressure reference percentile curves representative sample of preschool children in shanghai.

**Methods** We collected data for 4 619 healthy preschool children from 2 to 6 years of age. All these children were live born from Shanghai Minhang Maternal and Child Health Hospital. After each child had rested in the sitting position for 5 min, the blood pressure and heart rate were measured on the right arm at the level of the heart, using automated BP recorder (Model 45NEO-E6, Welch Allyn, USA) All measurements were performed in the clinic room of the hospital. The temperature of the clinic room kept between 20 °C and 25 °C at the time. Children were kept natural posture when BP was measured by trained pediatricians. Centile curves for SBP and DBP were drawn by sex using LMS method, the 5<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup>, 95<sup>th</sup>, 99<sup>th</sup> percentile of SBP and DBP were compared with reference of normal blood pressure and hypertension in Japanese preschool children.

**Result** BP increases linearly with age for both boys and girls. Generally, the means of girls' SBP and DBP show slightly lower than boys (female: 5.55 mm Hg vs 2.05 mm Hg; male: 6.62 mm Hg vs 4.62 mm Hg) respectively. The references of study were significantly differing from the Japanese reference. For example, the SBP 95<sup>th</sup> percentile of current study was significantly lower than Japanese references for boys and girls aged 2 – 6 by 6 – 11 mm Hg. The DBP 95<sup>th</sup> percentiles of boys aged 2 were slightly lower than Japanese reference, however they remained the same levels after from 3 – 6 years old. The percentiles of girls at 2 – 3 years old were lower than the Japanese reference, and exceeded at 3 – 4 years old and kept slightly higher to age of 6. Compared the study population of height and developmental level with the Japanese reference, we found the study children's height were lower than Japanese reference during the age range for both boys and girls (male) 1.16, 3.16, 6.06, 7.54, and 6.3 (female) 1.15, 2.27, 6.68, 8.23, and 7.33).

**Conclusion** This study provides the median, 90<sup>th</sup> and 95<sup>th</sup> percentile reference values of SBP and DBP based on a single large sample of children aged 2 – 6. These reference percentiles may be useful for the early screening and prevention of hypertension in children.

### Influence of regional economic status and healthcare insurance on secondary prevention following coronary artery bypass grafting in China

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**Objective** The present study aims to investigate the influence regional economic status and healthcare insurance on the secondary prevention patterns among patients after coronary artery bypass grafting in China.

**Methods** Data on 47 hospitals distributed in 17 provinces in China and 15 083 patients who underwent isolated CABG and discharged alive during 1 Jan. 2004 and 31 Dec. 2008 were enrolled. Hospitals were categorized as from the east coastal area or from the mid and west hinterland which stands for different economic status in China.

Healthcare insurance and use of discharge medication including aspirin, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs),  $\beta$ -blockers and lipid-lowering were collected and compared.

**Result** 10 of the 47 hospital were from the mid and west hinterland (21.3%), from which 1 854 patients were enrolled (12.3%). 47.8% of these patients got healthcare insurance, and the rate was significantly lower than that from the east area (61.2%;  $P < 0.001$ ). However, the proportion of prescription with more than 2 discharge medications was 59.8% in hinterland and 38.3% in the east ( $P < 0.001$ ). ACEI or ARB (49.1% for the west, 20.5% for the east;  $P < 0.001$ ), and lipid-lowering (40.7% for the west, 32.0% for the east;  $P < 0.001$ ) were prescribed in less than 50% of patients. After multivariable adjustment, hospitals located in the east (adjusted OR = 1.597, 95% CI: 1.426 – 1.788;  $P < 0.001$ ), patients without insurance for healthcare (adjusted OR = 1.206, 95% CI: 1.119 – 1.300;  $P < 0.001$ ) were independent factors for poor performance in evidence-based medication prescription.

**Conclusion** Both variation among regions with different economic status and healthcare insurance have significant influence on the patterns of medication prescription in patients undergoing CABG in China. However, high level of economic status does not correlate to better use of evidence-based medication.

### Hospital characteristics and evidence-based medication discrepancies at discharge among patients undergoing coronary artery bypass grafting in China

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**Objective** Benefit of evidence-based medication after coronary artery bypass grafting (CABG) has been widely confirmed. This study sought to evaluate hospital-based adherence and medication discrepancies at discharge among patients undergoing CABG in China.

**Methods** We studied patients from Chinese Cardiac Surgery Registry who underwent isolated CABG and discharged alive between 1 Jan. 2004 and 31 Dec. 2008. 47 hospitals distributed in 17 provinces and a total of 15 083 patients were analyzed. Hospital characteristics and discharge medication including aspirin, angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blockers (ARBs),  $\beta$ -blockers and lipid-lowering were collected. Treatment was categorized as adherence if patients were prescribed more than either 2 of these medications.

**Result** The proportion was 40.9% for adherence group among all patients. Private hospitals and tertiary hospitals account for 2.13% and 95.7% separately among all participating sites. Compared with non-military hospitals, military hospitals had better adherence (64.6% vs 38.9;  $P < 0.001$ ). Categorized as affiliated hospital to a university or not, non-affiliated hospitals got an adherence rate of 60.1%, higher than that of affiliated hospitals (31.1%;  $P < 0.001$ ). The rate for specialty hospitals and general hospitals was 38.4% and 43.0% ( $P < 0.001$ ), respectively. After multivariable adjusted, non-military hospitals (adjusted OR, 2.716; 95% CI: 2.329 – 3.168), affiliated hospitals (adjusted OR, 2.716; 95% CI : 2.329 – 3.168), and specialty hospitals (adjusted OR = 2.716; 95% CI: 2.329 – 3.168) were independent factors resulting in poor performance in

evidence-based medication prescription.

**Conclusion** The poor use of evidence-based medication at the time of discharge among Chinese patients undergoing CABG is closely correlated to the categories of hospital. Appropriate secondary prevention measures should be taken to improve the performance of hospital adherence.

### Gaps between clinical guidelines and secondary prevention performance after coronary artery bypass grafting in China

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**Objective** Evidence-based medications are recommended by clinical guidelines as significant strategy for secondary prevention following coronary artery bypass grafting (CABG). The gap between clinical guidelines and secondary prevention performance after CABG in China is rarely known.

**Methods** A national analysis was conducted on treatment rates with evidence-based medications from throughout the 2 time periods during 2004 – 2005 and 2007 – 2008. A total of 15 083 patients undergoing isolated CABG and discharging alive from 47 hospitals distributed in 17 provinces were enrolled into the analysis. Use of medication including aspirin,  $\beta$ -blockers, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) and lipid-lowering was investigated and compared with 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery.

**Result** In the time period of 2004 – 2005 and 2007 – 2008, aspirin was prescribed at a percentage of 94.1% and 95.9% ( $P < 0.001$ ), respectively. The use of  $\beta$ -blockers increased from 79.3% to 83.8% ( $P < 0.001$ ). However, prescriptions for ACEI or ARB therapy at hospital discharge covered only 1/4 of the whole population, and decreased from 25.1% to 23.0% between the two periods ( $P = 0.002$ ). 33.0% of patients during 2004 – 2005 and 33.1% during 2007 – 2008 were prescribed with lipid-lowering treatment ( $P = 0.972$ ). In adjusted logistic regression analyses, evidence-based medications were more likely to be prescribed among patients with diabetes ( $P = 0.034$ ), hyperlipidemia ( $P < 0.001$ ), hypertension ( $P < 0.001$ ), and who had undergone prior percutaneous coronary intervention (PCI) ( $P < 0.001$ ). During 2004 – 2005, 40.5% of patients received more than 2 categories of medication at discharge, while the proportion increased slightly to 41.4% during 2007 – 2008 (adjusted OR = 0.917; 95% CI 2.329 – 3.168;  $P = 0.022$ ).

**Conclusion** Although the use of guideline-recommended medications has improved gradually among CABG patients at discharge in China, significant difference exists between the real-world situation and the documented criteria.



## Influence of regional economic status and healthcare insurance on secondary prevention following coronary artery bypass grafting in China

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**Objective** Regional economic status and healthcare insurance may affect clinical strategies. The present study aims to investigate the influence regional economic status and healthcare insurance on the secondary prevention patterns among patients after coronary artery bypass grafting in China.

**Methods** Data on 47 hospitals distributed in 17 provinces in China were abstracted from Chinese Cardiac Surgery Registry. 15 083 patients who underwent isolated CABG and discharged alive during 1 Jan. 2004 and 31 Dec. 2008 were enrolled. Hospitals were categorized as from the east coastal area or from the mid and west hinterland which stands for different economic status in China. Healthcare insurance and use of discharge medication including aspirin, angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blockers (ARBs),  $\beta$ -blockers and lipid-lowering were collected and compared.

**Result** 10 of the 47 hospital were from the mid and west hinterland (21.3%), from which 1 854 patients were enrolled (12.3%). 47.8% of these patients got healthcare insurance, and the rate was significantly lower than that from the east area (61.2%;  $P < 0.001$ ). However, the proportion of prescription with more than 2 discharge medications was 59.8% in hinterland and 38.3% in the east ( $P < 0.001$ ). ACEI or ARB (49.1% for the west, 20.5% for the east;  $P < 0.001$ ), and lipid-lowering (40.7% for the west, 32.0% for the east;  $P < 0.001$ ) were prescribed in less than 50% of patients. After multivariable adjustment, hospitals located in the east [adjusted OR, 1.597, 95% CI, 1.426 – 1.788;  $P < 0.001$ ], patients without insurance for healthcare (adjusted OR 1.206, 95% CI, 1.119 – 1.300;  $P < 0.001$ ) were independent factors for poor performance in evidence-based medication prescription.

**Conclusion** Both variation among regions with different economic status and healthcare insurance have significant influence on the patterns of medication prescription in patients undergoing CABG in China. However, high level of economic status does not correlate to better use of evidence-based medication.

## Association of fasting plasma free fatty acids with plasma lipid levels

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**Objective** Free fatty acids (FFAs) play a key role in providing energy for tissues, particularly in fasting conditions. Increasing evidences suggest that elevated FFA concentrations are related to insulin resistance, and individuals with insulin resistance are at high risk for disordered lipoprotein metabolism, cardiovascular diseases, type 2 diabetes, central obesity, primary hypertriglyceridaemia, nephrotic syndrome and hyperthyroidism. Here, we investigate the association of fasting plasma FFAs with plasma lipid levels for healthy adults.

**Method** A total of 399 healthy Chinese adults ( $54.7 \pm 21.5$  years; Male:Female, 200:199) participated in study, which were after a rigorous physical examination in Zhongnan Hospital of Wuhan University. High performance liquid chromatography (HPLC) was used to determine fasting plasma levels of lauric (C12:0), eicosapentaenoic (C20:5), myristate (C14:0), palmitoleic (C16:1), arachidonic (C20:4), linoleic (C18:2), palmitic (C16:0), oleic (C18:1) and stearate (C18:0). Plasma lipid levels were assayed with commercial kits on an automatic analyzer.

**Result** HDL-C level is related to C16:1, C16:0, C18:1 ( $P < 0.05$ ). LDL-C level is related to C18:2 and C18:0 ( $P < 0.05$ ). TC level is related to C16:0 ( $P < 0.05$ ). TG level is related to C20:4, C18:2, and C18:0 ( $P < 0.05$ ).

**Conclusion** Different plasma FFAs are related to different plasma lipids.

## Short sleep duration is associated with hypertension: a meta-analysis

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**Objective** Growing evidence suggests an association between short sleep duration and hypertension. Elucidation of this association has implications for assessing and managing hypertension. A meta-analysis was performed to access the relationship between duration of sleep and prevalence of hypertension.

**Methods** A systematic search of publications in PubMed, Embase, and the Cochrane Library without language restrictions was performed. Studies were included if they were cross-sectional, involved adult population over 18 years of age, and reported participants' sleep duration, as well as the prevalence of hypertension in different sleep duration categories. Odds ratios (OR) and 95% confidence interval (CI) were pooled using a random effect model. Publication bias was assessed with funnel plots and Egger regression test. The heterogeneity among studies was tested by Q-statistic and I-statistic.

**Result** Overall, 13 studies including 173 301 male and female participants were included and evaluated. In the pooled analysis, short sleep duration was associated with higher prevalence of hypertension (OR: 1.14; 95% CI: 1.07 – 1.22;  $P < 0.001$ ) with no evidence of publication bias ( $P = 0.475$ ), but with significant heterogeneity between

studies ( $I^2 = 64.5\%$ ;  $P = 0.001$ ). The pooled ORs for the subcategories with sleep duration 6 h, 6–7 were 1.35 (95% CI: 1.26–1.44) and 1.07 (95% CI: 1.02–1.11) respectively compared with the subcategory with 7–8 h.

**Conclusion** Short sleep durations are significantly associated with the prevalence of hypertension in adults.

### Type 2 diabetes incidence attributable to abdominal obesity in China

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**Objective** Abdominal obesity, using waist circumference (WC) as indicators, is a strong risk factor for type 2 diabetes and has been increasingly prevalent in economically developing regions of the world. The aim was to estimate type 2 diabetes incidence attributable to abdominal obesity in China.

**Method** We conducted cohort studies: Multicenter Collaborative Study of Cardiovascular Epidemiology and Cardiovascular Health study in China since 1998 and 2000. Data on WC and other risk factors were collected at a baseline examination using a standard protocol. Follow-up evaluation was conducted in 2007 to 2008, with a response rate of 79.8%. We used multivariable-adjusted hazard ratio and prevalence of abdominal obesity in each age group, stratified according to sex, to calculate type 2 diabetes incidences attributable to abdominal obesity.

**Result** There was a significant association between abdominal obesity and incident diabetes in both men and women after adjustment for multiple risk factors ( $P < 0.001$ ). We estimated that 19.3% of type 2 diabetes incidence (95% CI: 14.2%–24.7%) was attributable to abdominal obesity among men and 27.5% (95% CI: 20.5%–34.3%) among women in China.

**Conclusion** Our study documents that abdominal obesity is a major risk factor for incident type 2 diabetes in China. Continued strengthening of national programs and initiatives for abdominal obesity prevention is needed to reduce abdominal obesity-related diabetes in China.

### Real world practice of community-based cardiovascular disease preventive care and practice characteristics in Beijing

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**Objective** To observe the real world practice of community-based cardiovascular disease preventive care and practice characteristics in Beijing and to realize self-confidence and barriers for delivering cardiovascular disease (CVD) preventive interventions recommended by guidelines among general practitioners (GPs). And to analysis the influencing factors and barriers for incorporating of CVD preventive care into practice for GPs.

**Methods** 1. Selection of investigating district/counties: 2 districts and 3 counties were chosen from 4 districts in Beijing by multi-stage cluster random sampling Methods. All the Community Health Service

Centers (CHSCs) with daily outpatient number more than 20 in the selected district/counties were recruited as the study sites. 2. Methods of GPs selection: 50 outpatients (aged 50 years and over) who visiting any selected CHSC during 3-month period were recruited. The survey contents included demographic characteristics, duration of hypertension, measurements and documents of blood pressure, lipid profile and serum glucose levels, medications taking, unhealthy behaviors and acceptance of diagnostic and therapeutic interventions delivered by GPs. 3. General practitioners' survey: 4–6 GPs in each selected CHSC were surveyed by face-to-face interview by trained interviewers by using questionnaires on "Awareness and incorporation of CVD risk factors preventive care and self-evaluation of competency in helping patients preventing CVD". The cross-sectional survey in both patients and GPs were conducted by trained investigators by using unified special questionnaires from Jul. to Sep. 2011.

**Result** In patients with documented coronary heart disease, the medicine taking rate according to medication recommendations of aspirin, ACEI/ARB,  $\beta$ -blockers, lipid-lowering statins was 45%, 19.4%, 13%, 13.1% respectively. The percent of patients managed 100% consistency with the guidelines was less than 2%. The control rates of CVD risk factors for achieving the recommended level were low. The proportion of fully confident about their ability in helping patients prevent CVD and multiple risk factors based on self-reported from GPs were as follows: make patients being adherent with their prescribing medicines (21.5%), helping patients being awareness about the values of risk factors for CVD (20%), urging patients in healthy dietary intake (13.7%), blood pressure (BP) therapy and control to optimal level (10.4%). The most lowest self-reported ability in preventing acute myocardial infarction (AMI) were as successfully preventing AMI events (6.6%), delivering smoking cessation counseling (7%) and weight management counseling (8.5%). Key barriers to implementation of guidelines by GPs were seen as prescribing cost or non-reimbursement (39.7%), poor patient compliance (38.6%), guideline related reasons such as too many guidelines (29.2%), impracticality of guidelines (28.5%), etc; as well as lack of time (23.3%).

**Conclusion** 1. The majority of patients visiting CHSCs were not receiving standardized preventive interventions for CVD and its risk factors recommended by guidelines. The control rate of CVD risk factors were at low levels. 2. GPs in Beijing were lack of self-confidence in delivering CVD preventive care and incorporating CVD prevention guidelines into practice. Many barriers were observed in keeping consistency with guideline recommendations in real practice. Efforts should be directed toward the establishment of sustainable system to effectively disseminate CVD prevention guidelines and improve quality of CVD preventive care at the community-based level, and in the end enhance the effectiveness of CVD prevention and control.

### Investigation of the influence of antidepressant therapy on blood pressure and quality of life in elderly patients both with hypertension and depression

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**Objective** To explore the influence of antidepressant therapy on blood pressure and quality of life in elderly patients both with hypertension and depression.

**Method** A total of 67 elderly patients with hypertension and depression in the department of internal medicine of Xuanwu hospital during Aug.

2008 and Mar. 2011 were randomly divided into two groups based on the antihypertensive therapy: control group (amlodipine 5 mg/d) and therapy group (amlodipine 5 mg/d and cipramil 20 mg/d) for three months. The pretherapy and post-treatment changes in the two groups were compared between 24 h SBP, 24 h DBP, dSBP, dDBP, nSBP, nDBP and scores of the short form (36) health survey.

**Result** After treatment, 24 h SBP ( $128.74 \pm 3.79$  vs  $139.42 \pm 10.19$  mm Hg), 24 h DBP ( $72.10 \pm 7.65$  vs  $78.64 \pm 8.03$  mm Hg), dSBP ( $130.81 \pm 4.50$  vs  $143.39 \pm 12.32$  mm Hg), dDBP ( $76.03 \pm 9.46$  vs  $81.53 \pm 9.20$  mm Hg), nSBP ( $126.94 \pm 3.69$  vs  $136.53 \pm 9.03$  mm Hg), nDBP ( $68.52 \pm 6.89$  vs  $75.44 \pm 7.57$  mm Hg) were much lower in therapy group than the control group ( $P < 0.01$ ). Besides physical functioning of quality of life, the other dimensions were much higher (role physical  $70.84 \pm 9.90$  vs  $62.31 \pm 10.16$ , bodily pain  $74.71 \pm 8.51$  vs  $63.33 \pm 8.48$ , general health  $62.19 \pm 8.39$  vs  $50.64 \pm 7.07$ , vitality  $64.03 \pm 8.26$  vs  $56.11 \pm 6.82$ , social functioning  $70.94 \pm 6.94$  vs  $62.92 \pm 7.46$ , role-emotional  $70.32 \pm 6.93$  vs  $62.14 \pm 8.18$ , mental health  $69.94 \pm 6.44$  vs  $61.69 \pm 8.83$ , total score  $68.70 \pm 3.29$  vs  $60.40 \pm 3.40$ , all  $P < 0.01$ ).

**Conclusion** Besides antihypertensive therapy, antidepressant therapy also should be put more attention in the elderly hypertensive people with depression.

### The relationships between serum uric acid and impaired fasting glucose or diabetes in male

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**Objective** Explore the relationships between serum uric acid and impaired fasting glucose or diabetes in male in order to provide scientific evidence for the prevention and clinical treatment of diabetes.

**Methods** The blood pressure, height, weight and waist circumference were measured and factors such as smoking, alcohol intake, family history of hypertension, etc. were investigated and blood glucose, blood lipid, serum uric acid were tested for 1 168 men aged  $\geq 30$  years who lived in Jinchang district of Suzhou. The concentrations of uric acid were categorized into four levels according to the quartiles of serum uric acid. The relationships between serum uric acid and impaired fasting glucose or diabetes were calculated by multiple logistic models.

**Result** There were 114 participants with impaired fasting glucose, the prevalence was 9.76%; and there were 148 participants with diabetes, the prevalence was 12.67%. The uric acid concentrations in participants with diabetes were higher than that in participants with impaired fasting glucose or normoglycemia. Whether adjusted for other factors or not, the association between uric acid levels and impaired fasting glucose was not significant. Compared to the lowest quartile of serum uric acid, the second, third and fourth quartile could decrease the prevalence of diabetes (OR = 0.236 – 0.458,  $P < 0.05$ ). And the prevalence of diabetes decreased along with the increasing of uric acid levels ( $P$  trend  $< 0.001$ ).

**Conclusion** The prevalence of diabetes decreased along with the increasing of uric acid levels in male.

### Circulating adipocyte–fatty acid binding protein levels and clinical significance in patients with coronary heart disease

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**Objective** The aim of the study is to investigate the changes of circulating A-FABP levels in patients with CHD, to study the variation of A-FABP in genders and its relationship with Gensini scores, and to define the A-FABP as a risk factor of CHD and the association with severity of coronary artery stenosis.

**Methods** A total of 102 subjects were recruited from the first affiliated hospital of the university of South China, who underwent the coronary angiography (CAG) during 2010 to 2012. Based on the CAG, the subjects were divided into following groups: non-CHD of 35 cases and CHD group of 67 cases. According to clinical presentation, ECG and the serological markers, CHD group was further classified into two subgroups: 28 cases of stable angina pectoris (SAP) group and 39 cases of acute myocardial infarction (AMI) group. According to the coronary artery lesion, all subjects can be divided into four groups: non-CHD group (35 cases), CHD single-vessel lesion group (26 cases), CHD double-vessel lesions group (20 cases), and CHD triple-vessel lesions group (21 cases). The quantitative assessment of the severity of coronary artery lesion was made in line with Gensini scores. The severity of coronary artery stenosis was assessed by the number of coronary artery lesion and the sum of the Gensini scores. According to the median level of A-FABP ( $P_{50} = 24.79$  ng/mL), all subjects can be divided into two groups: A-FABP of A group is  $< 24.79$  ng/mL, A-FABP of B group is  $\geq 24.79$  ng/mL. The A-FABP levels were determined by enzyme-linked immunosorbent assay (ELISA). The levels of CK, CK-MB, cTnT, ESR, hs-CRP, TG, TC, LDL-C, HDL-C, and FPG were also detected. Gensini score was calculated and the correlation between A-FABP, serological markers and clinical presentation, severity of coronary artery disease were analyzed. The SPSS 18.0 software was used for data analysis.

**Result** There was no statistically significant difference in A-FABP levels between CHD group and non-CHD group ( $26.60 \pm 2.62$  ng/mL vs  $24.27 \pm 3.14$  ng/mL,  $P > 0.05$ ). The A-FABP levels in AMI group were higher compared with SAP group ( $30.57 \pm 3.14$  ng/mL vs  $24.27 \pm 2.69$  ng/mL,  $P < 0.05$ ) and non-CHD group ( $30.57 \pm 3.14$  ng/mL vs  $24.27 \pm 3.14$  ng/mL,  $P < 0.05$ ). The risk rate of suffering from AMI for patients with A-FABP  $\geq 24.79$  ng/mL is 2.541 times as much as that for patients with A-FABP  $< 24.79$  ng/mL. In the non-CHD group, females had higher A-FABP levels compared with males ( $31.20 \pm 2.80$  vs  $21.04 \pm 2.21$  ng/mL,  $P < 0.05$ ); in the CHD group, A-FABP levels were more closely associated with Gensini scores in females than in males ( $R = 0.504$ ,  $P < 0.05$  vs  $R = 0.319$ ,  $P < 0.05$ ). The A-FABP levels in CHD triple-vessel lesions group were higher than non-CHD group ( $31.46 \pm 1.94$  vs  $24.27 \pm 3.14$  ng/mL,  $P < 0.05$ ) and CHD single-vessel lesion group ( $31.46 \pm 1.94$  vs  $23.07 \pm 1.72$  ng/mL,  $P < 0.05$ ). The A-FABP levels were positively correlated with cTnT ( $R = 0.328$ ,  $P < 0.05$ ), hs-CRP ( $R = 0.389$ ,  $P < 0.05$ ), involved coronary artery branches ( $R = 0.386$ ,  $P < 0.05$ ) and the Gensini scores ( $R = 0.280$ ,  $P < 0.05$ ).

**Conclusion** The A-FABP levels may contribute to CHD risk stratification. The A-FABP levels in female may become one independent risk factor for CHD. The A-FABP levels may predict the severity of CHD.



## Genome-wide linkage and positional candidate gene study of renal function in Chinese: the GenSalt study

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**Objective** The heritability of renal function has been established. However, our understanding of the genomic mechanisms underlying these traits remains limited. We performed a genome-wide linkage scan and positional candidate gene analysis to identify genetic determinants of estimated glomerular filtration rate (eGFR) and serum creatinine among the participants of the GenSalt study.

**Method** The GenSalt study was conducted among 3142 participants from 633 Chinese families. The eGFR was estimated based on gender, age, and serum creatinine, using the Modification of Diet in Renal Disease (MDRD) equation. The eGFR and serum creatinine phenotypes were inverse-normal transformed, adjusted for age, gender, field center, body mass index, systolic blood pressure, glucose and smoking status in all analyses. Multipoint quantitative trait linkage-analysis was performed using SOLAR software. A systematic literature search was used to identify candidate genes for renal function phenotypes under the linkage peaks (LOD > 2). The additive associations between single SNPs in the candidate genes and the phenotypes were assessed using a mixed linear regression model to account for familial correlations.

**Result** Suggestive linkage signals were identified for eGFR at 12p13.33 - 12p13.2 and 20q13.13 - 20q13.2, with maximum multipoint LOD scores of 3.2 and 2.2, respectively. For serum creatinine, we observed suggestive linkage signals at 6p12.3 and 12p13.33 - 12p13.31, with maximum multipoint LOD scores of 2.2 and 2.7, respectively. The strongest association signal for both eGFR and creatinine was found for marker rs10744670, located in the 3' flanking region of the KCNA1 gene at 12p13.32 ( $P = 4.4 \times 10^{-4}$  and  $6.2 \times 10^{-4}$ , respectively). KCNA1 encodes a voltage-gated potassium channel that is involved in magnesium reabsorption in the kidney.

**Conclusion** Linkage regions on chromosomes 6, 12 and 20 may harbor susceptibility loci for renal function. In addition, the marker near KCNA1 showed consistent associations with eGFR and creatinine.

## Basic Cardiovascular Medicine

### Protective effect of hydrogen sulfide on myocardial ischemia reperfusion injury in rats

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**Objective** To explore the effects and function mechanism of hydrogen sulfide on myocardial ischemia reperfusion arrhythmia in Rats.

**Method** We used sodium hydrosulfide (NaHS) as the donor of H<sub>2</sub>S, SD rats were randomly divided into sham group, myocardial ischemia reperfusion group (IR group), IR+NaHS group, and IR+NaHS+glibenclamide group. We monitor the hemodynamics of rats, including heart rate, arterial pressure, left ventricular pressure, et al. We also observe the rate of ventricular arrhythmia in each group.

**Result** H<sub>2</sub>S can significantly reduce rats' heart rate, arterial pressure and left ventricular pressure. Its also reduces the rate of ventricular arrhythmia in myocardial ischemia reperfusion rats (H<sub>2</sub>S 66.5% vs I/R 33.5%,  $P < 0.05$ ; H<sub>2</sub>S  $2.6 \pm 0.7$  vs I/R  $4.3 \pm 0.9$ ,  $P < 0.05$ ). The KATP Channel Blocker glibenclamide can weaken the H<sub>2</sub>S' antiarrhythmic effects (H<sub>2</sub>S  $2.6 \pm 0.7$  vs H<sub>2</sub>S+GLI  $4.1 \pm 0.7$ ,  $P < 0.05$ ).

**Conclusion** H<sub>2</sub>S possesses protective effect against myocardial ischemia reperfusion. The function mechanism may be associated with the KATP signal transduction pathway in cells.

### Effect of delayed remote ischemic preconditioning on the mitochondrial microRNA-181c level in isolated perfused rat hearts

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**Aim** Although delayed remote ischemic preconditioning (DRIPC) has been proved effective in cardioprotection in various animal and human studies, limited data concerning the underlying mechanisms has been reported. Mitochondrial microRNA-181c (miR-181c) has been found to confer cardioprotective potential. Hence, this study was designed to investigate this effect on the mitochondrial miR-181c level in isolated perfused rat hearts.

**Method** Isolated rat hearts were perfused with 95% oxygen oxygenated Krebs – Henseleit buffer solution (KHBs) in a Langendorff apparatus. After 30-min balanced perfusion, hearts were subjected to 30 min ischemia followed by 60 min reperfusion except a total of 90-min perfusion for control (ischemia/reperfusion, I/R). DRIPC was conducted with 4 cycles 5-min occlusion/5-min reflow at the unilateral hindlimb one day before heart isolation. Heart rate (HR), left ventricular developed pressure (LVDP), and maximum LVDP increase (+dp/dt) and decrease

(-dp/dt) rate were continuously collected. Infarct size and cardiac troponin I levels was measured. The total RNAs was extracted in isolated mitochondrial pellet. The expression of miR-181c was detected by real-time reverse transcription polymerase chain reaction using TaqMan method.

**Result** DRIPC improved the recovery of heart function (HR, LVDP, ± dp/dt), and reduced the release of cTnI ( $P < 0.05$ ). DRIPC limited the infarct size caused by ischemic reperfusion injury ( $22.34 \pm 4.02\%$  vs  $33.50 \pm 4.55\%$ ,  $P < 0.001$ ). Compared with control, I/R did not affect the miR-181c level ( $6.21 \pm 4.87$  vs  $4.61 \pm 0.63$ ,  $P > 0.05$ ). However, DRIPC significantly increased this level ( $9.16 \pm 2.68$  vs  $4.61 \pm 0.63$ ,  $P < 0.05$ ).

**Conclusion** DRIPC offers cardioprotective effect and increases the mitochondrial miR-181c level.

### The role of p66shc adapter protein in cardiac mitochondrial damage in selenium deficiency rats

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**Objective** To study the expression of p66shc adapter protein in selenium deficiency rat hearts, and its effect on the cardiac mitochondria.

**Methods** Twenty male Sprague-Dawley rats were randomized into normal control group ( $n = 8$ ) and selenium deficiency model group ( $n = 12$ ). When rats were fed for twenty weeks, the cardiac function was measured by hemodynamic studies. The cardiac mitochondrial structure was observed under electron microscopy, and the mitochondrial stereological parameters including surface density (Sv), volume density (Vv) and specific surface (Rsv, surface-to-volume ratio) were further studied. The protein expression of p66shc in the whole myocardium and mitochondrial fraction was measured using western-blot.

**Result** Compared with the control group, the rats in the model group had reduced systolic and diastolic function. Under electron microscopic observation, the cardiac mitochondria in the model group were swelling with fractured or dissolved cristae. Further stereological study showed that notable decreases in Sv and Rsv, and remarkable increase in Vv in the selenium deficiency rat hearts compared with the control group ( $P < 0.05$ ). The protein expression of phosphorylated p66shc in the whole myocardium and total p66shc in the cardiac mitochondria were both significantly increased in the model group compared with the control group ( $P < 0.05$ ). Pearson linear correlation analysis showed that the protein expression of total p66shc in the cardiac mitochondria had positive correlation with Vv, and negative correlations with Sv and Rsv ( $P < 0.01$ ).

**Conclusion** Selenium deficiency may increase the protein expression of total p66shc in the cardiac mitochondria, which may result in cardiac mitochondrial injury and the ultimate progress of heart failure.

### The dynamic change of mitochondrial cytochrome c is involved in myocardial cell Apoptosis in selenium deficiency rat hearts

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**Objective** To study the protein expression of cytochrome c in

cardiac mitochondria in selenium deficiency rats and its effect on myocardial cell apoptosis.

**Methods** Thirty-six rats were randomized into normal control group (n = 18) and selenium deficiency model group (n = 18). When rats were fed for 20 weeks, 30 weeks and 40 weeks respectively, the cardiac function was detected by carotid artery intubation. At the corresponding time points, the alterations of cardiac mitochondria were observed under the electron microscopy, and the myocardial cell apoptosis rate was detected by immunohistochemistry (SP method). The cardiac mitochondria were extracted from the rats at the corresponding time points for detecting the protein expression of cytochrome c by western-blot.

**Result** Compared with the corresponding control group, the cardiac function in the model group was significantly decreased ( $P < 0.05$ ). Morphometric analysis showed that cardiac mitochondria in the model group were notable swelling with fractured or dissolved cristae. Myocardial cell apoptosis rates were significantly increased in the model group compared with the corresponding control group, and the increases were greater as the time extension of selenium deficiency ( $P < 0.05$ ). The protein expression of cytochrome c in the cardiac mitochondria of selenium deficiency rats was significantly decreased compared with the corresponding control group, and the decreases were greater as the time of selenium deficiency prolonged ( $P < 0.05$ ). Pearson linear correlation analysis showed that the protein expression of mitochondrial cytochrome c had a negative correlation with myocardial cell apoptosis rate ( $r = -0.858$ ,  $P < 0.01$ ).

**Conclusion** Selenium deficiency can down-regulate the protein expression of cytochrome c in the cardiac mitochondria, which is involved in mitochondria-mediated myocardial cell apoptosis.

### Quantitative analysis of mitochondrial DNA deletions in patients with viral myocarditis and dilated cardiomyopathy

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**Objective** To study the mitochondrial DNA (mtDNA) deletions in myocardial biopsy samples from the patients with viral myocarditis (VMC) and dilated cardiomyopathy (DCM), and the relation between mtDNA deletions and peripheral lymphocytes.

**Method** mtDNA4977 base pair (mtDNA4977) and mtDNA7436 base pair (mtDNA7436) deletion rates of myocytes and lymphocytes were measured by the method of quantitative PCR in VMC patients (n = 20), DCM patients (n = 12) and control bases (12 myocardial samples from the healthy cases died of accident, and 23 blood samples of lymphocytes from the blood donors).

**Result** mtDNA4977 and mtDNA7436 deletions were observed in both controls (0.175%) and patients with VMC (0.385%) and DCM (3.004%). The severity of mtDNA deletions in VMC and DCM cases were 1.2 and 16.2 fold higher than in normal subjects respectively. mtDNA deletion rates in patients with DCM were 6.8 fold higher than that in patients with VMC ( $P < 0.05$ ). The degree of mtDNA deletions in peripheral lymphocyte was similar with that in myocardium, and also showed good correlation with that in myocardium ( $r = 0.960$ ,  $P < 0.001$ ).

**Conclusion** mtDNA deletions in myocardium might play an important role in the pathogenesis of VMC as well as its development to DCM. The value of peripheral lymphocyte in the study of myocardial mtDNA deletion needs to be further investigated.

### Quantitative analysis of mitochondrial proliferation and loss of mitochondrial membrane phospholipids in lymphocytes from patients with viral myocardial disease

Jin Wei, Ming Zhang, Hu Shan, Lin Lin

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**Objective** To study the degrees of mitochondrial proliferation and loss of mitochondrial membrane phospholipids in peripheral blood lymphocytes from the patients with viral myocardial disease and their relations to cardiac function.

**Method** Mitochondrial proliferation and loss of mitochondrial membrane phospholipids in peripheral blood lymphocytes from patients with viral myocardial disease (50 with viral myocarditis and 33 with dilated cardiomyopathy) were studied using Dermer's tricomplex flocculation technique under the electron microscope. And the severity of mitochondrial proliferation and loss of mitochondrial membrane phospholipids in peripheral blood lymphocytes was further analyzed according to NYHA cardiac function. 23 healthy blood donors were selected as the controls.

**Result** The levels of the mitochondrial proliferation and the loss of mitochondrial membrane phospholipids in peripheral blood lymphocytes were significantly increased in patients with viral myocardial disease compared with those in the controls. The mitochondrial proliferation and the loss of mitochondrial membrane phospholipids in patients with normal cardiac function were different from those in the controls and showed positive relations to the severity of cardiac function.

**Conclusion** The impairment of mitochondrial membrane phospholipids in peripheral blood lymphocytes might play an important role in the pathogenesis of viral myocardial disease.

### The deletion of mitochondrial DNA in patients with viral myocardial disease and its relation to cardiac function

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**Objective** To study the mitochondrial DNA (mtDNA) deletion rate in peripheral blood lymphocytes in patients with viral myocardial disease, and its relation to cardiac function.

**Methods** 83 patients with viral myocardial disease including viral myocarditis (n = 50) and dilated cardiomyopathy (n = 33), and 23 blood donors as the control cases were selected to be investigated. mtDNA 4977 base pair (mtDNA4977) and mtDNA 7436 base pair (mtDNA7436) deletion rates in peripheral blood lymphocytes were measured by the method of quantitative polymerase chain reaction (qPCR). Correlation analysis was used to study the relation between the mtDNA deletion rate and cardiac function.

**Result** mtDNA4977 and mtDNA7436 deletions were observed in all groups. The mtDNA deletion rates in viral myocarditis and dilated cardiomyopathy were both significantly increased compared with the control values ( $P < 0.001$ ). The degree of mtDNA deletion rate showed well accordance with the severity of cardiac function, which was (0.145 ± 0.090)% in patients with NYHA class I and increased to (3.451 ± 1.214)% in patients with NYHA class IV. mtDNA deletion rate had



positive correlations with NYHA classification, cardiothoracic ratio, and the diameters of left atrium and ventricle. And the correlation coefficients of mtDNA4977 and mtDNA7436 deletion rates with left ventricular ejection were -0.681 and -0.675 respectively (both  $P < 0.05$ ).

**Conclusion** The degree of mtDNA deletion in patients with viral myocardial disease is closely related to the impairment of cardiac function, which might play an important role in the pathogenesis of viral myocardial disease.

### Vasoprotective effect of the combination of amlodipine and atorvastatin in salt-sensitive hypertension

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**Objective** Current treatment for the secondary prevention of cardiovascular (CV) diseases frequently requires the prescription of several concomitant agents, particularly antihypertensives and the HMG-CoA reductase inhibitors, statins. We have previously shown that in salt-sensitive (SS) hypertension either the statin atorvastatin (AT) or the calcium channel blocker amlodipine (Aml) are endowed with vasoprotective effects. Here, we investigated in Dahl (DS) SS rats the effect of combination therapy of Aml and AT on aortic endothelial function, superoxide ( $O_2^-$ ) production, and the expression of endothelial nitric oxide synthases (eNOS), and the proinflammatory/proatherogenic genes monocyte chemoattractant protein-1 (MCP-1) and lectin-like oxidized LDL receptor-1 (LOX-1).

**Method** Groups of DS rats were fed either a normal (NS, 0.5% NaCl) or a high (HS, 4% NaCl) salt diet for 6 weeks. In addition, 3 separate groups of HS rats were given AT (15 mg/kg/day), Aml (5 mg/kg/day) or combination AT (15 mg/kg/day)/Aml (5 mg/kg/day). Systolic blood pressure (SBP) was measured by tail-cuff method; endothelium-dependent relaxation (EDR) to acetylcholine or endothelin (ET) 1-induced vasoconstriction was determined by using organ chamber bath, superoxide ( $O_2^-$ ) production in aorta rings by lucigenin chemiluminescence, the protein expression of eNOS and proinflammatory cytokines MCP1 and LOX1 by Western blot.

**Result** HS rats developed hypertension ( $207 \pm 7$  mm Hg vs  $153 \pm 4$  mm Hg in NS rats,  $P < 0.05$ ) aortic (25%) and cardiac (30%) hypertrophy, accompanied by upregulation of MCP-1 (80%) and LOX-1 (45%), downregulation of eNOS phosphorylation in the aorta, increased plasma C-reactive protein (CRP) level, and aortic  $O_2^-$  (230%), and impaired EDR to acetylcholine ( $E_{max} 64 \pm 9$  vs  $96 \pm 4\%$  in NS rats,  $P < 0.05$ ) and ET1-induced vasoconstriction. Aml reduced SBP, aortic hypertrophy, plasma CRP, vascular  $O_2^-$ , and MCP-1 expression and improved EDR. AT reduced aortic hypertrophy and plasma CRP, improved EDR, eNOS phosphorylation (Ser1179), normalized vascular  $O_2^-$ , MCP-1 and LOX-1 despite only a 10% reduction in SBP. Combination therapy further reduced SBP, normalized aortic hypertrophy, eNOS phosphorylation, EDR, and plasma CRP.

**Conclusion** The present study has provided evidences to support clinical data suggesting that combination with amlodipine

and atorvastatin has synergistic effects on cardiovascular system and preventing end-organ damage. Complementary mechanisms of action by two appear to facilitate the increased beneficial effects. Our findings may provide the scientific basis for the combination therapy of statin with antihypertensive agents to reduce and prevent cardiovascular events and atherosclerotic diseases.

### Analysis of SCN5A mutation in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia

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**Aim** Arrhythmogenic right ventricular cardiomyopathy/Dysplasia (ARVC/D) is a genetically determined disorder, characterized by the two components: cardiomyopathy and arrhythmia. To date, the molecular pathogenesis underlying this phenomenon is poorly understood. Whether the ion channel defect involved in the ARVC/D is unknown. The aim of this study was systematically evaluate the sodium channel variants in ARVC/D.

**Method** The patients according to the diagnostic guideline of ARVC/D revised in 2010 were collected. Genomic DNA was extracted from peripheral blood lymphocytes. All the exons and exon-intron boundaries of the SCN5A gene and desmosomal genes known to be associated with ARVC/D, including DSC2, DSG2, DSP, JUP and PKP2 were sequenced through the direct DNA sequencing.

**Result** A total of 13 unrelated index patients were collected. A new missense heterozygote mutation I137M in SCN5A gene was found in one proband 5. The mutation sited at the exon 4 of the SCN5A and the S1 segment in Domain I of Nav1.5, consisted of an C-to-G substitution at nucleotide site 411 (c.411C > G), which predicted a substitution of isoleucine for methionine at codon site 137 (P. Ile137Met, I137M). I137M was not detected in the 400 healthy control chromosomes from individuals of the same ethnic background, which indicated that this mutation was a conservative site in SCN5A gene and the encoding protein - Nav1.5 may have a functional defect.

**Conclusion** Our study for the first time systematically evaluates the sodium channel variants in patients with ARVC/D and find a new SCN5A mutation - I137M. The result increases the insight of genetic pathogenesis in ARVC/D. The mutational sodium channel may destroy the "desmosomal-related complex" and cause the genesis of ARVC/D.

### Paracrine action of MSCs in mouse infarcted hearts

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**Background** Mesenchymal stem cells (MSCs) have recently been demonstrated as a promising stem cell type to rescue damaged myocardium after acute infarction. One of the most important mechanisms underlying their therapeutic effects is the secretion of paracrine factors. However, the expression profile of paracrine factors of MSCs in infarcted hearts, especially at single cell level, is poorly defined.

**Aim** We aimed to depict the transcriptional profile of paracrine factors secreted by MSCs *in vivo*, with particular interest in the comparison between normal and infarcted hearts.

**Result** MSCs were isolated and injected into mice hearts immediately after infarction surgery. Bioluminescence imaging indicated a proportion of cells still alive even up to 12 days post surgery. Paralleled with survived cells, cardiac function was significantly improved after MSCs injection compared to that in PBS-injected mice, indicated by echocardiography and MRI. Despite increased number of vessels in MSCs-injected hearts, endothelial cells and cardiomyocytes transdifferentiation were rarely observed in infarcted hearts 5 days after infarction. Furthermore, laser capture microdissection followed by high through-put real time PCR was employed in our study, uncovering that the injected MSCs, compared to local cardiomyocytes, displayed elevated levels of secreted factors. To further investigate the regulation of those factors, we performed single cell analysis to dissect the gene expression profile of 48 MSCs in infarcted and normal hearts, respectively. Consistent with the *in vivo* observation, a similar regulation pattern of those factors was detected in cultured MSCs.

**Conclusion** Our study, for the first time, elucidated gene expression profiles, as well as regulation of paracrine factors, of MSCs at single cell level *in vivo*, indicating that paracrine factors from MSCs account for the improvement of cardiac function after infarction.

### The effect of different chemical compounds on rescuing nonsense mutations of HERG gene associated with LQT syndrome

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**Objective** It is known that aminoglycosides can promote readthrough of nonsense codons to produce full-length proteins in many genetic diseases caused by nonsense mutation. Recently, PTC124 with low toxicity has been indicated as a new compound for the treatment of nonsense mutations. The purpose of this study was to explore the effect of three different aminoglycosides sharing a 4, 6-disubstituted ring and PTC124 on rescuing nonsense mutations of HERG gene associated with LQT2 syndrome.

**Methods** Cultured human embryonic kidney cells (HEK293) were transiently transfected with equal amount of WT or HERG nonsense mutant cDNAs. Pharmacological rescue of different compounds was studied by adding G418, gentamicin, tobramycin or PTC124 into Dulbecco's modified Eagle's culture medium (DMEM) for 24 hours. Western blot was performed to evaluate the protein expression of WT or mutant HERG genes with and without drugs. Patch clamp was used to test the function of I<sub>Kr</sub> before and after adding drugs.

**Result** We found that G418 promoted significant level of readthrough with R1014X nonsense mutation in a dose-dependent manner (0 vs 14.26% ± 1.9%, 25.36% ± 1.89%, 39.07% ± 4.11%,  $P < 0.05$ ). In spite of the lower maximal level of readthrough induced by gentamicin, the overall pattern was similar to G418 (0 vs 11.75% ± 1.2%, 18.57% ± 4.28%, 14.68% ± 1.84%,  $P < 0.05$ ). PTC124 could slightly induced readthrough of R1014X nonsense mutant. However, tobramycin was unable to show a significant readthrough effect on the expression of R1014X. The readthrough effects of G418, gentamicin and PTC124 on the expression of W927X, R863X and E698X HERG mutants were

also tested. The Result showed that as the mutation site more close to N-terminal, the rescue efficiency was deprived with these compounds.

**Conclusion** These Result indicate that chemical compounds can induce different patterns of read-through effect on nonsense mutations of HERG gene. And the site of mutations influenced the rescuing efficiency of them.

### Attenuating effect of estrogen on furazolidone induced cardiomyocyte apoptosis is dependent on p66shc adapter protein

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**Objective** To study the role of p66shc adapter protein in the cardiomyocyte apoptosis induced by furazolidone, and the pretreatment effect of estrogen.

**Methods** Neonatal rat cardiomyocytes were prepared from 1 to 2 days old Sprague-Dawley rats, and were randomly divided into normal control group, furazolidone treated groups, and the group treated with estrogen and furazolidone. The cell viability was measured by MTT. The level of reactive oxygen species (ROS) and cell apoptosis rate were measured by flow cytometry. Mitochondrial membrane potential (MMP) was measured using a fluorescence microplate reader, and the protein expression of phosphorylated and total p66shc was detected using western blot.

**Result** When cardiomyocytes were stimulated with furazolidone from 6.25 μM to 100 μM for 48 h, cell viabilities and MMP levels were gradually decreased, and the levels of ROS in the whole cells and the cell apoptosis rates were both increased ( $P < 0.05$ ). The protein expression of phosphorylated p66shc in the whole cell lysates and total p66shc in the mitochondria were both increased in a dose-dependent manner when cardiomyocytes were exposed to 6.25 – 100 μM furazolidone for 24 h ( $P < 0.05$ ). When cardiomyocytes were stimulated with 50 μM furazolidone, the pretreatment of estrogen could significantly attenuate the cardiomyocyte injury induced by furazolidone, and down-regulate the protein expression of phosphorylated p66shc in the whole cell lysates and total p66shc in the mitochondria ( $P < 0.05$ ).

**Conclusion** Estrogen could attenuate furazolidone induced cardiomyocyte injury through down-regulating the protein expression of p66shc.

### Relationship between ischemia duration and expression of heat shock protein 70 in ischemia-reperfusion canine hearts

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**Background** Heat shock protein 70 (HSP70) has been shown to exert a protective effect in hearts subjected to ischemia-reperfusion and alleviate adverse effects of myocardial ischemia-reperfusion injury (MIRI). However, little is known about the influence of ischemia time on HSP70 expression. The effects of ischemic duration on the content of HSP70 transcripts in ischemia-reperfusion myocardium were

investigated in this article.

**Methods** Male mongrel dogs underwent a 15- or 60-min occlusion of the left anterior descending coronary artery, followed by a 120-min reperfusion. Additionally, a sham-operation group was assigned. The animals were killed after 120-min reperfusion and the heart was quickly removed. The myocardium was examined pathologically by electron microscopy. HSP70 mRNA expression both in intact and ischemic myocardium was measured by a semiquantitative reverse transcriptase-polymerase chain reaction (RT-PCR) method using complementary DNA normalized against the housekeeping gene  $\beta$ -actin.

**Result** (1) No ultrastructural changes of microvessels and myocardial cells except a slight loss of mitochondrial granules were noted in reperfusion myocardium from dogs of 15-min ischemia group. In 60-min ischemia group, endothelial cells of capillaries were slightly swelling, and the intercellular linking gaps of endothelial cells slightly widened. As for myocardial cells, intercellular, intermyofibrillar, and intermyofibrillar edema were present. Besides, the fractures of a few myofilaments, the granule loss and swelling of mitochondria were also seen. (2) HSP70 mRNA expression level in both ischemia-reperfusion zone and intact myocardium in 15-min ischemia group was markedly higher than in sham-operation group ( $36.2 \pm 6.5$  vs  $22.0 \pm 4.0$ ,  $P = 0.005$ ;  $29.8 \pm 4.5$  vs  $22.2 \pm 4.7$ ,  $P = 0.050$ ). Compared with sham-operation group, however, no changes in mRNA HSP70 levels in 60 min ischemia group ( $25.7 \pm 7.5$  vs  $22.0 \pm 4.0$ ,  $P = 0.681$ ;  $28.5 \pm 4.7$  vs  $22.2 \pm 4.7$ ,  $P = 0.118$ ) were seen. The ratio of HSP70 mRNA expression content in ischemia-reperfusion zone to that in intact myocardium in 15-min ischemia group was not significantly different from sham-operation group ( $1.22 \pm 0.16$  vs  $1.01 \pm 0.22$ ,  $P = 0.233$ ), but remarkably higher than 60-min ischemia group ( $1.22 \pm 0.16$  vs  $0.89 \pm 0.17$ ,  $P = 0.019$ ).

**Conclusion** The change of HSP70 expression in ischemia-reperfusion myocardium is associated with ischemia time, that is, short duration ischemia promotes HSP70 expression, whereas long time ischemia does not. Furthermore, the HSP 70 expression changes consist with the protective extent of myocardial ultrastructures.

### Identification of novel pre-translational regulatory mechanisms for NF- $\kappa$ B activation

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NF- $\kappa$ B controlled transcriptional regulation plays a central role in inflammatory and immune responses. Currently understanding about NF- $\kappa$ B activation mechanism emphasizes I $\kappa$ B-tethered complex inactivation in the cytoplasm. In the case of NF- $\kappa$ B activation, I $\kappa$ B phosphorylation leads to its degradation followed by NF- $\kappa$ B relocating to the nuclear and trans-activation of NF- $\kappa$ B targeted genes. Pre-translational mechanism mediated NF- $\kappa$ B activation remains poorly understood. In this study, we investigated NF- $\kappa$ B pre-translational regulation by performing a series of data-base mining analysis and using

six large national experimental data-bases; NCBI Unigene EST profile database, Gene Expression Omnibus (GEO) database, Transcription Element Search System (TESS) database, AceView database and Epigenomics databases, and TargetScan software. We reported the following findings: 1) NF- $\kappa$ B signaling genes are differentially expressed in human and mouse tissues; 2) Heart and vessels are the inflammation privilege tissues and less easy to be inflamed because lacking of key NF- $\kappa$ B signaling molecular expression; 3) NF- $\kappa$ B signaling genes are induced by cardiovascular disease risk factors oxidized-phospholipids and pro-inflammatory cytokines in endothelial cells; 4) Transcription factors C/EBPs and NF- $\kappa$ B have higher binding site frequencies in the promoters of Pro-inflammatory cytokine-induced NF- $\kappa$ B genes; 5) Most NF- $\kappa$ B signaling genes have multiple alternative promoters and alternatively spliced isoforms; 6) NF- $\kappa$ B family genes can be regulated by DNA methylation; 7) 27 out of 38 NF- $\kappa$ B signaling gene can be regulated by microRNAs. Our findings provide important insight into the mechanism of NF- $\kappa$ B activation, which may contribute to cardiovascular disease, inflammatory diseases and immunological disorders.

### Caspase-1 promotes endothelial progenitor cells (EPC) undergo pyroptosis and weakens EPC's angiogenesis after myocardial infarction

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We examined an important question whether endothelial progenitor cells (EPCs) have caspase-1 pathway, which can sense dyslipidemia, a risk factor for cardiovascular disease, as a metabolic danger-associated molecular pattern (DAMP), and activate EPC death and weaken EPC repairing. Using techniques including immunological, biochemical, gene deficient mice, cell therapy, and myocardial infarction model, we have made the following findings: 1) Dyslipidemia induces the decrease of mouse EPC numbers and promotes EPC undergo inflammatory cell death (Pyroptosis); 2) Stimulation with proatherogenic oxidation product, oxidized low density lipoprotein (oxLDL), decreases mouse EPC numbers and promotes EPC undergo pyroptosis; 3) Caspase-1 activation inhibits vascular endothelial growth factor receptor (VEGFR) expression on EPCs and weakens VEGF inhibition of oxLDL-induced EPC decrease; 4) Caspase-1 gene deficient (-/-) mouse Sca-1+ progenitor cell therapy improves mouse cardiac function after myocardial infarction; and 5) Caspase-1-/- Sca-1+ progenitor cell therapy improves capillary density, increases peripheral EPC percentages, inhibits caspase-1 activities and improves VEGFR2 expression on EPCs after myocardial infarction. Our Result have provided a first insight on how caspase-1 in EPCs senses hyperlipidemia, promotes EPC pyroptosis and weakens EPC repairing, and our Result have also demonstrated a potential of caspase-1 inhibitory EPC therapy for myocardial infarction.



## The comparative study of the right ventricle training Result between the young and old sheep by gradually increasing the pressure

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**Objective** To study the different Result of the right ventricle training between the young and old sheep induced by gradually increasing the after load.

**Methods** 12 male sheep, 5 – 6 months old, 26 – 37 kg, were randomly divided into experimental and control group, each comprising 6 animals (respectively  $29.00 \pm 2.78$  kg, and  $28.36 \pm 4.24$  kg, no statistically significant difference); 12 male sheep, 5 – 6 years old, 72 – 83 kg, were randomly divided into experimental and control group, each comprising 6 animals ( $75.63 \pm 4.57$  kg and  $76.38 \pm 3.62$  kg respectively, no statistically significant difference). After opening the chest through the second left intercostals, pulmonary trunk was dissociated and the adjustable pulmonary artery banding device was put around it. Then the balloon of the device was gradually inflated to narrow the pulmonary artery and to train the right ventricle. The shape of the right ventricle was studied by echocardiogram and the changes of the hemodynamic and myocardial histopathology were observed.

**Result** Young and old sheep both were able to achieve the aim of ventricular training (right ventricular pressure/left ventricular pressure greater than 0.6). After training the right ventricular systolic and diastolic function of the two groups were enhanced, although the added value of  $\pm dp/dt$  in the young sheep were higher than old, but there was no statistical significant difference between the two groups. Pathological Result showed that both right ventricular hypertrophy index were both added, but no significant difference. The myocardial histopathology in the old experimental group were observed degeneration of myocardial cells, interstitial edema, focal fibrosis and a small number of pathological changes such as fatty degeneration, liver biopsy showed central venous congestion and expansion of sinusoidal liver cells such as hepatic congestion with mild degeneration performance.

**Conclusion** The young and old sheep were successfully able to achieve the aim of ventricular training by gradually increasing the after load, but the old sheep occurred myocardial pathologic changes and heart dysfunction.

## Pigment epithelium–derived factor exerts different effects on the survival and function of endotheliocytes and cardiomyocytes in rat myocardial infarction

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**Background** Ischemic heart disease (IHD) is of increasing importance in aging populations. Alternative forms of treatment have

been studied in an attempt to reduce myocardial ischemia and relieve of symptoms. Gene therapy is an option that may induce angiogenesis, establish collateral circulation, reperfuse ischemic myocardium and recover cardiac function. Although there is much interest in a therapeutic angiogenesis strategy for IHD, Result have been modest because angiogenic inhibiting factor has been overlooked, so there vascular regeneration is poor in infarcted myocardium. Pigment epithelium-derived factor (PEDF) is a pleiotropic gene with anti-inflammatory, antioxidant, neurotrophic and powerful anti-angiogenic properties. The role of PEDF on endothelial cells/ cardiomyocytes function and survival, however, remains unclear.

**Methods** Adult Sprague-Dawley rats myocardial infarction models were surgically established. PEDF-RNAi-LV or PEDF-LV was respectively delivered into the ischemic myocardium for 4 weeks. Reverse transcription-polymerase chain reaction, western blotting and immunofluorescence staining were used to detect gene and protein expression. The apoptosis of endothelial cells/cardiomyocytes, vessel density, vascular permeability, inflammation and animal cardiac function were also evaluated.

**Result** The expression of PEDF and VEGF are opposite each other in the myocardium, so that when one is up the other is down. The inhibited PEDF expression activated the mitochondria and death receptor domain apoptotic signal pathway, promoted the apoptosis of cardiomyocytes, impaired cardiac function, and also leads to endogenous VEGF/VEGFR2 up-regulation. VEGF/VEGFR2 pathway mediated protection of endothelial cells, induced endothelial cells' sprouting, and initiated angiogenesis locally. The new vessels at this stage, however, were unstable. Relative over-expression of PEDF reduced the cardiomyocytes' apoptosis, protected cardiac function, but induced apoptosis of endothelial cells, and inhibited angiogenesis.

**Conclusion** Expression of PEDF in myocardial tissue leads to significant changes in the myocardial internal environment. Survival of endothelial cells and cardiomyocytes was increased or decreased respectively via multiple apoptosis signal pathways in infarcted myocardium. Moreover, PEDF expression inhibited angiogenesis of infarcted myocardium, and the cardiac function was significantly influenced.

## Probucol prevents atrial remodeling by inhibiting reactive oxygen species production and NF- $\kappa$ B activation in alloxan–induced diabetic rabbits

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**Objective** This study sought to assess the effects of probucol on atrial remodeling and atrial fibrillation (AF) promotion in alloxan-induced diabetic rabbits and to elucidate the underlying mechanisms.

**Background** Diabetes mellitus (DM) is an independent risk factor for AF. However, the underlying mechanisms for the increased propensity for AF in DM and the effects of probucol on atrial remodeling remain unclear.

**Methods** 40 Japanese rabbits were randomly assigned to a normal control group (C, n = 10), a alloxan-induced diabetic group (DM, n = 10), probucol-treated group (CPR, n = 10) and probucol-treated diabetic group (DPR, n = 10). Rabbits in the DPR and CPR groups were orally administered Probucol (1000 mg/day) for 8 weeks. Plasma malonaldehyde (MDA) levels were measured by chemical colourimetric Methods. The protein expression of NF- $\kappa$ B and TGF- $\beta$  in left atrial tissue

were analyzed by western blot, the mRNA expression levels of TNF- $\alpha$  were analysed by RT-PCR Methods. Isolated Langendorff perfused rabbit hearts were prepared to evaluate atrial refractory effective period (AERP) and its dispersion (AERPD), interatrial conduction time (IACT) and vulnerability to AF. Atrial interstitial fibrosis was evaluated by Sirius-Red staining.

**Result** The DPR rabbits exhibited significant alleviation of oxidative stress displayed as decreased plasma MDA compared with diabetic rabbits ( $P < 0.05$ ). Probucol significantly downregulated atrial NF- $\kappa$ B, TGF- $\beta$  protein expression and TNF- $\alpha$  mRNA expression in left atrial tissue of alloxan-induced diabetic rabbits. Probucol administration increases stability of vulnerable atrial fibrillation in diabetic rabbits ( $P < 0.05$ ). Histological analysis revealed suppression of DM-related histological changes (interstitial fibrosis) by probucol.

**Conclusion** Probucol prevented atrial remodeling and suppressed AF development in alloxan-induced diabetic rabbits. Its inhibition of ROS Production, NF- $\kappa$ B, TGF- $\beta$  and TNF- $\alpha$  overexpression may contribute to its antiremodeling effects.

### Role of GRK4 in the regulation of arterial AT<sub>1</sub> receptor in hypertension

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**Background** G protein-coupled receptor kinase 4 (GRK4) gene variants, via impairment of renal dopamine receptor and enhancement of renin-angiotensin system function, decrease the ability to excrete a sodium load, resulting in sodium retention and an increase in blood pressure. Increased aortic stiffness, a risk factor in cardiovascular disease, may be related to increased activity of the renin-angiotensin system. Whether or not GRK4 and the angiotensin type 1 receptor (AT<sub>1</sub>R) interact in the aorta is not known.

**Methods** GRK4 expression in vascular smooth muscle cells (Vs MCs) of the aorta was analyzed by confocal microscopy of double-stained, RT-PCR and immunoblotting. AT<sub>1</sub>R protein expression and function in GRK4 variant 142V transfected A10 cells and WT cells was quantified by immunoblotting and AT<sub>1</sub>R-mediated intracellular calcium concentration. AT<sub>1</sub>R phosphorylation level was determined by immunoprecipitation. The interaction between GRK4 and AT<sub>1</sub>R was determined by immunoprecipitation and confocal microscopy of double-stained. NF- $\kappa$ B activity was analyzed by electrophoretic mobility shift assay (EMSA). Angiotensin II-mediated vasoconstriction of the aorta from 142V-transgenic mice and WT mice was analyzed by tension measurement of the artery rings.

**Result** In this study, we find that GRK4 is expressed in Vs MCs of the aorta. Heterologous expression of the GRK4 variant 142V in aortic A10 cells increased AT<sub>1</sub>R protein expression and AT<sub>1</sub>R-mediated increase in intracellular calcium concentration. The increase in AT<sub>1</sub>R expression was related, in part, to an increase in AT<sub>1</sub>R mRNA expression via NF- $\kappa$ B, because blockade of NF- $\kappa$ B abolished those effects of GRK4 142V. As compared with control (vector-transfected cells), cells expressing GRK4 142V had greater NF- $\kappa$ B activity with more NF- $\kappa$ B bound to the AT<sub>1</sub>R promoter. The increased AT<sub>1</sub>R expression in cells expressing GRK4 142V was also associated with decreased AT<sub>1</sub>R degradation, which may be ascribed to lower AT<sub>1</sub>R phosphorylation. There was a direct interaction between GRK4 and AT<sub>1</sub>R in A10 cells that was decreased by GRK4 142V and could have caused the lower

AT<sub>1</sub>R phosphorylation. The regulation of AT<sub>1</sub>R expression by GRK4 142V in A10 cells was confirmed in GRK4 142V transgenic mice; AT<sub>1</sub>R expression was higher, while AT<sub>1</sub>R phosphorylation was lower in the aorta in GRK4 142V than GRK4 wild-type (WT) mice. Angiotensin II-mediated vasoconstriction of the aorta was also higher in GRK4 142V than GRK4 WT mice.

**Conclusion** This study provides a mechanism by which GRK4, via regulation of arterial AT<sub>1</sub>R expression and function, participates in the pathogenesis of conduit vessel abnormalities in hypertension.

### c-Met overexpression promote reendothelialization and inhibit neointimal formation after balloon injury

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**Aim** To explore the effect of c-met overexpression in EPCs on reendothelialization after balloon injury.

**Methods** EPCs derived from mouse bone marrow were isolated and cultured. 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide assays were used to evaluate EPC proliferation. Adenoviral vector expressing c-Met was generated using the AdEasy system. To evaluate the role of HGF/Met in vascular repair in vivo, we used balloon-injured rat carotid artery model. Evans Blue dye was administered to evaluate reendothelialization after 10 days injury, and the neointimal formation was assessed at 21 days following vascular injury.

**Result** The effect of HGF on EPC proliferation was examined 48 h after exposure to different quantities of HGF (range 2 – 20 ng/ml). The proliferation effect was strongly dose-dependent and significantly increased in c-met-EPCs group compared with EPCs group. After transfusion of c-met-EPCs or EPCs to balloon-injured rat via vessel, Evans Blue dye was administered to evaluate reendothelialization after balloon injury. Reendothelialized area was significantly larger in c-met-EPCs group than in EPCs group ( $64.25 \pm 8.90\%$  vs  $43.21 \pm 7.24\%$ ,  $n = 5$ ,  $P < 0.01$ ). A marked decrease in the neointimal area and I/M ratio was found in c-met – EPCs compared with EPCs group at day 21 ( $0.29 \pm 0.06$  vs  $0.63 \pm 0.13$ ,  $n = 5$ ,  $P < 0.01$ ).

**Conclusion** c-Met overexpression improve EPCs proliferation, promote reendothelialization and inhibit neointimal formation after balloon injury.

### The effects of anticoagulant therapy on coagulant state and platelet function following transcatheter closure of atrial septal defect

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**Background** Several studies have demonstrated coagulant system was activated after transcatheter closure of ASD, but changes of platelet function still remain controversial. Currently, it is not clear which anticoagulant regiment is more effective to prevent thrombosis and embolic events after device implantation. This study was to compare the

effects of three anticoagulant regimens on coagulant state and platelet function following transcatheter closure of atrial septal defect (ASD).

**Methods** A total 138 patients who underwent transcatheter closure of ASD were randomized into three groups to receive different anticoagulant therapy: unfractionated heparin (UFH) for 24 hours, low molecular weight heparin (LMWH) for 24 hours, and LMWH for 72 hours (pLMWH). Aspirin was given to all patients for 6 months after intervention. The laboratory measurements included beta-thromboglobulin ( $\beta$ -TG), platelet factor 4 (PF4) and prothrombin fragment 1+2 (F1+2) which were done before intervention as baseline, immediately after, and day 1, 2, 3, 7, 30 and 90 after intervention.

**Result** In 3 groups,  $\beta$ -TG, PF4 and F1+2 elevated immediately after implantation procedure.  $\beta$ -TG and PF4 declined slightly on day 1 and 2, and rose to a highest level on day 3, then fell down to baseline on day 7. The F1+2 gradually returned to baseline on day 90. However, the F1+2 in pLMWH group was markedly lower than that in UFH and LMWH groups on day 3. No thrombo-embolic events were noted during follow-up.

**Conclusion** Transcatheter closure of ASD was associated with significant activation of both platelets and coagulation. These findings support an antithrombotic regimen after procedure including anticoagulant and antiplatelet agents. The F1+2 level fell down earlier in pLMWH group. However, there were no differences of clinical outcomes among three groups on day 90 after intervention. Therefore, a larger size and longer follow-up study is needed to further clarify this issue.

## Dopamine D<sub>1</sub>-like receptors suppress proliferation of vascular smooth muscle cell induced by Insulin-like Growth Factor-1

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**Objective** Proliferation of vascular smooth muscle cells (VSMCs) participates in the pathogenesis and development of cardiovascular diseases, including essential hypertension and atherosclerosis. Our previous study found that stimulation of D<sub>1</sub>-like dopamine receptors inhibited insulin-induced proliferation of VSMCs. Insulin-like growth factor-1 (IGF-1) and insulin share similar structure and biological effect. However, whether or not there is any effect of D<sub>1</sub>-like receptors on IGF-1-induced proliferation of VSMCs is not known. Therefore, we investigated the inhibitory effect of D<sub>1</sub>-like dopamine receptors on the IGF-1-induced VSMCs proliferation in this study.

**Method** VSMC proliferation was determined by [3H]-thymidine incorporation, the uptake of 3-(4, 5-dimethylthiazol-2-yl)-5-diphenyl tetrazolium bromide (MTT) assay and cell number. Phosphorylated/non-phosphorylated IGF-1 receptor, Akt, mTOR and p70S6K expressions were determined by immunoblotting. The oligodeoxynucleotides were transfected to A10 cells to identify the effect of D<sub>1</sub> and D<sub>5</sub> receptors respectively.

**Result** IGF-1 increased the proliferation of VSMCs, while in the presence of fenoldopam, IGF-1 mediated stimulatory effect was reduced. Use of either the antisense for D<sub>1</sub> or D<sub>5</sub> receptor partially inhibited the fenoldopam-induced anti-proliferation effect of VSMCs. Use of both

D<sub>1</sub> and D<sub>5</sub> receptor antisenses completely blocked the inhibitory effect of fenoldopam. In the presence of PI3k and mTOR inhibitors, the IGF-1 mediated proliferation of VSMCs was blocked. Moreover, IGF-1 increased the phosphorylation of PI3k and mTOR. The inhibitory effect of fenoldopam on VSMC proliferation might be due to the inhibition of IGF-1 receptor expression and IGF-1 phosphorylation, since in the presence of fenoldopam, the stimulatory effect of IGF-1 on phosphorylation of IGF-1 receptor, PI3k and mTOR is reduced, the IGF-1 receptor expression was reduced in A10 cells.

**Conclusion** Activation of the D<sub>1</sub>-like receptors suppressed the proliferative effect of IGF-1 in A10 cells via the inhibition of the IGF-1R/Akt/mTOR/p70S6K pathway.

## Association between -1562 C > T polymorphism in the promoter region of matrix metalloproteinase-9 (MMP-9) and coronary artery disease: A meta-analysis

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**Objective** To determine the association between -1562 C>T polymorphism in the promoter region of matrix metalloproteinase-9 (MMP-9) and coronary artery disease (CAD) risk.

**Methods** This meta-analysis was on the basis of 26 studies including 12 776 cases and 6 371 controls. The was assessed by the Q-statistic test and the I<sup>2</sup>-statistic test. Sensitivity analysis was conducted by sequentially omitting any single study and recalculating the ORs and 95% CIs. Funnel plots and Egger's test were performed to test the potential publication bias. All the data were analyzed by using STATA version 12.0.

**Result** We found that -1562 C>T polymorphism did not contribute to susceptibility to CAD in the overall Result (ORCC vs TT = 0.99, 95% CI = 0.94 – 1.04, P heterogeneity = 1.000; ORCC + CT vs TT = 0.99, 95% CI = 0.95 – 1.04, P heterogeneity = 1.000; ORCC vs CT + TT = 0.96, 95% CI = 0.92 – 1.01, P heterogeneity = 0.992; OR allele C vs allele T = 0.98, 95% CI = 0.95 – 1.01, P heterogeneity = 1.000; ORCT vs TT = 0.98, 95% CI = 0.89 – 1.07, P heterogeneity = 1.000). But the stratified analysis by ethnicity and source of control indicated -1562 C>T polymorphism may be a risk factor for the CAD risk in Asians and hospital populations.

**Conclusion** Our meta-analysis supported the fact that -1562 C > T polymorphism was not associated with the susceptibility to CAD. Further larger studies are required to confirm our findings.

## Effects of prescription of Jiashen on ventricular remodeling and infiltration of monocyte/macrophages in the early period after myocardial infarction in rats

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**Objective** This study was designed to test the hypothesis that PJS modulates inflammatory processes to prevent cardiac functional deterioration and reduce ventricular remodeling after MI.

**Methods** Male Sprague-Dawley rats (9 – 10 weeks) were subjected



to sham-MI or MI by ligating the left anterior descending coronary artery for 1 and 4 weeks. The rats were divided into five groups: sham, MI, PJS (3 g/kg/day), PJS (6 g/kg/day), and losartan (an AT<sub>1</sub> antagonist, 10 mg/kg/day). The vehicle, PJS, or losartan was given by oral gavage once a day after MI. Cardiac functions were determined by echocardiographic measurements at 1 and 4 weeks after MI. Fibrinogen at the site of infarction and in ischemic myocardium were determined by Masson staining. Result of quantitative analysis were used to detect the level of hydroxyproline. Monocyte/macrophages expression was detected by immunohistochemistry staining and quantitative analysis.

**Result** The echocardiographic measurement showed that Both LVEDd and LVESd in the PJS-6 and Losartan groups were significantly shorter than in the MI group at both week 1 and week 4 post-MI. both FS and EF were well-maintained in the PJS-6 and Losartan groups than in the MI group at both week 1 and week 4 post-MI. Masson trichrome staining of cardiac sections: At 1 and 4 weeks after myocardial infarction, fibrinogen proliferation was much more obvious in MI group than in sham operation group. A detectable reduction of fibrinogen with PJS-6 and Losartan groups at the site of infarction was not found but was reduced at ischemic sites. Result of quantitative analysis shows: compared to the MI group, the PJS-6 and losartan groups significantly decrease at both the infarction and ischemia areas the level of fibrinogen. Immunohistochemical Result of monocyte/macrophages shows: At 1 and 4 weeks after myocardial infarction, monocyte/macrophages was much more obvious in MI group than in sham operation group. Compared to the MI group, the PJS-6 and losartan groups significantly decrease at both the infarction and ischemia areas of monocyte/macrophages.

**Conclusion** Our studies demonstrate that the PJS improves cardiac function, inhibits cardiac remodeling and suppresses infiltration of monocyte/macrophages after myocardial infarction. The data indicate that PJS inhibits its ventricular remodeling possibly via inhibiting infiltration of monocyte/macrophages. The Result suggest that PJS may have a promising potential for the prevention and treatment of MI.

### Protective effects of aliskiren on ischemia–reperfusion–induced renal injury in rats

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**Background** The protective effect of aliskiren on ischemia-reperfusion (I/R) injury in the heart and brain has been reported. Whether or not the protective effect exists in renal I/R injury is not known. Therefore, we investigated this effect in kidney in this study.

**Methods** Sprague-Dawley rats were randomly divided into four groups: sham group; sham control with aliskiren pretreatment; I/R group; I/R with aliskiren pretreatment. Renal ischemia was induced by occluding the left renal pedicle, and maintained ischemia for 45 min, the reperfusion lasted for 24 hrs. Aliskiren was administrated 15 min before ischemia. Blood samples and the kidneys were collected to check for renal function, angiotensin II (Ang II), apoptosis and oxidative stress levels.

**Result** Compared with the sham rats, serum creatinine (SCR) and blood urea nitrogen (BUN) were significantly increased in I/R rats, accompanied by histopathological damage of the kidney, including

tubular cell swelling, desquamation, and cast formation. There were more apoptotic cells and leukocyte infiltration in I/R rats than in the sham rats. Pretreatment with aliskiren ameliorated I/R induced renal injury, i.e. reduced SCR and BUN levels, ameliorated renal histopathological changes, and decreased the apoptosis of cells and leukocyte infiltration in kidney. I/R injury also decreased superoxide dismutase (SOD) and glutathione (GSH-reduced form) levels, which were blocked with the aliskiren pretreatment.

**Conclusion** Aliskiren pretreatment exerts a protective effect on ischemia/reperfusion injury in the kidney, via amelioration of oxidative stress, and reduction in leukocyte infiltration and cellular apoptosis.

### Low density lipoprotein contained microRNAs as potential novel atherogenic factors

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**Objective** Circulating microRNAs (miRNAs) are gaining more substantial research in recent years. They may serve as biomarker of certain diseases, and they are also biological active in disease progression. High density lipoprotein (HDL) was proved to be a novel endogenous circulating miRNA transporters. Low density lipoprotein (LDL) is similar to HDL in molecular structure, can also transport miRNAs in plasma. The aim of the study was to prove the existence of miRNAs in LDL, and reveal the changes in patients in coronary artery disease.

**Methods** Samples from 3 patients with coronary angiography diagnosed CAD and 3 healthy controls. LDL (1.019-1.063 g/ml) was isolated from the plasma by sequential ultracentrifugation, followed by desalting and dehydration by ultrafiltration. The LDL was then further purified by fast protein liquid chromatography. The expression of Ago2, NPM1 and CD 63 in plasma and LDL were detected by western-blot Methods. Total RNA was isolated from the highly purified LDL by mirVanaTM miRNA isolation kit. The miRNA expression profiles were analyzed by miRCURY TM LNA Array (v.18.0) chip.

**Result** Ultracentrifugation and FPLC can separate the LDL from other miRNA protein transporters. The apolipoprotein in highly purified LDL was apoB100, without any HDL components (apoAI). The miRNA chip revealed that LDL contains up to 280 miRNAs. LDL from CAD patients contains more miR-4778-5p than that from the healthies. Biological information studies reveal that the potential target genes of miR-4778-5p is ABCA1 and ABCG1. miR-4778-5p might regulate cholesterol efflux by regulating ABCA1 and ABCG1 directly.

**Conclusion** LDL is a novel endogenous miRNA transporter. The expression profiles were significantly changed in CAD patients. The miRNAs in LDL might be biological active in atherosclerosis.

### Effects of prescription of Jiashen on TGF-β/Smads pathway after myocardial infarction in rats

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**Objective** This study was designed to study the effect of PJS on

TGF- $\beta$ /Smads pathway after MI in rats.

**Methods** Male Sprague-Dawley rats (9–10 weeks) were subjected to sham-MI or MI by ligating the left anterior descending coronary artery for 1 and 4 weeks. The rats were divided into five groups: sham, MI, PJS (3 g/kg/day), PJS (6 g/kg/day), and losartan (an AT<sub>1</sub> antagonist, 10 mg/kg/day). The vehicle, PJS, or losartan was given by oral gavage once a day after MI. The expressions of TGF- $\beta$ 1, p-smad2, p-smad3 in the myocardium were assayed using Western-blot at 1 week or 4 weeks after MI.

**Result** At 1 week after MI, administration of PJS (3 or 6 g/kg/day) attenuated the increases in myocardial expression levels of TGF- $\beta$ 1, p-smad2 and p-smad3 compared with MI group (TGF- $\beta$ 1:  $1.21 \pm 0.06$  or  $1.06 \pm 0.03$  vs  $1.37 \pm 0.09$ ,  $P < 0.05$ ; p-smad2:  $1.88 \pm 0.04$  or  $1.52 \pm 0.11$  vs  $2.09 \pm 0.24$ ,  $P < 0.05$ ; p-smad3:  $0.83 \pm 0.01$  or  $0.5 \pm 0.02$  vs  $1.05 \pm 0.120$ ,  $P < 0.05$ ). The greater effect was achieved at a dose of 6 g/kg/day. Losartan treatment also inhibited the increases in myocardial expression levels of TGF- $\beta$ 1, p-smad2 and p-smad3 compared with MI group (TGF- $\beta$ 1:  $0.58 \pm 0.03$  vs  $1.37 \pm 0.09$ ,  $P < 0.05$ ; p-smad2:  $1.27 \pm 0.02$  vs  $2.09 \pm 0.24$ ,  $P < 0.05$ ; p-smad3:  $0.23 \pm 0.01$  vs  $1.05 \pm 0.12$ ,  $P < 0.05$ ). At 4 week after MI, administration of PJS (3 or 6 g/kg/day) attenuated the increases in myocardial expression levels of TGF- $\beta$ 1, p-smad2 and p-smad3 compared with MI group (TGF- $\beta$ :  $0.58 \pm 0.03$  or  $0.69 \pm 0.02$  vs  $0.78 \pm 0.01$ ,  $P < 0.05$ ; p-smad2:  $0.57 \pm 0.04$  or  $0.77 \pm 0.02$  vs  $0.88 \pm 0.05$ ,  $P < 0.05$ ; p-smad3:  $0.50 \pm 0.01$  or  $0.65 \pm 0.02$  vs  $0.78 \pm 0.01$ ,  $P < 0.05$ ). The greater effect was achieved at a dose of 6 g/kg/day. Losartan treatment also inhibited the increases in myocardial expression levels of TGF- $\beta$ 1, p-smad2 and p-smad3 compared with MI group (TGF- $\beta$ 1:  $0.42 \pm 0.01$  vs  $0.78 \pm 0.01$ ,  $P < 0.05$ ; p-smad2:  $0.24 \pm 0.57$  vs  $0.88 \pm 0.05$ ,  $P < 0.05$ ; p-smad3:  $0.39 \pm 1.87$  vs  $0.78 \pm 0.01$ ,  $P < 0.05$ ).

**Conclusion** Our studies showed PJS administered can significantly inhibit TGF- $\beta$ /Smads pathway after MI in rats. The data indicate that PJS improves cardiac remodeling possibly via inhibiting TGF- $\beta$ /Smads pathway. The Result suggest that PJS may have a promising potential for the prevention and treatment of MI.

### Tirofiban improves renal outcome in a rat model of ischemia/reperfusion injury by modulating NO synthases

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3. Division of Nephrology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA.

**Aim** Renal ischemia/reperfusion (I/R) injury is a common clinical disease. We have known that NO-signal transduction has an important effect on renal I/R injury. NO is produced by NO synthases. Endothelial NO synthase (eNOS) plays a protective role while inducible NO synthase (iNOS) induces impairment. There is evidence that tirofiban may cause alteration of NO production by affecting eNOS/iNOS. So in present study, we investigated whether tirofiban can affect NO Synthases and improve renal outcome in a rat model of I/R injury.

**Methods and Result** Tirofiban (100  $\mu$ g/kg) was intraperitoneally administered to Sprague-Dawley rats, which were divided into four groups: sham operated control group (N = 3); sham operated plus tirofiban (100  $\mu$ g/kg) group (N = 3); I/R group (N = 3); I/R plus tirofiban group (N = 3). After 24 h reperfusion, kidney and blood were collected

to estimate renal function, oxidative stress, apoptosis of renal tissues and plasma NOx – production. In I/R group, the level of serum urea, Scr, and AST was much higher compared with control. Pathological damage score was also much higher in I/R group. Tirofiban improves renal function damaged by I/R injury and reduce histopathological changes. Besides, tirofiban also decrease oxidative stress, apoptosis and the level of plasma NOx.

**Conclusion** Tirofiban plays a protective role in renal I/R injury. And the alterations of NO-transduction related to eNOS/iNOS may participate in the mechanism of tirofiban protection.

### lincRNA-p21 feedback enhances P53 activity via interaction with MDM2 function in vascular smooth muscle cells proliferation dominantly neointimal hyperplasia of atherosclerosis

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**Objective** To investigate the relationship and molecular mechanism of lincRNA-p21 in the development of atherosclerosis (AS).

**Methods** Firstly, we detected the expression of lincRNA-p21 expression in the aortic plaque of apoE<sup>-/-</sup> mice fed with high-fat diet and peripheral blood mononuclear cells of clinical coronary disease patients. Then we observed the role of lincRNA-p21 in cell proliferation and apoptosis using mice macrophage cell line RAW264.7 and human vascular smooth muscle cell line HA-Vs MCs by loss-of-function and gain-of function approaches. Meanwhile, the expression of mRNA and protein levels of apoptosis-related downstream targeting of p53 also been detected. Furthermore, we performed bioinformatics prediction, RNA-Immunoprecipitation (RIP), RNA-pulldown and deletion mapping experiments to test the potential interaction and specific interaction pattern between lincRNA-p21 and MDM2. Then co-Immunoprecipitation (co-IP) and Chromatin- Immunoprecipitation (ChIP) assays were performed to verify the possible influence on p53 transcriptional activity of this binding. We further investigated whether or not lincRNA-p21 was involved in the formation of neointimal hyperplasia in vivo, therefore recombinant lentivirus vector expressing Si-RNA against lincRNA-p21 was injected into the injured area of mouse carotid arteries.

**Result** In this study, we have indentified lincRNA-p21 was down-regulated in apoE<sup>-/-</sup> AS model mice. By loss-of-function and gain-of function approaches, we found that both lincRNA-p21 and p53 could repress proliferation and induce apoptosis in Vs MCs. LincRNA-p21 knockdown blocked P53 signaling and the effect of p53 on Vs MC proliferation and apoptosis. MDM2 is a key factor to regulate p53 activity by prevention of P300-induced p53 acetylation. We found that lincRNA-p21 can binding to MDM2 directly, which makes the MDM2 dissociation with p53, therefore, leads to p53 acetylation by P300, increases p53 activity. This finding is of significance, because after treatment with SiRNA against lincRNA-p21, the neointimal hyperplasia is increased dramatically in the injured carotid artery in mouse. Therefore, lincRNA-p21 might be a switch of MDM2, via indirectly effect on p53 activity, affect Vs MC proliferation and apoptosis, which is involved in the pathogenesis of atherosclerosis.

**Discussion** It is well-known that p53 plays an important role on the pathogenesis of AS. Both the quantity and transcriptional activity of p53 can be regulated by multiple ways, but the epigenetic modifications

especially ubiquitination and acetylation seems to be the most important patterns. MDM2, a p53 positive responsive gene, take part in both this two pathways. The quantity of p53 can be degraded by MDM2. On the other hand, p53 is well-known to be acetylated by the acetyltransferase CBP/p300, which dramatically induce p53 activity by acetylation. Nevertheless, this effect can be reduced when MDM2 combine with P53 through decrease the formation of P300-p53 complex. Therefore, the P300-MDM2-p53 complex play a key important role in the regulation of p53 and an intact MDM2 protein may be a core regulator in the whole process. lincRNA-p21 could bind to the RING domain of MDM2 through its 5' end 728-2057nt region, prevent the binding of MDM2 with p53, therefore, there would be more p53 binding with P300, which leads to p53 acetylation, increased p53 activity. Transfection of p53 have the similar effect with lincRNA-P21, while after knockout of lincRNA-P21 with Si-RNA, the effects of p53 on Vs MCs proliferation and apoptosis is blocked. After treatment with siRNA of lincRNA-p21, the neointimal hyperplasia is increased in the injured carotid artery in vivo.

**Conclusion** In conclusion, lincRNA-p21 might be a switch of MDM2, the binding of lincRNA-p21 with MDM2 would release freer P53, which would be binding with P300, leads to P53 acetylation, indirectly affect on P53 activity, increases Vs MC proliferation and decreases Vs MCs apoptosis, involved in the pathogenesis of atherosclerosis.

### PHD2 silencing enhances the survival and paracrine function of transplanted adipose-derived stem cells in infarcted myocardium

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**Rationale** Transplantation of stem cells into damaged hearts has had modest success as a treatment for ischemic heart disease. One of the limitations is the poor stem cell survival in the diseased microenvironment. Prolyl hydroxylase domain protein 2 (PHD2) is a cellular oxygen sensor that regulates two key transcription factors involved in cell survival and inflammation, hypoxia-inducible factor (HIF) and nuclear factor- $\kappa$ B (NF- $\kappa$ B).

**Objective** We studied if and how PHD2 silencing in human adipose-derived stem cells (ADSCs) enhances their cardioprotective effects after transplantation into infarcted hearts.

**Methods and Result** ADSCs were transduced with lentiviral shPHD2 to silence PHD2. ADSCs with or without shPHD2 were transplanted after myocardial infarction (MI) in mice. ADSCs reduced cardiomyocyte apoptosis, fibrosis and infarct size and improved cardiac function. shPHD2-ADSCs exerted significantly more protection. PHD2 silencing induced greater ADSCs survival, which was abolished by

shHIF-1 $\alpha$ . Conditioned medium (CM) from shPHD2-ADSCs decreased cardiomyocyte apoptosis. Insulin-like growth factor 1 (IGF-1) levels were significantly higher in the CM of shPHD2-ADSCs vs ADSCs, and depletion of IGF-1 attenuated the cardioprotective effects of shPHD2-ADSCs CM. NF- $\kappa$ B activation was induced by shPHD2 to induce IGF-1 secretion via binding to IGF-1 gene promoter.

**Conclusion** PHD2 silencing promotes ADSCs survival in MI hearts and enhances their paracrine function to protect cardiomyocytes. The pro-survival effect of shPHD2 on ADSCs is HIF-1 $\alpha$  dependent and the enhanced paracrine function of shPHD2-ADSCs is associated with NF- $\kappa$ B-mediated IGF-1 up-regulation. PHD2 silencing in stem cells may be a novel strategy for enhancing the effectiveness of stem cell therapy after MI.

### The relative contribution of paracrine effect vs direct differentiation on adipose-derived stem cell transplantation mediated cardiac repair

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Department of Cardiology, Daping Hospital, Third Military Medical University, Chongqing

**Background** Recent studies have demonstrated that transplantation of adipose-derived stem cell (ADSC) can improve cardiac function in animal models of myocardial infarction (MI). However, the mechanisms underlying the beneficial effect are not fully understood. In this study, we characterized the paracrine effect of transplanted ADSC and investigated its relative importance vs direct differentiation in ADSC transplantation mediated cardiac repair.

**Methodology/Principal Findings** MI was experimentally induced in mice by ligation of the left anterior descending coronary artery. Either human ADSC, conditioned medium (CM) collected from the same amount of ADSC or control medium was injected into the peri-infarct region immediately after MI. Compared with the control group, both ADSC and ADSC-CM significantly reduced myocardial infarct size and improved cardiac function. The therapeutic efficacy of ADSC was moderately superior to ADSC-CM. ADSC-CM significantly reduced cardiomyocyte apoptosis in the infarct border zone, to a similar degree with ADSC treatment. ADSC enhanced angiogenesis in the infarct border zone, but to a stronger degree than that seen in the ADSC-CM treatment. ADSC was able to differentiate to endothelial cell and smooth muscle cell in post-MI heart; these ADSC-derived vascular cells amount to about 9% of the enhanced angiogenesis. No cardiomyocyte differentiated from ADSC was found.

**Conclusion** ADSC-CM is sufficient to improve cardiac function of infarcted hearts. The therapeutic function of ADSC transplantation is mainly induced by paracrine-mediated cardioprotection and angiogenesis, while ADSC differentiation contributes a minor benefit by being involved in angiogenesis.



## Experiment of cellular repressor of E1A–stimulated genes (CREG) delivery via nanoporous Stent in a porcine coronary mode

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**Background** In this study we investigate the *in vitro* pharmacokinetic of nanoporous CREG eluting-stent (CREGES) and evaluate the efficacy and safety of nanoporous CREGES in inhibiting neointima proliferation in porcine coronary model.

**Methods** (1) The human 293F cells were transfected with pcDNA3.1 myc-His/hCREG using Lipofectamine 2000. (2) For the absorption of the CREG protein by the nanoporous stent, the stents were totally immersed and kept vertical in solution of CREG protein in a phosphate buffer. *In vitro* proliferation assays were performed using isolated endothelial and smooth-muscle-cells from to investigate the cell-specific pharmacokinetic effect of CREG protein and rapamycin. (3) The nanoporous bare metal stent (BMS), nanoporous CREGES and sirolimus-eluting stent (PARNTER) were implanted in left anterior descending coronary, left circumflex coronary and right coronary artery of forty porcines in random. And after 7, 14 and 28-day, animals were sacrificed for histomorphologic and pathologic score analysis.

**Result** The lysates of 293F cells transfected pcDNA3.1 myc-His/hCREG plasmid were detected by Western blot with Anti-hCREG, Anti-myc and Anti-His respectively. The recombinant fusion protein about 30 kD was identified in transfected cells by Western blot using Anti-myc and Anti-His. The recombinant hCREG protein was purified with Ni-NTA column according to 6×His affinity chromatographic theory. After the elution was concentrated with Centrprep centrifugal filter devices, the concentration of recombinant protein was determined to be 1.6 mg/mL by BCA assay. The purity of recombinant protein reached 92% identified with image-J software analysis. Stents eluting the CREG protein were tested for their adsorption characteristics by radioisotope technique with <sup>125</sup>I-labeled CREG protein. The amount of CREG protein adsorbed onto the nanoporous bare metal stent was dependent on the concentration and duration of immersion in the solution. We had tested three different concentrations for 48 h. Maximal CREG protein binding was therefore defined as the amount of agent bound to stent wires after 48 hours immersion in a 1.5 mg/ml solution. We implant the CREG eluting stents and 316L stainless steel stents as the control in pig model, to study the bio-security validity of prevention ISR by sliding microtome, SEM, transmission electron microscope (TEM), immunohistochemistry, tissue stain and biochemistry Methods.

**Conclusion** The nanoporous CREGES represents a novel promising device in preventing in-stent restenosis by inhibiting the thrombosis and neointimal hyperplasia via accelerating the endothelialization of the stent surface and inhibiting the smooth muscle cell proliferation.

## Rosuvastatin prevents contrast–induced nephropathy in diabetic nephropathy rats

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**Background** The aim of the present study was to assess the effects of rosuvastatin on contrast-induced nephropathy (CIN) in diabetic nephropathy rats.

**Methods** Male SD rats, using a single intraperitoneal injection of streptozotocin (STZ) to create a diabetic nephropathy model. The model rats were randomly grouped into diabetic nephropathy group, contrast group and the rosuvastatin+ contrast group, 10 in each group. Intravenous injection of iopromide (3500 u/kg) given 72 hours later, the line serum creatinine testing, to determine the CIN formation. The serum total cholesterol, triglycerides, creatinine, nitric oxide, interleukin-6, and tumor necrosis factor alpha levels were analyzed. Urine samples were taken to measure the albumin/urinary creatinine ratio. Kidneys were sectioned and stained with hematoxylin/eosin and Masson's trichrome. Immunohistochemical analysis of the renal tissue was performed to detect macrophage infiltration of the glomeruli.

**Result** The contrast group had a significantly reduced nitric oxide level and an increased interleukin-6 and tumor necrosis factor alpha level, albumin/urinary creatinine ratio and number of macrophages in the renal glomeruli. Rosuvastatin increased the nitric oxide level and reduced the interleukin-6 and tumor necrosis factor alpha levels, glomerular macrophage number and albumin/urinary creatinine ratio in the contrast +rosuvastatin group.

**Conclusion** Rosuvastatin treatment reduced glomerular damage due to improvement in the inflammatory pattern independent of serum lipid level. These effects may lead to improvements in the treatment of CIN.

## Low density lipoprotein contained microRNAs as potential novel atherogenic factors

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**Objective** Circulating microRNAs (miRNAs) are gaining more substantial research in recent years. They may serve as biomarker of certain diseases, and they are also biologically active in disease progression. High density lipoprotein (HDL) was proved to be a novel endogenous circulating miRNA transporters. Low density lipoprotein (LDL) is similar to HDL in molecular structure, can also transport miRNAs in plasma. The aim of the study was to prove the existence of miRNAs in LDL, and reveal the changes in patients in coronary artery disease.

**Methods** Samples from 3 patients with coronary angiography diagnosed CAD and 3 healthy controls. LDL (1.019 – 1.063 g/ml) was isolated from the plasma by sequential ultracentrifugation, followed by desalting and dehydration by ultrafiltration. The LDL was then further purified by fast protein liquid chromatography. The expression of Ago2, NPM1 and CD63 in plasma and LDL were detected by western-blot

**Methods.** Total RNA was isolated from the highly purified LDL by mirVana™ miRNA isolation kit. The miRNA expression profiles were analyzed by miRCURY™ TLNA Array (v.18.0) chip.

**Result** Ultracentrifugation and FPLC can separate the LDL from other miRNA protein transporters. The apolipoprotein in highly purified LDL was apoB100, without any HDL components (apoA1). The miRNA chip revealed that LDL contains up to 280 miRNAs. LDL from CAD patients contains more miR-4778-5p than that from the healthies. Biological information studies reveal that the potential target genes of miR-4778-5p is ABCA1 and ABCG1. miR-4778-5p might regulate cholesterol efflux by regulating ABCA1 and ABCG1 directly.

**Conclusion** LDL is a novel endogenous miRNA transporter. The expression profiles were significantly changed in CAD patients. The miRNAs in LDL might be biological active in atherosclerosis.

### Comparison of biomarkers of endothelial dysfunction and risk of early organ damage between primary aldosteronism and essential hypertension

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**Objective** To compare plasma concentrations of biomarkers of endothelial dysfunction between primary aldosteronism (PA) and essential hypertension (EH), and to determine whether elevated levels of these biomarkers predict development of early organ damage.

**Methods** Thirty-six cases with PA and 39 controls with EH individually matched for age, sex, blood pressure and duration of hypertension were assessed in this study. Plasma levels of biomarkers reflecting endothelial dysfunction (von Willebrand factor [vWF], soluble intercellular adhesion molecule 1 (sICAM-1), and oxidized low density lipoprotein [ox-LDL]) were detected and compared between cases with PA and their matched controls. Left ventricular mass index (LVMI) determined by echocardiography, 24-hour urinary protein quantitative determination and urinary albumin excretion rate (UAER) were adopted to evaluate early organ damage. Left ventricular hypertrophy was defined as LVMI > 125 g/m<sup>2</sup> in men and > 120 g/m<sup>2</sup> in women, and microalbuminuria was defined as UAER of between 20 µg/min and 200 µg/min.

**Result** The biomarkers of endothelial dysfunction (vWF and sICAM-1), as well as ox-LDL, LVMI, 24-hour urinary protein quantitation (24 h UPQ) and UAER, were significantly higher in PA cases than in EH controls (vWF [%], 122.3 ± 53.8 vs 113.1 ± 68.3; sICAM-1 [ng/mL], 401.0 ± 74.1 vs 300.9 ± 87.0; ox-LDL [U/L], 13.6 ± 10.0 vs 8.1 ± 5.9; LVMI [g/m<sup>2</sup>], 124.7 ± 33.6 vs 109.1 ± 25.7; 24 h UPQ [g], 0.17 ± 0.10 vs 0.09 ± 0.04 and UAER [µg/min], 25.9 ± 7.7 vs 9.7 ± 5.9, all P values < 0.05). Elevated plasma vWF, sICAM-1 levels and plasma aldosterone concentration independently predicted incident microalbuminuria in multiple regression models; whereas, elevated plasma vWF and ox-LDL levels, plasma aldosterone concentration and systolic blood pressure independently predicted left ventricular hypertrophy.

**Conclusion** Patients with PA have greater endothelial dysfunction reflected by multiple biomarkers and early organ damage than with EH, and plasma aldosterone concentration and multiple endothelial dysfunction biomarkers predict early organ damage independently.

### Transcriptome analysis of chamber specific genes during heart development

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**Objective** To curate ventricle and atrium specific genes in heart development and propose a statistics method to discriminate chamber genes.

**Methods** Microarray data was downloaded from public NCBI GEO database. Gene expression pattern was validated by extensive literature search. Data analysis was performed by using free software R and graphic was generated by local R scripts. Significant result was reported if P-value was lower than 0.05.

**Result** We confirmed the accuracy of microarray data from public database by its consistency with published result. We then curated a collection of chamber-enriched genes by setting an empirical threshold and used these groups of genes to classify lineage (ventricle and atrium) specific cells.

**Conclusion** Cardiac regeneration is the holy grail of heart failure treatment. Embryonic stem cells (ESCs), induced pluripotent stem cells (iPSCs) and direct reprogramming of fibroblasts into cardiomyocytes are potential strategies in clinical practice to regenerate injured heart. However, the current problem is to assess the ability of those approaches to differentiate into chamber specific heart cells which include ventricle and atrial as well as pacemaker cardiomyocytes. Here, we proposed a statistic method to discriminate the ventricle and atrium lineage cells using combined gene expression pattern. In doing so, we first confirmed the accuracy of microarray data from public database by its consistency with published result. We then curated a collection of chamber-enriched genes by setting an empirical threshold and used these groups of genes to classify lineage (ventricle and atrium) specific cells. Our result indicates that current protocol of directed differentiation of embryonic stem cells might generate atrium and ventricle enriched gene expression pattern. Therefore, we infer that we should take a cautious step to apply these Methods to clinical translation and evaluate the possibility of eliciting environmental “niche” to induce lineage transformation.

### CFD analysis & PIV experimental Study on the flow in inlet & outlet cannulas of FW-2 ventricular assist pump

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**Objective** To analyze and test the hydraulic characteristics of the blood flow in the inlet and outlet cannulas of FW-2 ventricular assist pump with the Methods of computational fluid mechanics (CFD) and particle image velocimetry (PIV). Then the blood compatibility of the inlet and outlet cannulas was evaluated.

**Methods** According to the feature and applicability of CFD and PIV Methods, we determined to calculate the flow fields in the inlet

cannula with CFD Methods and test the flow fields in the outlet cannula with PIV Methods. The numerical model of inlet cannula was built by ANSYS software. The blood viscosity and density parameters were setup. The boundary conditions were set up as flow was 5 L/min and the outlet pressure was 0 MPa. Then the flow field was simulated. The risk of thrombogenesis was evaluated on the basis of the CFD Result of vortex and stagnant flow in the inlet cannula. The hemolysis characteristic was analyzed according to the distribution of shear stress in the inlet cannula. We tested the hydrodynamics characteristics in the central section of the assist pump outlet cannula on the two dimensional PIV system. And the hydrodynamics characteristics in the whole outlet cannula were tested. We selected the outlet section of the pump as the first test section and the last section was 20 mm far away from the first section. We tested ten sections totally. Then we analyzed the possibility of thrombosis in blood pump outflow cannula. The Result of the ten sections were arranged according to its spatial position to obtain the flow fields of the whole outlet cannula. The flow was set to 5 L/min in the testing. Finally we analyzed the possibility of thrombogenesis in outlet cannula according to the hydrodynamics characteristics of the outlet cannula.

**Result** The CFD Result displayed that the flow velocity in the inlet cannula was well-distributed and the maximum velocity was 1 m/s. There was no vortex or stagnant flow in the inlet cannula. The maximum shear stress was 40 Pa meanwhile the exposed time of the blood in the inlet cannula was less than 1 second. The PIV Result displayed that the flow velocity in the outlet cannula was well-distributed and mainly in the range of 1 m/s to 1.18 m/s. The maximum velocity was 1.4 m/s in the outlet cannula. The streamline displayed that there was no vortex flow in the outlet cannula. The blood velocity near the outlet cannula inner wall increased to the maximum rapidly outside the boundary layer so there was no flow stagnation. The 3D PIV Result displayed there was spiral flow near the cannula inner wall. The spiral flow disappeared away from the pump outlet 20 mm because it wears off along the outlet cannula.

**Conclusion** It is difficult to form thrombus in the FW-2 inlet cannula because there is no vortex or stagnant flow field in the inlet cannula. The well-distributed flow in the inlet cannula can improve the flow distribution in the assist pump and advance the biocompatibility of the pump. The influence of inlet cannula on hemolysis can be negligible because the red blood cells are unlikely be damaged by the shear stress in the inlet cannula. The blood is unlikely remain onto the inner wall of outlet cannula. The thrombus caused by low speed flow won't happen. The diffuser of the assist prevents the eddy diffusion effectively. The outlet cannula can eliminate the spiral flow.

### Ghrelin protects human pulmonary artery endothelial cells against hypoxia-induced injury via PI3-Kinase/Akt

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Center for pulmonary Vascular Disease, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100037, Peoples Republic of China

**Objective** To investigate the effect of the Ghr on the hypoxia-induced injury in human pulmonary artery endothelial cells (HPAECs) and on the involved transduction pathway.

**Methods** HPAECs were purchased from Cascade Biologics. HPAECs injury was induced by exposure of cells to hypoxia/serum-starving in a sealed GENbox hypoxic chamber. Effects were investigated by treating cells with varying concentrations of Ghr in the absence or

presence of inhibitors that target phosphoinositide 3-kinase (PI3K), in normoxic or hypoxic conditions for 24 h. Cell viability was determined using a cell counting kit-8 assay. Apoptosis was detected using the Hoechst/PI and terminal deoxynucleotidyl transferase-mediated dUTP-biotinnick end-labeling assays. The NO secreted by HPAECs was detected by nitric acid reduction method. Western blot analysis was used to examine the changes in the expression levels of endothelial nitric oxide synthase (eNOS), phospho-eNOS, phospho-Akt, Akt, mammalian target of rapamycin (mTOR), phosphor-mTOR, B-cell lymphoma-2 (Bcl-2), and Bcl-2 associated X protein (Bax).

**Result** Our Result indicated that the treatment with 10<sup>-7</sup> mol/l Ghr significantly enhanced cell viability (10<sup>-7</sup> mol/l) significantly increased NO secretion and eNOS phosphorylation in comparison with the hypoxia or normoxia alone group (P < 0.05, n = 4) Nevertheless, the treatment with LY294002 (20 μmol/l) decreased the Ghr-induced NO release as well as the eNOS activity.

**Conclusion** In conclusion, we have demonstrated that Ghr could promote HPAECs survival and improve its function under hypoxic condition. We also have shown that the Ghr strongly activated Akt and eNOS, and this potentially beneficial effect of the Ghr was at least partly mediated by the PI3K/Akt pathway in these cells. The bcl-2/bax ratio was also involved in the protective action of the Ghr in HPAECs.

### Influence of genetic polymorphisms of uptake (OATP1B1) and efflux (BCRP/MRP2) transporters on the pharmacokinetics of rosuvastatin

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**Objective** The aim of the present study was to investigate the contribution of genetic polymorphisms of uptake (OATP1B1) and efflux (BCRP/MRP2) transporters on the pharmacokinetics of rosuvastatin in Chinese subjects, and provide molecular mechanism to the individual differences in drug disposition and response caused by membrane transporters.

**Methods** After genotyping screening, twenty four healthy Chinese subjects were enrolled in the following study groups: OATP1B1 521TT (n = 15) and 521TC+CC (n = 9), BCRP 421CC (n = 15) and 421CA+AA (n = 9), and MRP2-24CC (n = 13) and -24CT+TT (n = 11). Each subject was given multiple oral doses of rosuvastatin for 7 days. The plasma and urine concentrations of rosuvastatin were determined by LC-MS/MS. The pharmacokinetic parameters of rosuvastatin, including area under the plasma concentration-time curve (AUC), peak plasma concentration (C<sub>max</sub>), and terminal half-life (t<sub>1/2</sub>), were compared according to genotype groups

**Result** After single oral dose of rosuvastatin, the AUC<sub>0-12</sub>, C<sub>max</sub> and percent of cumulative amount eliminated into the urine (Percent<sub>excretion</sub>) were significantly higher in BCRP 421CA+AA group than those in the 421CC wild-type group (P = 0.030, 0.015 and 0.041, respectively), whereas there was no difference in the t<sub>1/2</sub> and T<sub>max</sub> between these groups. In contrast, no significant differences were found between the two genotype groups in terms of AUCs, C<sub>max</sub>, total clearance and renal clearance values at steady state (P > 0.05), but a prolonged t<sub>1/2</sub> was observed in 421CC wild-type group compared with that in 421CA+AA group (P = 0.035). In addition, the OATP 1B1 521T>C and MRP2 -24C>T variants were not associated with differences in the



pharmacokinetic parameters of rosuvastatin.

**Conclusion** The BCRP421C>A variant, rather than MRP2-24C>T and OATP 1B1 521T>C, is one of the determinant factors governing the interindividual variability in the pharmacokinetics of rosuvastatin.

### Tongxinluo dose-dependently decreases apoptosis of mesenchymal stem cells under hypoxia and serum deprivation via the MEK/ERK1/2 pathway

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**Background** and Objective Mesenchymal stem cells (MSCs) are one of the optimal candidates for myocardial infarction. However, the survival ratio of implanted cells in the infarcted heart is low. Tongxinluo (TXL) is a traditional Chinese herbal medicine with multiple cardiovascular protective effects and has been widely used in China to treat patients with coronary heart disease. MEK/ERK pathway plays an important role in mediating cell survival. Therefore, we hypothesized that TXL could promote MSCs survival under hypoxia and serum deprivation (H/SD) via MEK/ERK pathway.

**Methods** MSCs from the Sprague-Dawley rats bone marrow (60 – 80 g, male) were pretreated with TXL (100 – 800 µg/ml) for 6 hours under H/SD. For inhibitor studies, the cells were preincubated with MEK1/2 inhibitor U0126 (10 µM) for 1 hour prior to the addition of TXL (800 µg/ml). Cell apoptosis was assessed using Annexin V/propidium iodine (PI) by flow cytometry, apoptosis related protein bax, cytochrome C and bcl-2 was assessed by western blot. The expression of ERK1/2 and phosphorylation of ERK1/2 were measured by western blot.

**Result** We found that cell apoptosis was significantly upregulated under H/SD conditions compared with the normal. TXL decreases the apoptosis level in a dose-dependent manner especially in the 800 mg/ml concentration, demonstrated by reduced apoptosis rate, decreased expression of pro-apoptotic protein bax and cytochrome C and increased expression of anti-apoptotic protein bcl-2. Further, TXL upregulated the phosphorylation of ERK1/2. And treatment with U0126 attenuated the protective role of TXL coupled with downregulated phosphorylation of ERK1/2.

**Conclusion** TXL protects MSCs from H/SD injury via MEK/ERK1/2 pathway. It provides a further explanation for the protective effects of TXL on MSCs survival.

### Increased plasma level of haptoglobin is associated with stable coronary heart disease

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**Purpose** Haptoglobin (HP) is an acute phase protein and has been shown to play an anti-inflammatory role by binding free haemoglobin.

The role and implication of HP in patients with stable coronary heart disease (CHD) are not completely defined. This study is to assess the plasma level of HP in patients with CHD and explore the relationship between the concentration of HP and the severity of CHD.

**Methods** Two hundred and fifty-five patients with CHD, defined as more than 50% stenosis in at least one main vessel by coronary angiography, were enrolled in the CHD group and 157 age and gender-matched subjects without CHD were selected as the control group. Patients with diabetes were all excluded. The severity of CHD was determined by the Gensini score and patients in the CHD group were divided into three sub-groups according to the score: less than 40, between 40 and 90, and more than 90. The plasma levels of HP were detected with an immunoturbidimetric method in all patients.

**Result** The plasma level of HP in the CHD group (n = 255) was significantly higher than that in the control group (n = 157) (98.6 ± 55.1 mg/dl vs 85.7 ± 43.6 mg/dl, P < 0.01). Plasma levels of HP were 95.7 ± 53.6 mg/dl, 97.1 ± 61.3 mg/dl, and 103.7 ± 53.6 mg/dl in each CHD sub-group with Gensini score less than 40, between 40 and 90, and more than 90, respectively, with no statistical difference of HP levels among the three sub-groups (P = 0.881). In addition, no linear correlation was observed between the plasma HP levels and Gensini scores (r = 0.014, P = 0.868).

**Conclusion** The plasma level of HP is significantly higher in the patients with CHD and might associated with CHD, but not in accordance with the severity of CHD assessed using the Gensini score. The mechanism, accounting for the association, is worth to discuss.

### Salt induces endothelial cell dysfunction by activating oxidative stress and p38 MAPK pathway

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**Background** Dietary salt plays a major role in the regulation of blood pressure. However, the mechanisms underlying endothelial cell dysfunction induced by sodium have not yet been completely elucidated.

**Methods** SD rats were randomly divided into high salt group (n = 10, 1.5% NaCl in drinking water) and control group (n = 10, no NaCl in drinking water). Systemic blood pressure (SBP) was measured weekly by the tail-cuff method. Blood samples were collected at 8 and 12 weeks for later analysis. Human coronary artery endothelial cells were firstly cultured in medium containing aldosterone at physiological concentration (0.45 nmol/L) for 3 days. Secondly sodium at different concentrations, i.e. 125, 135, 145, 155, 165 mmol/L, was applied to these cells for 3 hours. For mechanical study, SB203580 and tempol were used for 1 hour prior to NaCl stimulation. Cells and supernatant were collected after NaCl stimulation for later analysis. F-actin of endothelial cells was observed by immunofluorescence. The plasma and cell supernatant Nitric Oxide (NO) were determined by Nitrate reductase method. The plasma and cell supernatant ONOO<sup>-</sup> were assessed by ELISA. The endothelial nitric oxide synthetase (eNOS), gp91, p-P38 and p-HSP27 in endothelial cells were detected by Western Blot.

**Result** Compared to control group, administration of 1.5% NaCl water to rats for 8 or 12 weeks significantly increased blood pressure (P < 0.05), decreased plasma NO generation (P < 0.05) and improved plasma ONOO<sup>-</sup> generation (P < 0.05). F-actin of endothelial cells was

unaffected by acute changes under sodium concentration  $\leq 135$  mmol/L but rose steeply under sodium concentration  $\geq 145$  mmol/L. NO generation and expression of eNOS were found down-regulated, but ONOO<sup>-</sup> generation, the expression of gp91, p-P38 and p-HSP27 were found up-regulated in endothelial cells cultured in sodium concentration  $\geq 145$  mmol/L. Tempol and SB203580 markedly inhibited NaCl-induced alterations in endothelial actin reorganization and activation of p38 MAPK. Tempol markedly inhibited NaCl-induced alterations in the generation of NO, ONOO<sup>-</sup>, the expression of eNOS and gp91, but SB203580 did not prevent these responses.

**Conclusion** The Result suggest that salt may induce endothelial cell dysfunction and thus control vascular tone by activating oxidative stress and p38 MAPK.

### Transplantation of cellular repressor of E1A-stimulated gene modified embryonic stem cells improves heart function post-myocardial infarction through blocking MAPK-ERK1/2 pathway

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**Background** Cellular repressor of E1A-stimulated genes (CREG) is a mannose-6-phosphate-containing secreted glycoprotein of 220 amino acids. It has been proposed that CREG acts as a ligand that enhances differentiation and/or reduces cell proliferation. In humans, the potential therapeutic role of embryonic stem cells (ESCs) in ischemic heart disease is subject to intense investigation. Particularly, the contribution of ESCs to angiogenesis and cardiomyogenesis in myocardial ischemia is not well established. In our studies, we induced myocardial infarct (MI) in mouse model, and monitored the effects of CREG modified ESCs transplantation on cardiac function.

**Methods** pCXN2-Flag-wtCREG, pCXN2-Flag-mutCREG and pCXN2-Flag-EGFP plasmids were transfected into ESCs by lipofectamine 2000. Myocardial infarction was induced by coronary artery ligation in seven- to nine-week-old mice. A total of  $2 \times 10^5$  ESC over-expressing wild type CREG (wtCREG), glycosylation mutant CREG (mutCREG) and EGFP or 20  $\mu$ l PBS were injected into the peri-ischemic area. Four groups of mice were analyzed for hemodynamic and pathologic parameters 1 and 2 months after MI and injection. Heart functions were assessed by small animal ultrasound system. Left ventricular pressure was measured by catheterization through right carotid artery. Fibrosis and collagen synthesis were assessed by Masson staining. Apoptosis was determined by TUNEL assay. Protein possibly involved in signaling pathway was detected by Western Blot.

**Result** wtCREG and mutCREG-ESCs significantly improved murine cardiac function after MI, as compared with EGFP-ESCs or PBS. The beneficial effect of wtCREG and mutCREG-ESCs may mostly be ascribed to their notable resistance to apoptosis and fibrosis, and to their anti-inflammatory action, since cardiomyogenesis was limited. These beneficial effects were associated with attenuation of the mitogen-activated protein kinase (MAPK)-extracellular signal-regulated kinase 1 (MAPK-ERK1)/2-dependent signaling cascade. In addition, CREG expression attenuated fibrosis and collagen synthesis through blocking MAPK-ERK1/2-dependent Smad2/3 activation in vivo.

**Conclusion** Therefore, the expression of CREG improves cardiac

functions and inhibits inflammation and fibrosis through blocking MAPK-ERK1/2-dependent signalling.

### Effect of apelin on the cardiac hemodynamics in hypertensive rats with heart failure

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**Background** Apelin has definite protective effects on various cardiovascular diseases, but the mechanism of how hypertension with heart failure (H-HF) is influenced by pyroglutamylated apelin-13 (Pyr-AP13) remains unclear.

**Methods** Male SD rats (200 – 220 g) were divided into five groups: (i) sham group (n = 8), (ii) H-HF group (n = 8), (iii) H-HF group, infusion of 0.1 mg Pyr-AP13 or 5%GS (n = 8), (iv) H-HF group, infusion of 1 mg Pyr-AP13 or 5%GS (n = 8), (v) H-HF group, infusion of 10 mg Pyr-AP13 or 5% GS (n = 8). Histological determination of the fibrosis was performed using hematoxylin eosin or Masson's trichrome staining. The concentration of cyclic adenosine 3', 5'-monophosphate (cAMP) was determined using ELISA method.

**Result** The expression of membrane and cytosol proteins was evaluated with Western blot analysis. Significant cardiac and perivascular fibrosis was observed in the H-HF group. After infusion of Pyr-AP13, the systolic and diastolic function was significantly improved in cardiac hemodynamic parameters in H-HF group. Apelin receptor (APJ) activated by exogenous infusion of Pyr-AP13, partially recycled from cytoplasm back to the plasma membrane, but membrane APJ was eventually down-regulated in H-HF rats than the sham rats.

**Conclusion** Our findings suggested that a complex was formed after Pyr-AP13 combined with cellular membrane APJ receptor, which may activate the phosphorylation of extracellular signal-regulated kinase 1/2 (P-ERK1/2) regulated by cAMP. However, endogenous down-regulation of APJ receptor Result in benefits from the exogenous administration of apelin reduction.

### Molecular genetics and clinical features of Chinese IPAH and HPAH patients

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**Objective** To improve knowledge of the genetic origin of PAH in Chinese patients with the disorder.

**Methods** We investigated 15 unrelated families with PAH and 290 sporadic PAH patients for BMPR2 mutations. Direct sequencing to detect mutations in coding regions and flanking splice sites, in addition to analysis of exon dosage across the entire gene using multiplex ligation-dependent probe amplification (MLPA®) showed a wide BMPR2 mutation spectrum in Chinese patients with PAH.

**Result** Our study reports an extensive molecular investigation of the BMPR2 gene in Chinese patients with PAH. The overall genetics of PAH in Chinese patients was similar to that of other populations already explored for this disease, although few characteristics were noteworthy. We found polymorphisms of the BMPR2 gene which are important to know in the context of genetic investigation of the disease in Chinese patients. The predisposing effect of the BMPR2 gene was similar to that

of other populations, and the younger age at diagnosis suggests that the BMPR2 mutation constitutes the first hit that increases the probability of an early onset of the disease.

**Conclusion** Our study provides an extensive investigation of the genetic etiology of Chinese heritable and idiopathic PAH which gives insight into the variety of BMPR2 mutations among different ethnic groups.

### Oestradiol ameliorates monocrotaline pulmonary hypertension via NO, PGI<sub>2</sub> and ET-1 pathways

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**Objective** Pulmonary hypertension (PH) continues to be a serious clinical problem with high mortality. As oestrogen is a potential vasodilator of the pulmonary circulation, this study examined the mechanisms by which 17 $\beta$ -oestradiol improves monocrotaline (MCT)-induced PH.

**Methods** Female Sprague-Dawley rats underwent bilateral ovariectomy or sham operations. The rats received MCT (50 mg/kg) and were treated with 17 $\beta$ -oestradiol (1 mg/kg/day) for 5 weeks or only from Week 4 to Week 5. Plasma 17 $\beta$ -oestradiol concentrations were decreased in sham-operated, MCT-treated rats compared with sham-operated rats ( $17.7 \pm 4.7$  vs  $50.3 \pm 15.4$  pg/mL;  $P = 0.029$ ). The 17 $\beta$ -oestradiol anabolic enzyme cytochrome P450 (CYP) 19 was decreased by MCT treatment, while the catabolic enzymes CYP 1A1 and 1B1 were increased.

**Result** Ovariectomized and MCT-treated rats had more severe PH. 17 $\beta$ -oestradiol suppressed pulmonary arterial smooth muscle cell proliferation and macrophage infiltration, and enhanced apoptosis by increasing nitric oxide and prostacyclin levels and reducing endothelin-1 levels. PI3K and Akt phosphorylations were markedly increased but were inhibited by 17 $\beta$ -oestradiol treatment in PH rats.

**Conclusion** Oestrogen deficiency may aggravate development of PH. 17 $\beta$ -oestradiol improved PH via activation of the PI3K/Akt pathway to regulate nitric oxide, prostacyclin and endothelin-1 expression.

### MicroRNA-31 regulate phenotypic modulation of human vascular smooth muscle cell via its target gene CREG

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**Background** Cellular repressor of E1A-stimulated genes (CREG) plays an important role in phenotypic modulation of Vs MCs, but the mechanism of its upstream signaling regulation is not clear. Recently, microRNAs (miRNA) have been found to play a critical role in cell differentiation and proliferation, suggesting that miRNA may be an upstream regulator of CREG. Thus, we aimed to investigate which miRNA bind to CREG directly and involved in CREG-mediated effect

on Vs MCs phenotypic modulation.

**Methods** Human Vs MCs were stimulated by platelet derived growth factor (PDGF) and serum starvation to establish phenotypic modulation model. Expression of CREG and Vs MC differentiation marker genes in different phenotypic Vs MCs were determined by Western blot. Computational analysis has suggested that miR-31 is able to bind to CREG mRNA 3'-UTR. To find the miRNA which has a negative relationship with CREG, CREG and miR-31 expressions were determined by qRT-PCR in Vs MCs with different phenotype. To overexpress and knockdown miRNA expression, miRNA mimic and inhibitor were used. SM  $\alpha$ -actin and CREG expressions were analyzed by Western blot and qRT-PCR. To identify miR-31 can bind to CREG directly, luciferase expression of a firefly luciferase reporter construct containing CREG mRNA 3'-UTR was measured by using a dual luciferase reporter system. At last, CREG was knocked down by its shRNA in Vs MCs and miRNA inhibitor was transfected into CREG deficient cells, SM  $\alpha$ -actin expression were determined by Western blot.

**Result** In cultured Vs MCs, Vs MC differentiation marker genes and CREG expressions were downregulated in differentiated Vs MCs and upregulated in proliferative cells. As expected, miR-31 and CREG have a negative relationship at protein and mRNA level in Vs MCs with different phenotype. Furthermore, gain-of-function and loss-of-function showed that SM  $\alpha$ -actin and CREG expressions are suppressed by miR-31 mimic and are increased by miR-31 inhibitor in vitro. More importantly, miR-31 mimic decreased luciferase expression driven by the construct of CREG mRNA 3'-UTR in HEK293 cells, confirming CREG is a direct target of miR-31. Finally, knockdown of CREG in Vs MCs, the effect of miR-31 inhibitor on SM  $\alpha$ -actin expression is decreased.

**Conclusion** We conclude that miR-31 directly binds to CREG and modulate Vs MC phenotype through its target gene CREG, and miR-31 can act as a more efficient biomarker of vascular diseases with pathological lesion based on Vs MC phenotypic modulation.

### CREG promotes vasculogenesis of embryonic stem cells by activating PI3K/Akt/VEGF pathway

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**Background** Vasculogenesis plays an important role under both physiological and pathological conditions. Factors controlling vasculogenesis is still far to be fully elucidated. Cellular repressor of E1A activating gene (CREG) has been reported to be highly expressed in endothelium and prevent injured endothelial cells from apoptosis, suggesting its potential role in regulating vasculogenesis. The aim of this study was to investigate the role and mechanism of CREG in regulating vasculogenesis of embryonic (ES) stem cells.

**Methods** CREG over-expression (wtCREG) and knock-down (shCREG)ES cell lines were established by transfection of wild type ES cell R1 (wtR1) with pCXN2-Flag-CREG-IRES-EGFP and mouse CREG shRNA vectors respectively, using ES cells expressing EGFP as a control (ctlR1). We first detected CREG expression during wtR1 and ctlR1 differentiation by Western Blot. Then embryoid bodies (EB) derived from 4 groups of ES cells were plated on fibronectin coated cover slips and cultured for 10 days to make an in vitro vasculogenesis model. Endothelial network formation was detected by CD31



immunofluorescence. Transcription of CD31, VEGFR2 and VEGF were measured by real time polymerase chain reaction (RT-PCR). Protein involved in several signaling pathways, including JNK, ERK1/2, PI3K/Akt and VEGFR2, VEGF were detected by Western Blot. PI3K/Akt inhibitor and VEGF neutralizing antibody were used for blocking study in wtCREG group. VEGF were supplemented for rescue study in shCREG group.

**Result** Expression of CREG increased with differentiation of ES cells in control group (wtR1 and ctrlR1). wtCREG had significantly higher density of endothelial network formation identified by CD31 immunofluorescence in contrast to shCREG, which barely had endothelial network formation. RT-PCR also showed that transcription level of CD31, VEGFR2 and VEGF are up-regulated in wtCREG and down-regulated in shCREG. Western blot showed no difference in JNK, ERK1/2, but significant change of PI3K/Akt, VEGFR2, VEGF parallel to CREG expression in 4 groups. Blocking assay showed that PI3K/Akt inhibitor wortmannin and VEGF neutralizing antibody could effectively eliminate the CREG induced vasculogenesis, and VEGF could successfully rescue failed vasculogenesis due to CREG gene silence.

**Conclusion** CREG promotes vasculogenesis of ES cells by activating PI3K/Akt/VEGF pathway.

### Cellular repressor of E1A-stimulated genes accelerates endothelial angiogenesis via integrin-linked kinase-PINCH-Cdc42 activation

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**Background** Cellular repressor of E1A-stimulated genes (CREG) is an important endothelial-protective gene, which is reported to modulate the mobility of endothelial cells. The study aimed to investigate the effects of CREG on endothelial angiogenesis.

**Methods** Aortic expression of CREG protein was detected by western blot and immunostaining in CREG heterozygous (CREG<sup>+/+</sup>) mice and wild-type littermates. Perfusion recovery of hind limb was valued by laser Doppler in mice and wild-type littermates 14 days after the hind limb arterial ligation. The matrigel experiments *in vivo* and *in vitro* were performed after the human umbilical vein endothelial cells (HUVEC) were infected by adenovirus overexpressing CREG or adenovirus expressing GFP as control, and the filopodium formation was observed to evaluate the CREG function on neovascularization. Different integrin-linked kinase (ILK) subunit site mutant plasmids and small interfering RNA identified p-Cdc42 were transfected into HUVEC to explore the mechanism through which CREG-mediated endothelial angiogenesis.

**Result** Aortic expression of CREG protein was detected to reduce remarkably in CREG<sup>+/+</sup> mice compared to that in wild-type littermates. Meanwhile, laser Doppler perfusion imaging showed that perfusion recovery was significantly impaired in CREG<sup>+/+</sup> mice than that in wild-type littermates after 14 days hind limb arterial ligation (78.23 ± 7.2% vs 12.15 ± 2.058% in calf; 58.23 ± 6.5% vs 32.15 ± 3.514% in thigh; *P* < 0.001). Subsequently, overexpression of CREG in HUVEC increased endothelial cell network formation *in vitro*, enhanced neovascularization and improved limb perfusion *in vivo*, accompanied by filopodium formation and changes in cell shape. Mechanismly, integrin-linked

kinase (ILK), a key adhesion plaque protein, participated in CREG-mediated endothelial angiogenesis. Furthermore, studies using small interfering RNA identified p-Cdc42 to be a key downstream molecule of ILK involved in CREG-mediated endothelial cell filopodium formation. Transfection with binding-site-mutant plasmids of ILK and co-immunoprecipitation revealed that CREG activated the ILK-PINCH complex, which is involved in the regulation of p-Cdc42 activation.

**Conclusion** CREG overexpression stimulates the endothelial filopodium formation and regulates angiogenesis via the ILK/PINCH/p-Cdc42 signaling pathway, which provides the basis for future studies in the field of angiogenesis.

### Overexpressing Cellular repressor of E1A-stimulated genes promote hypoxia-induced VEGF paracrine via HIF-1 $\alpha$ in mesenchymal stem cells

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**Background** Hypoxia inducible factor-1 $\alpha$  (HIF-1 $\alpha$ ) is the key transcription regulator for multiple angiogenic factors, including vascular endothelial growth factor (VEGF). Cellular repressor of E1A-stimulated genes (CREG) has also been identified a potent promoter of angiogenesis. However, the mechanisms by which CREG promotes angiogenesis are not fully understood. Here, we show that CREG is an effective stimulator of HIF-1 $\alpha$  under hypoxia in bone marrow-derived mesenchymal stem cells (BMSCs).

**Methods** All experiments were performed on rat BMSCs. The level of VEGF was measured by ELISA. The HIF-1 $\alpha$  mRNA was analyzed by RT-PCR. The level of HIF-1 $\alpha$  protein and the mechanisms mediating these proangiogenic effects were determined by Western blotting.

**Result** We found that VEGF release from BMSCs was significantly increased in parallel with high level of HIF-1 $\alpha$  in BMSCs following anoxia or hypoxia in time-dependent manner. Furthermore, the level of VEGF released from BMSCs overexpressing CREG and the expression of HIF-1 $\alpha$  in BMSCs overexpressing CREG were higher than the normal BMSCs under hypoxia. Rather, HIF-1 $\alpha$  steady-state mRNA was also affected by CREG. This effect was associated with constitutive activation of phosphatidylinositol 3-kinase (PI3K)/Akt and its effector p70 S6 kinase (P70S6K), but not extracellular-signal regulated kinase 1/2. The use of small molecule inhibitors LY294002 or rapamycin to inhibit PI3K/Akt and p70S6K activities, respectively, resulted in diminished HIF-1 $\alpha$  activation and subsequent VEGF expression. RNA interference-mediated knockdown of HIF-1 $\alpha$  suppressed CREG-induced VEGF synthesis and angiogenic tube formation, confirming that the effect was HIF-1 $\alpha$  specific.

**Conclusion** Overexpressing CREG promote hypoxia-induced VEGF paracrine via HIF-1 $\alpha$  in mesenchymal stem cells. Therefore, CREG could play a major role in angiogenesis and vascular remodeling.

## Relationship between paraoxonase 1 (PON1) gene polymorphisms, haplotypes, concentration, activity and immunohistochemical analysis with coronary artery disease risk in Chinese Han population

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**Background** Paraoxonase 1 (PON1) is a high-density lipoprotein (HDL)-associated enzyme capable of inhibiting the progression of atherosclerosis, thus preventing the development of coronary artery disease (CAD). The polymorphisms of PON1 gene are known to affect the PON1 concentration and activity, thereby affect the CAD risk. As to its crucial role in preventing of CAD, we determined PON1 polymorphisms and haplotypes, concentration and activity, in addition to the immunohistochemical analysis of PON1 in this population and correlated them with CAD.

**Methods** A total of 864 controls and 792 patients with CAD confirmed by angiography ( $\geq 70\%$  stenosis) were recruited in Shenyang Northern Hospital. The concentration of PON1 was measured with Human PON1 Elisa Kit. PON1 activity towards phenylacetate was determined by spectro-photometrically at 270 nm. In addition, genotypes were determined by polymerase chain reaction (PCR). The genotypes and haplotypes were determined by SHEsis and SNPStats softwares respectively. PON1 expression in coronary and carotid arteries was detected by immunohistochemical analysis.

**Result** Among all studied polymorphisms, only Q192R (rs662) had significant effect on the risk of CAD (Q192R,  $P < 0.001$ ). In a logistic regression model, after adjustment for the conventional risk factors for CAD, QR and RR genotypes of Q192R had significantly higher CAD risk. Haplotypes Q-L-T-C-G (OR: 0.511, 95% CI: 0.401 – 0.651) was also significantly associated with CAD. Both serum PON1 concentration and activity reduced significantly in CAD patients as compared to the controls ( $P < 0.001$ ). Immunohistochemical analysis showed that during the atherosclerosis of coronary artery, smooth muscle cell staining for PON1 was greatly reduced as compared to the controls, so did in the external carotid artery.

**Conclusion** The coding Q192R polymorphism and Q-L-T-C-G haplotype are all independently associated with CAD. Serum PON1 concentration and activity were lower in CAD patients than the controls. Additional with the evidence of immunohistochemical analysis, our data add support to the point that PON1 is a strong factor in predicting the risk of CAD.

## No association between PON1 gene single nucleotide polymorphisms and clopidogrel resistance in Chinese Han population

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**Background** Clopidogrel requires bioactivation in vivo to convert

the pro-drug into its active metabolite to show its antiplatelet effects. The variability in the clinical response to clopidogrel treatment has been attributed to genetic factors, but the specific genes and mechanisms underlying clopidogrel bioactivation remain unclear. Recent studies report that Paraoxonase-1 (PON1) as a key enzyme play vital part in clopidogrel bioactivation. The aim of our study was to assess whether PON1 gene polymorphisms are correlation with clopidogrel resistance (CR) in patients receiving clopidogrel after percutaneous coronary intervention (PCI).

**Methods** A total of 850 patients undergoing PCI were enrolled in this study, according to clopidogrel response which was assessed by post-treatment 20  $\mu\text{mol/L}$  ADP -induced platelet aggregation ratio (PRA), RPA (RPA  $\geq 70\%$ ) was defined as clopidogrel resistance (CR). We genotyped five SNPs of PON1 gene, the coding polymorphisms Q192R (rs662) and L55M (rs854560), the promoter polymorphisms -108C/T (rs705379), -162A/G (rs705381) and -909G/C (rs854572) variants by using polymerase chain reaction (PCR). In addition, activity level of PON1 towards phenylacetate was measured by spectro- photometrically at 270 nm. The SPSS 21.0 software was used to analyze all the included data.

**Result** The genotype frequencies of all studied SNPs were well to the Hardy-Weinberg equilibrium in both CR group and NCR group. Between the two groups, the five SNPs have the similar genotype and allele frequency (Q192R,  $P = 0.325$  and  $0.421$ ; L55M,  $0.806$  and  $0.499$ ; rs705379,  $P = 0.426$  and  $0.263$ ; rs705381,  $P = 0.513$  and  $0.484$ ; rs854572,  $P = 0.482$  and  $0.798$  respectively). The serum PON1 activity was lower in CR as compared to the NCR group, but not statistically significant ( $P = 0.554$ ). In the two groups, we did not observed any significant difference in PON1 gene polymorphisms and PON1 activity.

**Conclusion** This study demonstrates that neither PON1 gene polymorphisms nor PON1 activity are associated with CR in patients receiving clopidogrel after PCI.

## Association between polymorphism in the chemokine CCL21 gene rs10972201 and coronary artery disease in Chinese Han population

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**Background** Atherosclerosis is an inflammatory disease characterized by the formation of atherosclerotic plaques. Homeostatic chemokine CCL21 was up-regulated within the atherosclerotic lesions, which could potentially contribute to atherogenesis and plaque destabilization with subsequent thrombus formation and development of acute ischemic events. Although CCL21 expression may be genetically determined, the relationship between CCL21 polymorphisms and the risk of coronary artery disease (CAD) is unclear. The aim of this study was to investigate the relationship between the polymorphism of CCL21 rs10972201 and the CAD in a Chinese Han population.

**Methods** Matched case-control study was conducted between January 2010 to September 2011 among 282 patients with CAD and 258 hospitalized controls. All the subjects had undergone coronary angiography, and inclusion criteria for CAD were  $\geq 50\%$  narrowing of the lumen of at least 1 of the major coronary arteries by coronary angiography. Additionally, angiographic severity of disease was

defined as 0-, 1-, 2- or 3-vessel disease based on the number of luminal narrowing  $\geq 50\%$  in the three major coronary arteries. The control subjects were selected from the subjects admitted to the hospital for the evaluation of chest pain, whose major coronary artery had no stenosis, and did not have any vascular disease. The groups were matched for age, sex, body mass index, smoking, hypertension, hypercholesterolemia, and diabetes. Polymorphic genotypes were determined by polymerase chain reaction and sequencing analysis.

**Result** The genotype frequencies of GG, AG and AA in CCL21 rs10972201 polymorphism were 83.33%, 15.96%, 0.71% in CAD group, 84.49%, 15.12%, 0.39% in the control respectively. The A allele frequency of CCL21 rs10972201 polymorphism allele in CAD cases and controls were 8.69% and 7.95% respectively. No significant differences in the genotype or allele frequencies were revealed between the two groups ( $P = 0.864$  and  $0.659$ , respectively). Further stratification analysis between the polymorphism of CCL21 rs10972201 and angiographic severity of CAD also yielded negative Result ( $P > 0.05$ ).

**Conclusion** This study indicates that the CCL21 rs10972201 polymorphism is unlikely to be a major contributor to the pathogenesis of CAD.

### Combination of danhong injection and adipose-derived stem cells transplantation promote angiogenesis in ischemic hind limb of diabetic nude mice through a endogenous hydrogen sulfide dependent mechanism

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**Objective** To investigate the efficacy of Danhong injection (DH) combined with Adipose tissue-derived stem cells (ADSCs) transplantation on angiogenesis in diabetic hind limb ischemia model and the related molecular mechanism.

**Methods** Male nude mice were induced to diabetes by injection of streptozotocin intraperitoneal. Diabetes modeling success was identified by random blood glucose levels higher than 16 mmol/L twice. After 2 weeks, hind limb ischemia model was established by ligation and excision of femoral artery. Forty 8-week-old nude mice were randomly divided into four groups: group I ( $n = 10$ ): diabetic hind limb ischemia model, group II ( $n = 10$ ): ADSCs ( $1 \times 10^6$  cells, i.m.) transplantation, group III ( $n = 10$ ): DH ( $2 \mu\text{L/g} \times 7$  days) i.p., group IV ( $n = 10$ ): combination of DH and ADSCs transplantation. After 2 weeks, perfusions, vessel regeneration, and local VEGF expression of lower limbs among different groups were evaluated with LDPI, X-ray arteriography, real-time PCR and ELISA respectively. And microvascular densities of lower limb muscle were investigated using immunocytochemical staining of CD31. The expression of cystathionine beta synthase (CBS), cystathionine gamma lyase (CSE), 3-mercaptopyruvate sulfurtransferase (3-MST), which are three major sources for endogenous enzymatic production of hydrogen sulfide ( $\text{H}_2\text{S}$ ), were measured by western blot. Hydrogen sulfide tissue concentration in mice ischemic muscles was measured by pre-column derivatization with monobromobimane (mBrB) and the corresponding reversed-phase high performance liquid chromatography (RP-HPLC)- fluorescence quantitation method.

**Result** Only ADSCs transplantation or DH ip could significantly increase perfusion, promote the formation of collateral circulation, and

enhance local VEGF, CBS/CES/3-MST and  $\text{H}_2\text{S}$  expression after 2-week intervention compared with control group, without decreasing blood glucose and increasing serum  $\text{H}_2\text{S}$  and VEGF. And meanwhile capillary density of the ischemic hind limb showed similar trend by CD31 staining. While combination of DH and ADSCs transplantation could increase the protective effects further vs DH ip or ADSCs transplantation alone.

**Conclusion** ADSCs transplantation or DH ip alone could improve ischemia perfusion and vascular tube-like generation in diabetic hind limb models through endogenous hydrogen sulfide actions. And, combination of DH ip and ADSCs transplantation could exert more protective effects. Which might be a novel therapy strategy against diabetic hind limb ischaemia.

### Advanced Glycation End Products induces apoptosis and shortens telomere length in human adipose tissue-derived stem cells through modulation of MAPK pathways

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**Objective** To investigate the effects of advanced glycation end products (AGEs) on apoptosis and telomere length of human adipose tissue-derived stem cells (ADSCs) and the related molecular mechanism.

**Methods** ADSCs were obtained by combination with enzymatically digestion and centrifugation, and then were identified to observe cultured cells' morphology, induce differentiation towards adipocytes, osteocytes and chondrocytes, and determine by fluorescence activated cell sorter (FACS) analysis. The cells were exposed to AGE-HSA (concentration of 0, HSA 200, 10, 50, 100, 200  $\mu\text{g}/\text{ml}$ ) for 24 h. The apoptotic rates were investigated by Annexin V-FITC Apoptosis Detection Kit and Caspase-Glo™ 3/7 Assay. Telomere lengths were measured by quantitative PCR. The expression of RAGE, p-ERK1/2, p-p38 MAPK, p-JNK1/2 and caspase-3 was determined by western blot. Then the cells were preincubated with ERK, p38 and caspase-3 inhibitors before the stimuli, the apoptosis and telomere length of ADSCs were evaluated once more.

**Result** Compared with the 200  $\mu\text{g}/\text{ml}$  HSA group, AGE-HSA (50, 100, 200  $\mu\text{g}/\text{ml}$ ) could significantly inhibit the apoptosis, short telomere length, decrease phosphorylation-ERK1/2 (P-ERK1/2), and increase p-p38MAPK, but do not affect expressions of p-JNK1/2 in ADSCs. Moreover, treatment of ADSCs with 100  $\mu\text{g}/\text{ml}$  AGE-HSA resulted in activation of caspase-3. Furthermore, PD98059 (ERK1/2 inhibitor) significantly enhanced AGE-HSA induced apoptosis and shortened telomere length in ADSCs, whereas caspase-3 inhibitor or SB203580 (P-p38MAPK inhibitor), decreased apoptosis and longer telomere length in ADSCs.

**Conclusion** AGE-HSA could promote the apoptosis and shortened telomere length in ADSCs via of activation of RAGE-MAPK-Caspase3 pathway. These findings partly revealed a novel mechanism about telomere length participating in the dysfunction of ADSCs induced by AGE-HSA.



## Effects of advanced glycation end products on function and angiogenesis of adipose tissue-derived stem cells and protective effects of Danhong injection

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**Objective** To investigate the effects of Nε-(carboxymethyl) Lysine albumin (CMLs), a primary advanced glycation end products isoform in diabetic body, on function and angiogenesis of adipose tissue-derived stem cells (ADSCs) and protective effects of Danhong injection.

**Methods** ADSCs were obtained by combination with enzymatically digestion and centrifugation, and then were identified to observe cultured cells' morphology and induce differentiation towards adipocytes, osteocytes and chondrocytes. The cells were exposed to 5 different interventions respectively for 24 h, including PBS, 60 μg/ml BSA, 60 μg/ml CML-BSA, 0.5 μl/ml DH and 60 μg/ml CML-BSA+0.5 μl/ml DH. The proliferation capability of such cells were evaluated using WST-1 assay, migration ability were explored by transwell assay, the apoptotic rates were investigated by FCM, secreted VEGF in culture supernatant were measured by ELISA, and angiogenesis of such cells was observed in matrigel in vitro.

**Result** Compared with the BSA control group, proliferation, migration and secretion capability of ADSCs were inhibited by stimuli with CML-BSA (n = 6, P < 0.05), but the apoptosis of such cells were promoted. Finally, angiogenesis of ADSCs was significantly inhibited. DH (0.5 μl/ml) could promote proliferation, migration and secretion capability but inhibit apoptosis of ADSCs (n = 6, P < 0.05) vs PBS, and furthermore partially reverse the negative effects of CML-BSA (60 μg/ml) on ADSCs (n = 6, P < 0.05).

**Conclusion** CMLs could significantly inhibit proliferation, migration, but promote apoptosis and reduce VEGF expression and secretion of ADSCs. DH injection would partially reverses the negative effects of CMLs. CMLs could significantly inhibit angiogenesis of ADSCs, which would partially reversed by DH injection.

## Gene-gene interactions among PPAR α / δ / γ polymorphism for lipid accumulation product in Chinese Han population

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**Objective** This study aimed to investigate the association between 10 single-nucleotide polymorphism (SNPs) in the peroxisome proliferator-activated receptors (PPARs) and lipid accumulation product (LAP), and to discuss whether there is a gene-gene interaction among this 10 SNPs of PPARs.

**Method** We randomly selected 820 subjects of genetic

polymorphism research based on the Metabolic syndrome (MS) study in Jiangsu province, and no individuals were consanguineous. Ten SNPs (rs135539, rs4253778, rs1800206, rs9794, rs2016520, rs10865710, rs1805192, rs709158, rs3856806 and rs4684847) in PPARα/δ/γ were genotyped. The genetic polymorphism of rs4253778 was detected by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP), while other SNPs were determined by using the Taqman fluorescent probe. A linear regression model was used to analyze the relations between gene polymorphism and LAP. Mean difference (Difference) and 95% confident interval (95% CI) were calculated. Gene-gene interactions were explored by the method of generalized multifactor dimensionality reduction (GMDR).

**Result** The 10 SNPs were within Hardy-Weinberg equilibrium (P > 0.05). Linkage analysis showed that there was no significant linkage disequilibrium between these polymorphism (all D' < 0.75). There was significant difference in the rs709158 allele and genotype distribution between male and female participants (P = 0.011). The frequency of the G allele of rs709158 was higher in male participants (33.7% in male subjects Vs 27.6% in female subjects, P = 0.011). Single factor analysis showed that after adjusted for gender, age, smoking, alcohol consumption, high fat diet and low fiber diet, rs1800206, rs1805192 and rs3856806 were significantly associated with a higher level of LAP, the Difference (95% CI) were 35.39 (25.66 – 45.12), 13.56 (5.12 – 21.99) and 14.24 (6.04 – 22.45), respectively. While rs2016520 was significantly associated with a lower level of LAP, the Difference (95% CI) was – 15.64 (-23.80 – 7.48). GMDR analysis showed a significant gene-gene interaction among rs135539, rs1800206 of PPARα, rs2016520 of PPARδ and rs10865710, rs3856806, rs709158, rs1805192, rs4684847 of PPARγ for eight-dimension models (P = 0.001), in which prediction accuracy was 0.6151 and cross-validation consistency was 10/10.

**Conclusion** The rs1800206, rs2016520, rs1805192 and rs3856806 were significantly associated with the level of LAP, and had gene-gene interacted with rs135539, rs10865710, rs709158 and rs4684847. PPARα/δ/γ polymorphisms may contribute to the level of LAP independently and/or in an interactive manner.

## Regulatory effects of Shc-related phosphotyrosine adaptor proteins on vascular aging

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**Objective** p66shc (66-kilodalton isoform of Shc gene products) gene, which encodes a phosphotyrosine signal adapter protein, extends life span by 30%. To observe Regulatory effects of Shc-related phosphotyrosine adaptor proteins on vascular aging.

**Methods** On the base of regular observation of aortic structure changes in 4, 10, 16, 24 months old rats respectively, Malondialdehyde (MDA) and superoxide dismutase (SOD) level of aorta plasma were detected, and the compliance of rat carotid segment was measured by constant liquid injection. p66shc, Caspase-3 gene expression associated with senescence in healthy rats were analyzed by Western-blotting in the same periods.

**Result** With aging, aorta wall thickened, fibrosis degree increased. MDA concentration evidently d ascended (P < 0.05), but SOD markedly declined (P < 0.05). The carotid flexibility increased, especially flexibility area were significantly different (P < 0.05). The protein expressions of p66shc, Caspase-3 were increased in vascular ageing-related remodeling,

which suggests that p66shc, Caspase-3 activity may play an important role in regulating vascular senescence lifespan *in vitro*.

**Conclusion** Vascular aging has its specific structural alterations, one of its molecular mechanisms might be associated with increasing expression level of p66shc, Caspase-3 with aging. Further elucidating its underlying mechanism may provide theoretical bases for prevention and treatment of atherosclerosis.

### Study on Valsartan delaying endothelial cell senescence and gene expression of p16<sup>INK4a</sup>

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**Aim** To investigate the role of Valsartan on Angiotensin II (Ang II)-induced senescence of human umbilical endothelial cell senescence and gene expression of p16<sup>INK4a</sup>.

**Methods** HUVECs were cultured *in vitro* and intervened by Ang II (10<sup>-6</sup> mol/L) and Valsartan (Ang II type 1 receptor blocker). HUVECs were divided into 3 groups, the control group, Ang II group, Valsartan group.  $\beta$ -gal staining was used to identify cell aging status. Flow cytometry was used for analyzing the cell cycle changes; the positive cell rate of p16<sup>INK4a</sup> was detected by immunocytochemical staining, and the expressions of p16<sup>INK4a</sup> apotein were determined by Western-blotting.

**Result** Compared with the control cells, the positive cell number of  $\beta$ -gal staining was significantly higher in Ang II-induced cells (81.24  $\pm$  6.46)%; the cell cycle was at G<sub>0</sub>-G<sub>1</sub> (88.36  $\pm$  6.45)%. In Valsartan group, p16<sup>INK4a</sup> protein expression decreased evidently (P II group, which suggests that p16<sup>INK4a</sup> activity plays an important role in regulating vascular endothelial cell senescence lifespan *in vitro*).

**Conclusion** Cell Endothelial cell senescence is induced by Ang II. One of its molecular mechanisms might be associated with increasing the expression level of p16<sup>INK4a</sup> in aging cell, and then up-regulating the amount of cells blocking in G<sub>1</sub> phase of cell cycle. Valsartan could antagonize the process effectively and delay endothelial cell aging significantly.

### The regulatory effects of peroxiredoxin II on cardiac contractility and the underlying mechanisms

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Peroxiredoxin II (prxII), a cytosolic form of the anti-oxidant peroxiredoxin family, has been reported to protect cardiomyocytes from oxidative stress-induced injury. Interestingly, we found that prxII expression levels were decreased to 60% in failing human hearts, compared to donors. However, the expression levels of this cellular peroxidase were significantly increased in the hyperdynamic hearts of two genetically modified mouse models with: a) phospholamban ablation; and b) overexpression of the active inhibitor-1 of protein phosphatase 1. To determine whether alterations in prxII levels may contribute to altered cardiac contractility, we generated adenoviruses

with sense (Ad-prxII) and anti-sense prxII (Ad-prxII-AS) insertions and infected adult rat cardiomyocytes with these viruses. Myocyte contractility and calcium kinetics were then recorded after 24 hours of infection. Overexpression of Ad-prxII was associated with decreases in the basal rates of contraction and relaxation to 31 and 25%, respectively, of GFP control levels. The fractional shortening was also reduced to 36% of GFP controls. In parallel, calcium kinetics were inhibited as evidenced by 65% decreases in the peak of the calcium transient and prolongation in the time to 80% decay of calcium peak to 70% of controls. The caffeine-induced sarcoplasmic reticulum calcium content was also reduced to 80% of GFP controls. Isoproterenol stimulation abolished the inhibitory effects of prxII overexpression. On the other hand, Ad-prxII-AS infected cardiomyocytes exhibited enhanced contractile parameters and Ca-kinetics, compared to GFP controls under basal conditions, but the maximally stimulated parameters by Iso were similar among the 3 groups. Interestingly, the depressed or increased contractility by Ad-prxII or Ad-prxII-AS respectively was associated with parallel decreases or increases in phosphorylation of phospholamban (Ser16 and Thr17), compared to GFP-infected cells. There were no alterations in the expression levels of key SR calcium handling proteins: SERCA2, phospholamban, calsequestrin and ryanodine receptor in the infected cells. These findings indicate that prxII, an anti-oxidant protein, may regulate basal cardiomyocyte contractile performance through phospholamban phosphorylation.

### The expression of cystathionine gamma-lyase/hydrogen sulfide pathway in CVB3-induced myocarditis and the protective role of hydrogen sulfide

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**Objective** This study aimed to investigate the expression of cystathionine gamma-lyase/hydrogen sulfide pathway in CVB3-induced myocarditis and the protective role of hydrogen sulfide.

**Methods** A total of 140 five-week-old Balb/c male mice were randomly assigned to four groups: control group, viral myocarditis group, sodium bisulfide (NaHS) group (50  $\mu$ mol/kg), DL-propargylglycine (PAG) group (40 mg/kg). Experimental viral myocarditis was induced by injecting coxsackievirus B3 (CVB3). NaHS or PAG was administered intraperitoneally to mice with viral myocarditis from day 0 to day 10 after infection. On day 4 and day 10, ten mice of each group were sacrificed, and then blood and heart specimens were harvested. The heart sections were stained with hematoxylin and eosin. Levels of H<sub>2</sub>S, IL-6 and TNF- $\alpha$  were measured by ELISA. The expressions of CSE mRNA and CVB3 mRNA were investigated by quantitative real time PCR (qRT-PCR), and the expression of CSE protein was detected by western-blotting.

**Result** The levels of H<sub>2</sub>S, CSE mRNA and CSE protein were decreased in CVB3-induced myocarditis. Treatment of NaHS attenuated the histopathological severity of CVB3-induced myocarditis and upregulated the levels of serum and tissue H<sub>2</sub>S, while PAG as an irreversible CSE inhibitor aggravated myocardial injury, inflammatory cells infiltration and interstitial edema and inhibited the expression of H<sub>2</sub>S and CSE. Moreover, the RT-PCR also showed that NaHS inhibited the expression of CVB3 mRNA, while PAG upregulated the expression

of CVB3 mRNA.

**Conclusion** The CSE/H<sub>2</sub>S pathway is downregulated in CVB3-induced viral myocarditis. Treatment with PAG which inhibits the production of endogenous H<sub>2</sub>S can exacerbate the disease and promote virus propagation, while NaHS as a H<sub>2</sub>S donor, plays a protective role to infected myocardium and suppresses virus replication during the early stage.

### Panax notoginseng saponins ameliorates coxsackievirus B3-induced myocarditis by activating cystathionine gamma-methyltransferase/hydrogen sulfide pathway

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**Objective** This study aimed to investigate whether or not panax notoginseng saponins (PNS) ameliorates coxsackievirus B3-induced myocarditis by activating cystathionine gamma-methyltransferase (CSE)/hydrogen sulfide (H<sub>2</sub>S) pathway.

**Methods** A total of 140 five-week-old Balb/c male mice were randomly assigned to five groups: control group, viral myocarditis group, sodium bisulfide (NaHS) group (50 μmol/kg), DL-propargylglycine (PAG) group (40 mg/kg) and panax notoginseng saponins (PNS) group (100 mg/kg). After injection for four and ten days, ten mice of each group were sacrificed, then blood and heart specimens were harvested. Histopathology was performed using haematoxylin and eosin. ELISA was used to measure the concentration of H<sub>2</sub>S. Total RNA was collected for qRT-PCR of CVB3 mRNA and CSE mRNA, and total protein was collected for western blot analysis of CSE protein.

**Result** The serum and tissue H<sub>2</sub>S level, CSE mRNA and CSE protein levels were decreased in CVB3-induced myocarditis. PNS and NaHS treatments alleviated myocardial injury and upregulated the expression of H<sub>2</sub>S, CSE mRNA and CSE protein on post-infection day 4 and day 10. PAG, as an irreversible CSE inhibitor, aggravated myocardial injury and downregulated the expression of H<sub>2</sub>S, CSE mRNA and CSE protein. The qRT-PCR also showed that PNS and NaHS inhibited expression of CVB3 mRNA and PAG upregulated expression of CVB3 mRNA. Moreover, all the effects of PNS are much more positive than NaHS and no significant difference was observed between the groups on post-infection day 4 and day 10.

**Conclusion** The data indicated that PNS ameliorated myocardium injury and inhibited virus replication by activating the CSE/H<sub>2</sub>S pathway in CVB3-induced myocarditis. These results suggested that PNS played a potential role as a potential medication for viral myocarditis therapy.

### Ischemia/reperfusion-induced MKP-3 impairs endothelial NO formation via inactivation of ERK1/2 pathway

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Mitogen-activated protein kinase phosphatases (MKPs) are a family

of dual-specificity phosphatases. Endothelial cells express multiple MKP family members, such as MKP-3. However, the effects of MKP-3 on endothelial biological processes have not yet been fully elucidated. Here, we address the association between MKP-3 and endothelial Nitric oxide (NO) formation under ischemia/reperfusion (IS/RP) condition. Human umbilical vein endothelial cells (HUVECs) were subjected to IS/RP treatment. The MKP-3 expression and NO formation were examined. IS/RP induced endothelial MKP-3 expression and inhibited eNOS expression and NO formation, accompanied by an increase of endothelial apoptosis. The siRNA experiments showed that MKP-3 was an important mediator in impairing eNOS expression and NO production in endothelial cells. Transfection of HUVECs with constitutively active ERK plasmids suggested that the above mentioned effect of MKP-3 was via inactivation of ERK1/2 pathway. Furthermore, impairment of eNOS expression was restored by treatment of histone (HDAC) inhibitor and related to histone deacetylation and recruitment of HDAC1 to the eNOS promoter. Finally, Salvianolic acid A (Sala) markedly attenuated induction of MKP-3 and inhibition of eNOS expression and NO formation under endothelial IS/RP condition. Overall, these results for the first time demonstrated that IS/RP inhibited eNOS expression by inactivation of ERK1/2 and recruitment of HDAC1 to the gene promoter, leading to decreased NO formation through a MKP-3-dependent mechanism in endothelial cells, and Sala has therapeutic significance in protecting endothelial cells from impaired NO formation in response to IS/RP.

### Angiotensin II-Induced cardiomyocyte hypertrophy is attenuated by neuregulin receptor degradation protein-1

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**Objective** Recent studies indicate ubiquitin-proteasome system particularly the E3 ubiquitin ligase plays a key role in cardiac hypertrophy. We have previously shown that overexpression of Neuregulin receptor degradation protein-1 (Nrdp1) increased cardiomyocyte injury by inhibiting the target protein of ErbB3 and downstream signaling molecules. In the present study we asked whether overexpression of Nrdp1 might exhibit antihypertrophic effects, and therefore we tested this hypothesis both in vitro.

**Methods** Neonatal cardiomyocytes were treated with Ang-II for different times and different concentrations, along with RT-PCR and Western Blotting were used to detect the levels of Nrdp1 mRNA and protein. Neonatal cardiomyocytes were infected with adenovirus containing GFP (Ad-GFP) and Nrdp1 wild-type (Ad-Nrdp1), then treated with Ang-II for 24 hours. Quantitative real-time PCR was used to determine the expression of hypertrophy-related genes. Immunofluorescence and 3H-leucine incorporation assay were performed to detect the cell size.

**Result** Ang-II stimulation markedly downregulated Nrdp1 mRNA and protein expression in cardiomyocytes especially in 24 hours ( $P < 0.05$ ). After stimulated by Ang II, the area of cardiomyocytes and 3H-leucine incorporation rate of cardiomyocyte markedly decreased in Ad-Nrdp1 group compared with Ad-GFP control group ( $P < 0.05$ ). Furthermore, the mRNA levels of ANF and β-MHC in Ad-Nrdp1 group were significantly lower than that of Ad-GFP group ( $P < 0.05$ ).

**Conclusion** The E3 ligase protein Nrdp1 prevents Ang-II-induced



cardiomyocyte hypertrophy. Thus, overexpression of *Nrdp1* might represent a novel approach to attenuate pathological cardiac hypertrophy.

### The establishment and mechanism of spontaneous calcification of aortic interstitial cells in SD rats

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**Objective** Aortic valve interstitial cells (AVICs) play a vital role in the development of aortic valve stenosis. The aim of this study is to observe that whether or not AVICs calcified spontaneously and to detect the expression of osteogenic factors in the formation of calcified cell nodules.

**Methods** AVICs were cultured in explant method, calcification were detected by Von Kossa, alizarin red S stain and a calcium assay kit, and expression of osteogenic factors, such as *Cbfa1*/OC/BMP-2/BMP-4, were detected by RT-PCR and western-blot analysis at different times.

**Result** 1. AVICs aggregated and formed small cell nodules after 4–6 day culture, and the number of nodules become more and the diameter is bigger at day 12 than that at day 6.

2. The cell nodules were positive by Von Kossa and alizarin red S stain, which indicated that they were calcified nodules. The statistical analysis indicated that both the content of alizarin red S and calcium at day 12 were higher than that at day 0 and day 6 ( $F = 106.167$ ,  $F = 116.379$ , respectively;  $P < 0.001$ ).

3. The statistic analysis of the osteogenic gene expression indicated that the *Cbfa1*/OC/BMP-4 mRNA were lowest at day 0, higher at day 6 and highest at day 12 ( $F = 410.106$ ,  $\chi^2 = 7.200$ ,  $F = 38.463$ , respectively;  $P < 0.005$ ), and BMP-2 mRNA were lowest at day 0, higher at day 6 and day 12 ( $F = 56.565$ ,  $P < 0.001$ ). The statistic analysis of the osteogenic protein expression indicated that the BMP-2/4 protein expression were lowest at day 0, higher at day 6 and highest at day 12 ( $\chi^2 = 7.200$ ,  $F = 452.482$ , respectively;  $P < 0.05$ ).

**Conclusion** AVICs calcified spontaneously with extend culture time, in which the differentiation of AVICs into osteoblasts-like cells may play an important role in the process of calcification.

### Expression and significance of Fibulin-5 in the vessel wall of aortic dissection

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**Objective** To discuss the effect of Fibulin-5 on the integrity of aortic structure and function.

**Methods** EVG staining, SP immunohistochemistry and Western blot were used to identify the differential expression of Fibulin-5 between the AD group (AD group,  $n = 12$ ) and the control group (control group,  $n = 12$ ).

**Result** The morphology and arrangement of elastic fibers in the aortic media were anomalous in AD group. Immunohistochemistry showed Fibulin-5 positively expressed in the cytoplasm of smooth muscle cells, and the expression of Fibulin-5 was lower in the AD group than control group. Western blot also showed the expression of Fibulin-5

was lower in the AD group with statistical significance ( $P < 0.05$ ).

**Conclusion** Down-regulation of Fibulin-5 in the aortic media may affect the synthesis of elastic fibers, resulting in a decrease of elastic fibers in the media and structure disturbance of the media. Finally, it indicates that Fibulin-5 may play a crucial role in the formation of AD.

### Loss of cardioprotection by sevoflurane postconditioning against myocardial ischemia-reperfusion injury in old rats

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**Background** Sevoflurane postconditioning protects young hearts against ischemia-reperfusion injury. It is unknown whether the infarct-limiting effect is also maintained in aged cohorts, and whether there are age-associated differences in the underlying mechanisms.

**Methods** Young or old rats were subjected to 30 min of myocardial ischemia, induced by left anterior descending coronary artery occlusion, followed by 2 h of reperfusion with or without anesthetic postconditioning, administered by inhalation of 1.0 MAC (minimal alveolar concentration) sevoflurane initiated immediately upon reflow for 5 min in the presence or absence of LY294002 (PI3K inhibitor) or U0126 (MEK1/2 inhibitor). Myocardial infarct size was measured by Evans Blue and TTC staining. Cardiac expression level of phosphorylation of Akt and ERK1/2 was determined by Western blotting analysis. Myocardial NAD<sup>+</sup> content was measured to indicate mitochondrial permeability transition pore (mPTP) opening.

**Result** Sevoflurane postconditioning significantly decreased myocardial infarct size in young ( $35 \pm 4\%$  vs  $56 \pm 3\%$ ,  $P < 0.05$ ) but not old rats ( $45 \pm 3\%$  vs  $47 \pm 4\%$ ,  $P > 0.05$ ), compared with each control group. Sevoflurane postconditioning substantially augmented the phosphorylation level of Akt ( $0.74 \pm 0.03$  arbitrary units vs  $0.27 \pm 0.03$  arbitrary units,  $P < 0.05$ ) and ERK1/2 ( $0.85 \pm 0.04$  arbitrary units vs  $0.29 \pm 0.04$  arbitrary units,  $P < 0.05$ ) compared with control group, which was abolished by LY294002 and U0126 in young rat hearts respectively, but failed to activate Akt and ERK1/2 in old rat hearts. Cardiac NAD<sup>+</sup> content was significantly higher in response to sevoflurane postconditioning in young ( $118.57 \pm 9.27$  nmol/g tissue vs  $46.78 \pm 4.54$  nmol/g tissue,  $P < 0.05$ ) but not old rats ( $58.50 \pm 7.16$  nmol/g tissue vs  $61.15 \pm 5.50$  nmol/g tissue,  $P > 0.05$ ), compared to each control group. LY294002 or U0126 abrogated the infarct-sparing effect and inhibition of loss of NAD<sup>+</sup> induced by sevoflurane postconditioning in young rats respectively.

**Conclusion** Cardioprotection mediated by sevoflurane postconditioning in young rats is not effective in senescent rats, which may at least be the consequence of failure to activate Akt and ERK1/2, and resultant failure to inhibit mPTP opening.

### miRNA-16/21 as a biomarker for coronary atherosclerotic unstable plaques

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**Objective** To investigate the probability of circulating miRNA as the biomarker for coronary unstable plaque.

**Method** Outpatients of Fuwai hospital were divided into non-calcified plaque group, calcified plaque group and normal controls group, by CT examination and ACS symptoms. 11 kinds of miRNAs associated with plaque instability were detected (n = 12 cases); a further detection (n = 50 cases) was continued.

**Result** 5 miRNAs are variated; further detection (n = 50 cases) showed miR-16 levels was significantly higher in the non-calcified plaque group than other group (P = 0.024); miR-21 levels in the three groups was in ascending order (P < 0.001). ROC curve showed that AUC for miR-16 individually identified in patients with non-calcified plaque was 0.603 (P = 0.023, 95% CI 0.513 – 0.694); miR-21 was 0.640 (P = 0.013, 95% CI 0.534 – 0.746); miR-16 and miR-21 combination was 0.679 (P = 0.001, 95% CI 0.578 – 0.781).

**Conclusion** Serum levels of miR-16 and miR-21 may become biomarkers for unstable coronary plaques.

### Serum miRNA-21 as a biomarker for coronary unstable plaques

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**Objective** To investigate the probability of circulating miRNA as the biomarker for coronary atherosclerotic unstable plaque.

**Method** Outpatients of Fuwai hospital, from September 2011 to December 2012, were divided into three groups by 64-slice spiral CT examination and the clinical symptoms of ACS. Non-calcified plaque group, symptoms of ACS, typical non-calcified plaque (CT value < 50 HU) on the main coronary artery, and no calcified coronary plaque as well as mixed plaque; calcified plaque group: no symptoms of ACS, the presence of typical calcified plaques (CT values > 50 HU), and no non-calcified coronary plaque as well as mixed plaque; normal control group: no symptom and other history of chronic diseases, normal liver and kidney function, and no coronary plaque on the CT examination. 5 ml fasting serum samples were collected, and were stored at -80 °C for RNA extraction. 12 cases were selected in initial screening. 10 kinds of miRNAs associated with plaque instability were detected using TaqMan qRT-PCR method; by relative quantitative analysis, if the miRNA's expression in non-plaque group more than 1 fold than the normal group, a further detection in expanded sample size (n = 60 cases) was continued. The Result were transformed into logarithmic form, and were analyzed using SPSS17.0.

**Result** The screening Result showed four kinds of miRNA (miR-21/126/155/222) expressed in non-plaque group more than 1 fold than the normal group; in expanded size samples (n = 60 cases) showed that miR-

21 levels in the three groups was in ascending order (P < 0.001). ROC curve showed that AUC for miR-21 individually identified in patients with non-calcified plaque was 0.695 (P < 0.001, 95% CI 0.602 – 0.787); AUC for miR-21 individually identified in patients with calcified plaque was 0.614 (P = 0.029, 95% CI 0.515 – 0.714).

**Conclusion** Serum level of miR-21 is associated with coronary atherosclerotic plaque instability and may become early identification of biomarkers for unstable coronary plaques.

### Lysophosphatidic acid inhibits the role of hydrogen peroxide-induced apoptosis of bone marrow mesenchymal stem cells

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**Objective** Stem cell transplantation is becoming a new strategy of ischemic heart disease treatment in recent years. The survival rate of transplantation stem cell is the key problem to limit its curative effect. We Use hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) induced rat bone marrow mesenchymal stem cells (BMSC) apoptosis to build cell oxidative stress damage model for exploring anti-apoptosis role of a kind of endogenous bioactive molecules - hemolysis phosphatidic acid (LPA).

**Methods** Whole bone marrow of SD rats were separated and used to isolate and culture bone marrow mesenchymal stem cells. Different concentrations of H<sub>2</sub>O<sub>2</sub> stimulated BMSC for apoptosis test. LPA pretreatment cells given H<sub>2</sub>O<sub>2</sub> stimulate were observed after 4 hour of H<sub>2</sub>O<sub>2</sub>; LPA1/3 cell receptor antagonist (Ki16425) pretreatment for LPA role observe whether LPA mediates BMSC apoptosis through the two receptor subtypes. Flow cytometry instrument Annexin V method to detect apoptosis cell percentage; and Western blotting was used to detect the expression change of apoptotic cell markers Caspase 3, Bax and antiapoptotic marker Bcl 2.

**Result** H<sub>2</sub>O<sub>2</sub> can significantly induce BMSC apoptosis. Different concentrations (0.1, 1, 10, 25, 50 μM) of LPA preprocessing BMSC. Annexin V - PI double dye and Western Result showed that 100 μM H<sub>2</sub>O<sub>2</sub> can obvious induce apoptosis; 10 – 50 μM LPA can obviously decrease the percentage of apoptosis of BMSC. Annexin V - PI Result showed that the LPA can make BMSC survival rate increased by 80%. Western Result also showed that 10 – 50 μM LPA can significantly decrease the Caspase 3 and Bax expression and increase Bcl2 expression. LPA1/3 receptor antagonist (Ki16425) can obviously inhibit the rise of Bcl 2 and Result the increase of cleaved caspase3 and bax.

**Conclusion** H<sub>2</sub>O<sub>2</sub> can induce apoptosis showing concentration dependence. LPA shows obvious inhibition effect of apoptosis induced by H<sub>2</sub>O<sub>2</sub>. This kind of antiapoptotic effect may be mediated via LPA1/3 receptor.

## Novel mutations in the SCN5A gene associated with ischemic malignant ventricular arrhythmias

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**Objects** The purpose of this study is to explore whether the SCN5A gene mutations relates to sudden cardiac death in patients with coronary heart disease.

**Materials and Methods** (1) Clinical investigation: Detailed clinical evaluation was performed and congenital genetic causes of malignant ventricular arrhythmias were excluded. (2) Genetic Screening: Total coding region of SCN5A gene were screened by DNA direct sequencing. (3) Mutagenesis and Transfection: Mutated SCN5A channel cDNA was generated by site-directed mutagenesis system. Human embryo kidney (HEK) 293 cells were transfected with the WT- or mutated-SCN5A constructs with the help of liposomes. (4) Electrophysiological Analysis: We characterized the membrane current and the voltage dependence of steady-state activation (SSA) and steady-state inactivation (SSI) by whole-cell patch clamp.

**Result** (1) Clinical Findings: 20 unrelated patients with age ranging from 42 to 81 years old were enrolled. And among them 5 were females, 18 got VT and 2 got VF. (2) Genetics and Corresponding phenotype: Two heterozygous missense mutations were found in SCN5A gene respectively. Mutant A1427S composed of G-to-T substitution at nucleotide site 4338 (c.4338G>T), predicted a substitution of Alanine for Serine at codon site 1427 (P.Ala1427Ser). Mutant R812C consisting of C-to-T substitution at nucleotide site 2435 (c.2435C>T), predicted a substitution of Arginine for Cysteine at codon site 812 (P.Arg812Cys). The two mutations were not detected in the 200 healthy control chromosomes of the same ethnic background. (3) Electrophysiological Properties: Compared to WT, A1427S channel produced significant reduction of peak and current density of I<sub>Na</sub>, inducing a depolarization shift of the I-V relationship curve and voltage dependence of SSA of I<sub>Na</sub>. However, there was no statistic difference between WT and A1427S channel in SSI of I<sub>Na</sub>. Compared to WT, R812C channel produced significant increase of peak and current density of I<sub>Na</sub>, resulting in a depolarization shift of the I-V relationship curve, voltage dependence of SSA of I<sub>Na</sub>. But there was no statistic difference between WT and R812C channel in SSA and SSI of I<sub>Na</sub>.

**Conclusion** SCN5A A1427S and R812C mutation were first reported in patients of coronary heart disease with malignant ventricular arrhythmias. "Loss of function" or "gain of function" of SCN5A may be related to ischemic arrhythmias.

## Effects of atorvastatin on BMP/Smad signaling in pulmonary arterial smooth muscle cells derived from pulmonary hypertensive rats

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**Objective** The present study was to investigate the effects of atorvastatin on BMP/Smad signaling in pulmonary arterial smooth muscle cells (PASMCs) derived from pulmonary artery hypertensive

(PAH) rats.

**Methods** Animal Study: PAH was induced by a single intraperitoneal injection of MCT at a dose of 40 mg/kg. Mean pulmonary arterial pressure (MPAP) was measured by catheterization; right ventricular hypertrophy index (RVHI) were calculated [RVHI = RV/(LV+S)]. Cultured Cells Study Cultured PASMCs isolated from PAH rats was treated with atorvastatin in the concentrations ranging from 0 – 10<sup>-5</sup> mol/l for 24 h. Untreated PASMCs isolated from normal rats was used as control. The mRNA expressions of BMP2, BMPR2, Smad1 and Smad4 were determined by RT-PCR respectively, and the protein expressions of BMP2, BMPR2 and p-Smad1, Smad4 were determined by Western-Blot.

**Result** MPAP [(15.10 ± 0.72) vs (32.63 ± 0.98) mmHg] and RVHI (24.94 ± 4.66 vs 52.60 ± 3.40) were higher in PAH rats, as compared with normal rats (P < 0.05 respectively). The mRNA expressions of BMP2, BMPR2, and Smad1, Smad4 in PASMCs derived from PAH rats were obviously lower than that from normal rats (P < 0.05). Atorvastatin induced an increase in mRNA expressions in the cultured PASMCs derived from PAH rats in a concentration-dependent manner (P < 0.05). The protein expressions of BMP2, BMPR2, Smad4 and phosphorylation level of Smad1 in PASMCs derived from PAH rats were obviously lower than that from normal rats (P < 0.05). Atorvastatin induced an increase in protein expressions and phosphorylation level in the cultured PASMCs derived from PAH rats (P < 0.05).

**Conclusion** The expression of BMP/Smad signaling was abnormal in PASMCs derived from pulmonary artery hypertensive rats induced by MCT. Atorvastatin alleviated PAH may be related to

## Effect of atorvastatin on endothelium-independent relaxation of small pulmonary arteries in monocrotaline-induced PAH rats

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**Objective** To examine the preventive effect of atorvastatin on sodium nitroprusside (SNP)-induced endothelium-independent relaxation (EDiR) in small pulmonary artery (SPA) rings in monocrotaline (MCT)-induced pulmonary hypertension rats.

**Methods** 72 Male SD rats were randomly assigned into four groups: normal control (Ctr), pulmonary arterial hypertension (PAH), PAH preventively treated with 5 mg/kg/d (L<sub>Ator</sub>) and 10 mg/kg/d (H<sub>Ator</sub>) atorvastatin (A<sub>tor</sub>) respectively. Rats were sacrificed after 1, 2 and 4 wks drug gavage. Mean pulmonary artery pressure (mPAP), right ventricular hypertrophy index (RVHI%), and vasomotion function were determined. The potency of vascular relaxation was expressed as the pD<sub>2</sub>.

**Result** mPAP in PAH was significantly higher than that in Ctr 4 wks after MCT injection (32.19 ± 0.91 vs 14.39 ± 0.35, P < 0.01). While preventively treated with A<sub>tor</sub> for 4 wks, mPAP was significantly decreased in L<sub>Ator</sub> and H<sub>Ator</sub> rats as compared with PAH (19.13 ± 1.01, 17.55 ± 0.20 vs 32.19 ± 0.91; P < 0.01). RVHI% was significantly decreased 4 wks after preventively treated with A<sub>tor</sub> in L<sub>Ator</sub> and H<sub>Ator</sub> rats compared with PAH (36.09 ± 4.29 vs 56.76 ± 5.86; 28.93 ± 5.08 vs 56.76 ± 5.86, P < 0.01). SNP-induced EDiR of SPA rings in PAH was not significantly decreased 1 or 2 wks after MCT injection, and significantly decreased 4 wks after the injection (5.89 ± 0.97 vs 8.53 ± 0.91, P < 0.01). There were no difference in Snp-induced EDiR of SPA rings among Ctr, L<sub>Ator</sub> and H<sub>Ator</sub> rats 1 wk after preventively treated with different doses of A<sub>tor</sub>. However, Snp-induced EDiR was significantly ameliorated in SPA



rings 2 wks after the treatment in  $H_{AtoR}$  rats compared with Ctr rats ( $9.93 \pm 0.78$  vs  $8.53 \pm 0.91$ ,  $P < 0.01$ ). Snp-induced EDiR was decreased in both  $L_{AtoR}$  and  $H_{AtoR}$  rats 4 wks after the preventive treatment ( $6.81 \pm 0.76$ ,  $6.92 \pm 0.62$  vs  $8.53 \pm 0.91$ ,  $P < 0.05$ ).

**Conclusion** Early preventive treatment with high dose of atorvastatin has protective effects on the early damage of endothelium-independent vasodilatation function in small pulmonary artery of MCT-induced PAH rats.

### Krüppel-like factor 4 transcriptionally regulates TGF- $\beta$ 1, contributing to hypertensive cardiac fibrosis

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**Background** Angiotensin II (Ang II) plays a major role in the pathogenesis of cardiac fibrosis in hypertension. It is known that Ang II stimulates myofibroblast differentiation and cardiac fibrosis through regulating expression of a variety of transcription factors. However, it has not yet been fully elucidated that the type and function of the transcription factors involved in fibrotic injury caused by Ang II. As well, how transcription factors interact and constitute a network-control the development process of hypertension-induced heart inflammation and fibrosis is unknown.

**Methods** To study the role of Krüppel-like family transcription factors in hypertension, we prepared hypertensive mouse model with Ang II (1500 ng/kg/min) infusion for 7 day. We tested expression of Klf4 in heart tissue and different cell types after Ang II stimulation. In vitro, Klf4 were overexpressed by Ad Klf4 infection or knockdown by small Interfering RNA transfection to detect its role in myofibroblast differentiation and collagen synthesis. The Klf4 regulated target genes were determined by ChIP Seq. Furthermore, ChIP assay and pGL-3-TGF- $\beta$ 1-luc+ plasmids transfection were done to detect the Klf4 binding site at TGF- $\beta$ 1 promoter region. In vivo, myofibroblast-specific deletion of Klf4 (Klf4 fl/fl; alpha-SMA-Cre) and Klf4 fl/fl control mice were infused continuously with Ang II or saline for 7 day. The extracellular matrix deposition was evaluated by Masson trichrome staining. Myofibroblast formation was associated with alpha-SMA immunohistochemical staining. Mac-2 and MCP-1 protein expression were tested to determine macrophage infiltration and expression of inflammatory cytokines.

**Result** Klf4 was the highest expressed among the Klf members in Ang II-induced cardiac fibrosis. Klf4 promotes fibroblast-to-myofibroblast differentiation and collagen synthesis. Klf4 transcriptionally regulates fibrogenic genes including TGF- $\beta$ 1. The sites at -184 – -180 bp and -45 – -41 bp in the TGF- $\beta$ 1 promoter were responsible for Klf4 transactivation of the TGF- $\beta$ 1 promoter. Cardiac fibrosis area was significantly lower in Klf4 fl/fl; alpha-SMA Cre mice than that in Klf4 fl/fl mice ( $11.13 \pm 0.90\%$  vs  $7.22 \pm 0.89\%$ ,  $P < 0.05$ ). Alpha-SMA positive area was significantly decreased ( $3.90 \pm 0.71\%$  vs  $1.11 \pm 0.22\%$ ,  $P < 0.05$ ) in hearts of the Klf4fl/fl; alpha-SMA Cre mice. Mac-2 and MCP-1 positive area were both significantly lower ( $2.76 \pm$

$0.27\%$  vs  $2.07 \pm 0.35\%$ ,  $P < 0.05$ ;  $3.16 \pm 0.46\%$  vs  $1.47 \pm 0.75\%$ ,  $P < 0.05$ ) for Ang II-infused 7 day.

**Conclusion** Our studies demonstrate that AngII could directly activate Klf4 expression of cardiac fibroblasts. Klf4 transcriptionally regulated fibrosis related gene, which including TGF- $\beta$ 1. Klf4 plays a pivotal role in hypertension-induced cardiac fibrosis and inflammation.

### Genetic variant of endoglin gene is associated with sporadic intracranial aneurysms in the Chinese Han population

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**Background** It has been reported that the prevalence of unruptured IAs was significantly higher (10.5 – 13.5%) in a Japanese subgroup with a family history of IAs, indicating that genetics also plays a role. Endoglin plays a pivotal role in the in vascular development and disease. Variant of endoglin gene have been shown to be risk factors for IAs in different racial population. In the present study, we investigated the correlation between polymorphisms in the endoglin gene with IAs in Chinese Han population.

**Methods** The association of endoglin D366H variants (rs1800956) with sporadic IAs was tested in 313 patients with intracranial aneurysms, and 450 controls. A chi-square test was used to test for genotype/allele frequencies, the effects of the variant on risk of IAs were tested using a logistic-regression model. The covariables selected for logistic regression model were conventional vascular risk factors, including age, sex, blood pressure, smoking, and alcohol consumption.

**Result** The frequency of the GG+CG genotype of rs1800956 was significantly higher in patients with IAs than in the controls (22.0% vs 15.3%,  $P = 0.018$ ; crude OR, 1.56; 95% CI, 1.08 – 2.26). After adjustment for conventional vascular risk factors, including age, sex, blood pressure, smoking, and alcohol consumption, the G allele of rs1800956 conferred a high risk of IAs (adjusted OR, 1.56; 95% CI, 1.08 – 2.26,  $P = 0.019$ ).

**Conclusion** The variant rs1800956 of endoglin is genetic risk factors for sporadic IAs among individuals of Chinese Han ethnicity. This study confirms the association between endoglin and IAs.

### Rosuvastatin could modulate insulin signaling and inhibit atherosclerosis beyond its plasma cholesterol-lowering effect in insulin-resistant mice

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**Objective** To provide evidence that rosuvastatin could improve

insulin-resistance and inhibit atherogenesis by modulating insulin signaling, and whether this effect beyond its plasma cholesterol – lowering effect.

**Methods** Thirty-two 6-week-old low-density lipoprotein receptor deficient (LDLR<sup>-/-</sup>) mice were randomized into four groups (n = 8 in each group): Normal control group (NC); High fat and high fructose diet group (HFF); HFF plus rosuvastatin group (HFFR); HFFR plus mevalonic acid group (HFFRMA). After 12 weeks, we measured the fasting blood sugar (FBS), fasting insulin (FINS) and total cholesterol (TC); the morphological concentrations of the aorta artery and aorta sinus; the expression of insulin receptor substrate 2 (IRS-2), phosphorylated insulin receptor substrate 2 (P-IRS-2), protein kinase B (AKT, also known as PKB) and phosphorylated protein kinase B (P-AKT) in liver.

**Result** Compared with other groups, FBS and FINS increased significantly in HFF group. Furthermore, HFF group had an increase in the morphological concentrations of the aorta artery and aorta sinus, but there was a significant decrease in HFFRMA group and HFFR group. Moreover, there was a high expression of IRS-2, P-IRS-2, AKT and P-AKT in HFFRMA group and HFFR group, but a low expression in HFF group. And there is no significant difference regarding to each afore-mentioned index in HFFR group and HFFRMA group.

**Conclusion** Our data show that rosuvastatin could improve insulin-resistance and inhibit atherogenesis in HFF-fed mice by partially reversing the decrease in the insulin stimulated IRS-2/P13-K/AKT pathway in liver, and this effect is independent of its cholesterol-lowering effect.

### Autophagy flux mediates cardiac protection of sevoflurane post-conditioning

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**Objective** We have previously shown that sevoflurane, a major volatile anesthetic gas in cardiac surgery, protects cardiomyocytes from ischemia reperfusion (I/R) injury both in pre- and post-conditioning. However, its mechanism is not fully elucidated. It has been reported that sevoflurane induces autophagy, and may play a role in cardiac protection, but it has not been investigated whether I/R induced autophagy flux is associated with the cardioprotection afforded by sevoflurane post-conditioning.

**Methods** The Sprague – Dawley rats weighing between 250 and 300 g were randomly assigned into three groups: (I) sham group; (II) IR group, in which hearts subjected to 30 min of ischemia and 120 min of reperfusion; (III) SPoC group, in which sevoflurane (3%) administered at the first 15 min after reperfusion. Infarct size was delineated by tetrazolium staining and expressed as a percentage of the at-risk myocardium, as well as cardiomyocytes apoptosis by TUNEL assay was investigated at the end of 2 hours reperfusion. Counts and morphology of autophagosome for transmission electron microscopy (TEM), expression of microtubule-associated protein light chain 3-II, and mitochondrial permeability transition pores (MPTP) opening for calcein release were evaluated after the 30 min of reperfusion. To investigate whether the

efficacy of sevoflurane post-conditioning was maintained with CQ (chloroquine) treatment, additional rats was given CQ (10 mg/kg, i.p.) at 1 hours prior to surgery, (IV) Sham+CQ group, (V) IR+CQ group, (VI) SPoC+CQ group. Infarct size and ratio of apoptotic cardiomyocytes were evaluated. Moreover, number of autophagosomes, autophagic mark LC3 and MPTP were detected.

**Result** Sevoflurane post-conditioning was cardioprotective: infarct size was  $21.1 \pm 2\%$  in the SPoC group vs  $38.7 \pm 1\%$  in the IR group ( $P < 0.05$ ), respectively. Sevoflurane post-conditioning was associated with decreased expression of microtubule-associated protein light chain 3B-II (LC3B-II) ( $8.03 \pm 0.45$  vs  $5.95 \pm 0.41$ ,  $P < 0.05$ ,  $n = 3$ ) and the counts of autophagosomes were decreased in the SPoC group. Compared to IR group, SPoC group exhibited inhibition of MPTP opening in heart tissues, and attenuated the apoptosis of myocardiumocytes. Surprisingly, in adding CQ group, the cardiomyocytes protective effects were abrogated. Infarct size areas in SPoC+CQ was increased than those in SPoC group ( $21.1 \pm 2\%$  vs  $53.0 \pm 1\%$ ,  $P < 0.05$ ,  $n = 6$ ). The ratio of LC3-II/I was elevated ( $9.38 \pm 0.32$  vs  $5.95 \pm 0.41$ ,  $P = 0.0026$ ,  $n = 3$ ). Furthermore, SPoC+CQ group was associated with elevated apoptosis of cardiomyocytes and MPTP opening.

**Conclusion** Our Result demonstrate that sevoflurane post-conditioning attenuated I/R induced apoptosis of myocardiumocytes. Sevoflurane post-conditioning promotes autophagy flux in reperfusion period, which inhibits MPTP opening in I/R pathological process, at least partly contributing to the key step in the cardioprotection of sevoflurane.

### The Role of ER stress in the process of BH3-only protein Bim-mediated cardiomyocytes apoptosis induced by hypoxia

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**Objective** To investigate the role of endoplasmic reticulum stress in the injury induced by Bim of hypoxic cardiomyocytes.

**Methods** The Rat cardiomyocytes, 1 – 3 days after birth, were cultured primarily and identified by using antibody targeting  $\alpha$ -actin of striated muscle. Bim-siRNA were transfected transiently into cardiomyocytes by lipofectamine 2000. Establish a model of hypoxia (The cells after 48 h transfection, were given a deal with hypoxia for 12 h). The experiments were divided into five groups: Blank Control Group, Hypoxia Group, Hypoxia + Negative Control siRNA Group, Hypoxia + Mock control Group, Hypoxia + Bim-siRNA Group. The cell survival rate was determined by MTT method; the cell apoptosis rate and the change of the calcium concentration in cells were determined by flow cytometry; the expression of Bim and the markers of endoplasmic reticulum stress Caspase-12 and InSP3 were assessed by Western blot.

**Result** Immunohistochemical identification confirmed that rat cardiomyocytes were successfully cultured. Green fluorescence was observed in the cells transfected of negative control siRNA group though the fluorescence microscope. The Result of Western blot showed that the transfection of Bim-siRNA decreased the expression of Bim effectively ( $P < 0.01$ ). Compared with the blank control group, The MTT assay determined that the survival rate of cardiomyocytes was decreased ( $P < 0.05$ ) after the injured by hypoxia. And the Result of flow cytometry showed that hypoxia increased cell apoptosis rate ( $P < 0.01$ ) and the concentration of calcium ( $P < 0.01$ ), while the transfection of Bim-siRNA reduced the effects caused by hypoxia ( $P < 0.05$  or  $P < 0.01$ ). Compared with the hypoxia+Negative Control siRNA group, the transfection of Bim-siRNA increased the cell survival rate, decreased cell apoptosis rate

and the concentration of calcium ( $P < 0.01$ ). The Result of Western blot showed that the transfection of Bim-siRNA reduced the expression of Caspase-12 and InSP3 ( $P < 0.05$  or  $P < 0.01$ ), which were endoplasmic reticulum stress markers. And reduced the effects that hypoxia increased the expression of Caspase-12 and InSP3 ( $P < 0.05$  or  $P < 0.01$ ).

**Conclusion** Cardiomyocytes apoptosis induced by hypoxia can be inhibited by Silencing Bim gene. Caspase-12 and InSP3 which are the markers of endoplasmic reticulum stress may participate in the process of Bim-mediated rat cardiomyocytes apoptosis induced by hypoxia. It is likely to be a new direction for treatment of coronary atherosclerotic heart disease.

### The effect of BH3-only protein Bim silencing by siRNA on apoptosis induced by hypoxia in rat cardiomyocyte

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**Aim** To investigate the effect of BH3-only protein Bim (Bcl-2 interacting the mediator of the cell death) on apoptosis induced by hypoxia in rat cardiomyocyte.

**Methods** The Rat cardiomyocytes, 1-3 days after birth, were cultured primarily and identified by using antibody targeting  $\alpha$ -actin of striated muscle. Bim-siRNA was transfected transiently into cardiomyocytes by lipofectamine 2000. Establish a model of hypoxia (The cells after 48 h transfection were given a deal with hypoxia for 12 h). The experiments were divided into five groups: Blank Control Group, Hypoxia Group, Hypoxia + Negative Control siRNA Group, Hypoxia + Mock control Group, Hypoxia + Bim-siRNA Group. With the inverted microscopy, the Cardiomyocyte beat frequency and rhythm can be observed and recorded; the content of lactate dehydrogenase (LDH) in cell culture fluid was detected by automatic biochemical analyzer; The cell survival rate was determined by MTT method; the cell apoptosis rate was determined by flow cytometry; the expression of Bim, Bax, Bcl-2 and p-p38MAPK was assessed by Western blot.

**Result** Immunohistochemical identification confirmed that rat cardiomyocytes were successful cultured. The beat frequency of cardiomyocyte was slowed down after hypoxia stimulation, the rhythm was disordered ( $P < 0.01$ ). And the content of lactate dehydrogenase (LDH) in cell culture fluid increased obviously ( $P < 0.01$ ). The MTT result showed that the survival rate was decreased ( $P < 0.05$ ). And the Result of flow cytometry showed that hypoxia increased cell apoptosis rate ( $P < 0.01$ ), while the transfection of Bim-siRNA reduced the effects caused by hypoxia ( $P < 0.05$  or  $P < 0.01$ ). The Result of Western blot showed that the transfection of Bim-siRNA decreased the expression of Bim ( $P < 0.01$ ). It confirmed that Bim was silenced by Bim-siRNA effectively. The hypoxia increased the expression of Bax and p-p38 ( $P < 0.05$ ), and decreased the expression of Bcl-2 ( $P < 0.01$ ), while the transfection of Bim-siRNA reduced the effects caused by hypoxia ( $P < 0.05$ ). These were greatly related to the decreasing of apoptosis.

**Conclusion** The down-regulation of the expression of Bim can suppress the apoptosis of rat cardiomyocyte induced by hypoxia. Its mechanism is associated with the down-regulation of p-p38MAPK, Bax expression and up-regulation of Bcl-2. It is likely to be a new direction for treatment of coronary atherosclerotic heart disease.

### Clinical and genotype characteristics of arrhythmogenic right ventricular cardiomyopathy with left ventricular involvement

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**Objective** Arrhythmogenic right ventricular cardiomyopathy (ARVC) is mainly caused by mutation of genes encoding desmosomal proteins. It is supposed that both ventricles should be involved in the disease since the effect of ultrastructural and molecular dysfunction of desmosome plays an equal role on both ventricles. This study was aimed to identify the clinical and genotype characteristics of ARVC with left ventricular (LV) involvement.

**Methods** A total of 172 ARVC patients were enrolled for clinical evaluation. LV involvement was defined by echocardiography with at least one of the followings: LV end-diastolic diameter  $> 57$  mm, LV ejection fraction  $\leq 50\%$ , LV wall being thin, or LV dyskinesia. One hundred patients of the total sample underwent genetic screening for 9 reported ARVC-causing genes, including JUP, DSP, PKP2, DSG2, DSC2, TGFB3, TMEM43, DES, and LMNA. The genotype-phenotype correlation of the patients with LV involvement was analyzed.

**Result** Thirty-one (18%) patients were found to have LV involved. Compared with patients without LV involvement, the involved group had similar sex ratio, onset age, duration between onset and diagnosis, clinical manifestations, except more severe right ventricular structural impairment (58% vs 32%,  $P = 0.008$ ). Among the 64 mutation carriers, LV involvement was found in 11 (17%) patients. The involved group had more multi-mutation carriers (64% vs 30%,  $P = 0.046$ ), but less plakophilin-2 mutation carriers (36% vs 72%,  $P = 0.037$ ).

**Conclusion** In Chinese ARVC patients, 18% has echocardiography identified LV involvement, which is related to multi-mutation and right ventricular structural impairment progression.

### Metabolomic investigation of ischemic myocardial tissue in BA-MA mini-pigs with diabetes mellitus

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**Objective** The purpose of this study is to establish the small molecule fingerprints on acute ischemic myocardial model of diabetic and non-diabetic miniature swine using metabolites. We will utilize statistical analysis combined with clinical physiological indexes and network database to identify differential small molecule metabolic products, aiming to explore new molecules from metabolic view more sensitively, accurately, specifically as diagnostic markers of diabetic patients with acute myocardial ischemia.

**Methods** First, we injected STZ (150 mg/kg, iv) to set up a small pig model of diabetes, then collecting blood the day prior to administration, after administration for a week, monitoring fasting



blood glucose, serum insulin and C-peptide levels dynamically, continued increase of FBG (FBG  $\geq 7.0$  mmol/L) indicated successful model. Then, we used thoracoscopic to do minimally invasive coronary artery ligation of the left anterior descending (LAD) to establish diabetes and non-diabetic miniature swine with acute myocardial ischemia. Dynamic ECG was used for 48 h after coronary artery ligation. We collected blood before coronary clogging, coronary clog for 10 min, 4 h and 48 h respectively. Before animal's execution (48 h), we collected sinus blood and ischemic myocardium for metabolomics analysis. Finally, we used UPLC/TOF-MS and NMR to detect homogenates glucose, fatty acids, lactic acid, ketone bodies, amino acids fingerprinting of myocardial tissue according to time point. Then we compared the changes of metabolic products before and after ischemia and did related metabolites contour analysis, finding relations between specific metabolites and FBG, insulin levels, cardiac electrophysiology and cardiac function to clarify the pathogenesis of decreased tolerance of diabetic myocardial ischemia, aiming to look for new possible therapeutic targets.

**Result** FBG was significantly increased and maintained at 17.7–20.1 mmol/l after injection of STZ for 24 h, C-peptide and insulin levels were significantly lower. The total protein, alanine aminotransferase, aspartate aminotransferase, and creatinine were not significantly changed in model group, urea nitrogen and albumin decreased slightly, blood uric acid w significantly decreased. ( $P < 0.05$ ). Western blot Result showed that compared with the control group, pancreas, liver and renal tubular basement membrane glucose transporter protein 2 significantly reduced in model group. We confirmed that a one-time injection of high-dose STZ of can successfully establish type 1 diabetes miniature pig model, and there were significant effects on liver and kidney function. Metabolomics data obtained by the model is of confidence. After one week stable blood sugar of diabetic group, we did coronary artery ligation surgery (VATS). Serum troponin I (cTnI) and myoglobin (MYO) was significantly higher after VATS for 4 h, (10–100 times higher than normal limit), reaching the diagnostic criteria of myocardial infarction (5 times higher than the upper normal limit). Echocardiography, MRI and histopathological analysis showed that myocardial injuries were the apex, left ventricular anterior wall and septum. Diabetic miniature swine heart function was relatively lower; infarct area/higher risk infarct area ratio (diabetic group 18: 1 vs control group 5: 1); the myocardial infarction was heavier ( $> 75\%$ ), which was in line with poor tolerability of diabetes myocardial ischemia. Acute myocardial ischemia pathological changes were obvious in all animals, pathological Q waves formed after 48 h, the diabetic group QRS score was higher than the control group ( $6.9 \pm 2.4$  vs  $4.1 \pm 1.8$ ,  $P < 0.05$ ); and pathological staining showed that the infarction area was larger than the control group ( $29.2 \pm 5.1\%$  vs  $15.3 \pm 3.4\%$ ,  $P < 0.05$ ), the correlation coefficient was 0.92. We used SIMCA-P software to do PCAPLS-DA. The Result showed that there were 14 differential metabolites in ischemic myocardial tissue, including four types amino acids, they were a neutral amino acid (glycine, serine), a non-polar imino acid (Proline) and 1 acidic amino acids (glutamic acid), which decreased by 1.56 times, 1.62 times, 2.23 times and 3.76 times respectively compared with control group. 4 hexose (glucose, fructose, galactose, and pyran-galactose) increased slightly, rising by 1.4–2.6 times than control group on average; cholesterol content decreased by nearly 1.7 times. The most significant changes were peanuts arachidonic acid, nearly 5 times decrease, the difference had statistically significant.

**Conclusion** (1) high-dose STZ successfully established a type I diabetes miniature pigs model, which had little effect on liver and kidney function. (2) VATS surgery is a safe, effective method in doing diabetic AMI model. (3) Diabetes with acute myocardial ischemia would lead to myocardial necrosis easily; infarct size was significantly larger than that of the control group; ECG testing on determines infarct size had

good correlation with pathological method. (4) metabolomics studies showed that arachidonic acid, which was an important constituent of the myocardial cell membrane, may become diagnosis and prognostic candidate molecules marker in diabetic myocardial ischemia.

### Mechanical stretch induced cardiac fibroblasts proliferation, transdifferentiation and apoptosis is mediated by calcineurin pathway

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**Objective** To investigate if calcineurin pathway is involved in cardiac fibroblasts proliferation, transdifferentiation and apoptosis induced by mechanical stretch.

**Methods** Primary cardiac fibroblasts from 1- to 2-day-old Sprague-Dawley rats were isolated by trypsinization and purified by differential anchoring velocity technology. The cultured cells of passage 2-3 were divided into: control group, mechanical stretch group (MS group), calcineurin siRNA+mechanical stretch group (CaN-siRNA + MS group), FK506+mechanical stretch group (FK506+MS group), calcineurin overexpression+mechanical stretch group (CaN-overex + MS group). Calcineurin and downstream NFAT3 expressions were determined by western blot. Cardiac fibroblasts proliferation was determined by cell counting kit-8 and detection of proliferating cell nuclear antigen (PCNA), cell transdifferentiation was measured by alpha-smooth muscle actin (alpha-SMA) through western blot and apoptosis by Bax/Bcl-2.

**Result** Mechanical stretch promoted cardiac fibroblasts proliferation, as well as upregulation of alpha-SMA and increased Bax/Bcl-2 ratio, overexpression of calcineurin could promote more cardiac fibroblasts adverse remodeling similar to those induced by mechanical stretch. Pretreatment with calcineurin-siRNA lentivirus significantly attenuated cardiac fibroblasts proliferation, transdifferentiation and apoptosis when later stimulated by mechanical stretch, whereas pretreatment with FK506, a calcineurin inhibitor, only moderately inhibited cardiac fibroblasts proliferation and apoptosis with no obvious effect on cell transdifferentiation.

**Conclusion** This study demonstrates that mechanical stretch promoted cardiac fibroblasts proliferation, transdifferentiation and apoptosis via activating calcineurin/NFAT3, thus abolishing the calcineurin pathway might be beneficial for reversing myocardial fibrosis.

### Pulmonary microRNA expression changes in a piglet model of deep hypothermic low-flow cardiopulmonary bypass induced immature lung injury

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**Background** After cardiac surgery performed under deep

hypothermia with low-flow (DHLF) cardiopulmonary bypass (CPB), the lung injury often becomes more severe in infants, which is usually driven by diverse pathogenic etiologies. Due to their pleiotropic actions, microRNAs (miRNAs) are potential candidates involved in a diverse pathophysiological processes and diseases via regulating gene expression. The objective of this study was to investigate the changed miRNAs and their potential target genes in neonatal piglet lungs in response to DHLF-CPB.

**Methods** Piglets ( $n = 10$ ) aged  $18.2 \pm 1.55$  days, weight  $4.9 \pm 1.21$  kg, were randomly divided into 2 groups: sham-operated (Control,  $n = 5$ ), DHLF-CPB (CPB group,  $n = 5$ ). In CPB group, the DHLF-CPB was routinely established, which was cooled to  $25^{\circ}\text{C}$  with low-flow for 60 minutes (50 ml/kg/min) during in the 2 hours aortic cross-clamping. At 2 hours after weaning from CPB, the right lower lobe was harvested. Lung function indices were recorded and morphological changes in the lung were examined by haematoxylin and eosin. The levels of cytokine (TNF- $\alpha$ , IL-6 and SP-A) and the activity of NF- $\kappa$ B in lung tissue were measured by enzyme-linked immunosorbent assay (ELISA) and electrophoresis mobility shift assay (EMSA), respectively. The miRNA profiling was obtained by applying miRNA chip, and real-time quantitative polymerase chain reaction (RT-PCR) was used to validate the differentially expressed miRNAs in RNA samples from lungs of piglets.

**Result** The lung function indices shown greatly elevation of respiratory index, descent of oxygenation index and histopathological changes revealed the piglets' lungs were greatly impaired due to DHLF-CPB. There were a great increase in the levels of TNF- $\alpha$  [ $(36.1 \pm 6.5)$  pg/ml vs  $(15.6 \pm 1.5)$  pg/ml, ( $P < 0.05$ )], IL-6 [ $(175.47 \pm 29.58)$  pg/ml vs  $(133.03 \pm 26.28)$  pg/ml, ( $P < 0.05$ )] and decrease in the levels of SP-A [ $(9.26 \pm 0.71)$  pg/ml vs  $(11.00 \pm 1.23)$  pg/ml ( $P < 0.05$ )] in the CPB group. Using miRNA microarray we identified that there are 16 miRNAs expression significantly changed ( $P < 0.05$ ) and verified up-regulation of miR-21, miR-204 and down-regulation of miR-127, miR-145 in CPB group by RT-PCR analyses. Especially, miR-21 is known can be induced by activation of NF- $\kappa$ B and miR-204 putatively targets the SP-A mRNA, which is correlated with a strongly activation in the activity of NF- $\kappa$ B ( $P < 0.05$ ) and decrease of SP-A expression in CPB group in our study. And we found no significant changes in the expression of miR-324 and miR-885.

**Conclusion** Our Result show that DHLF-CPB induces great lung injury and dynamic changes in miRNA expression in piglet lungs. Moreover, the changes of NF- $\kappa$ B activity and SP-A expression may be important to understand the influence of differentially expressed miRNAs on DHLF-CPB induced immature lung injury.

### Involvement of calcineurin pathway in TGF- $\beta$ 1 induced cardiac fibroblasts proliferation

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**Objective** Transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1) and calcineurin (CaN) each plays a role in promoting cardiac fibroblasts proliferation. However, the regulatory effect of TGF- $\beta$ 1 on CaN

remains unknown yet. We therefore sought to investigate if calcineurin and its pathway are involved in TGF- $\beta$ 1 induced cardiac fibroblasts proliferation.

**Methods** Primary cardiac fibroblasts from 1- to 2-day-old Sprague-Dawley rats were isolated by trypsinization and purified by differential anchoring velocity technology. The cultured cells of passage 3 were stimulated by TGF- $\beta$ 1 either with a concentration gradient (0, 0.1 ng/ml, 0.5 ng/ml, 5 ng/ml, 10 ng/ml and 25 ng/ml) or at different time points (0, 30 min, 1 h, 2 h, 6 h and 12 h), calcineurin and downstream NFAT-3 expressions were examined, respectively. On the other hand, cardiac fibroblasts were divided into three groups: control group, CaN-siRNA group and CaN-overexpression group. CaN/NFAT-3 expressions and cell proliferation in each group were determined.

**Result** NFAT-3 is activated by TGF- $\beta$ 1 in a dose- and time-dependent manner in parallel with that of CaN. Pretreatment with CaN-siRNA lentivirus significantly attenuated cardiac fibroblasts proliferation induced by TGF- $\beta$ 1, while overexpression of CaN promoted the proliferation of CFs.

**Conclusion** The present study demonstrates that apart from Smads signaling cascade, TGF- $\beta$ 1 could also promote CF proliferation via activating calcineurin/NFAT-3 pathway, thus calcineurin might be a potential target of reversing myocardial fibrosis.

### Overexpressed HSP22 protects against hypoxia/reoxygenation-induced apoptosis in endothelial cells

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Vascular endothelial cells (VEC) injury induced by ischemic-reperfusion can lead to endothelial barrier dysfunction, thrombosis and edema. Further study indicated that apoptosis was first seen in the endothelial cells in the stages of reperfusion. Several studies demonstrate that the dysfunction and incompetence of VEC precedes myocyte cells apoptosis and restoration of its function is later than myocyte cells in ischemic-reperfusion. Therefore, it is of great significance to protect endothelial cells against ischemic-reperfusion injury. Several studies have shown that HSP22 could protect myocardial cells ischemia-reperfusion injury against apoptosis and oxidative stress. Recently, we found significant increase in HSP22 expression in vascular endothelial cells undergoing hypoxia/reoxygenation. But, it was so far not known whether HSP22 have beneficial effects on endothelial cells during hypoxia/reoxygenation injury. This problem was examined in a model of hypoxia-reoxygenation stress when endothelial cells were infected with virus-based vectors expressing HSP22 or green fluorescent protein (GFP) which exposed to 24 hours of hypoxia followed by reoxygenation. We further investigated the levels of Bcl-2, Bax and NF- $\kappa$ B, which were considered to the relational proteins of endothelial cells apoptosis. HSP22 inhibited hypoxia/reoxygenation-induced apoptosis associated with up-regulation of Bcl-2 and down-regulation of NF- $\kappa$ B levels at reoxygenation 0 h, 3 h, 6 h, and 12 h following 24 h hypoxia ( $P < 0.01$ ). Furthermore, Co-immunoprecipitation indicated HSP22 could directly bind to IKK- $\alpha$ , increase I $\kappa$ B- $\alpha$  level, then reduce NF- $\kappa$ B transcription activity.

## Argonaute HITS-CLIP decodes microRNA-mRNA interaction maps during heart development

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**Aims** MicroRNAs (miRNAs) are a family of small, non-coding RNAs that play critical roles in the regulation of embryonic development and cellular differentiation. Recently, high-throughput sequencing of RNAs isolated by crosslinking immunoprecipitation of (HITS-CLIP) provides an excellent method for comprehensively exploring the miRNA-mRNA interactions in vivo. The aim of this research was to study the miRNA-mediated gene regulatory networks during heart development by HITS-CLIP.

**Methods** By AGO-HITS-CLIP experiments combined with bioinformatics analysis, we systematically identify the miRNA-mRNA interactions in embryonic mouse heart tissues of three different developmental time points (e15.5, e18.5 and P2).

**Result** In total, we identified more than 30 thousands Ago-binding clusters composed of miRNAs, mRNAs, as well as other ncRNAs. We identified approximately ten thousands miRNA-mRNA interactions, corresponding to the in vivo target sites of 526 miRNAs. In-depth analysis of the targetomes of several heart-specific miRNAs, including miR-1, miR-133, miR-206, miR-208, miR-499, indicates that hundreds of genes involved in cell growth, developmental timing, differentiation and heart functions, are controlled by these miRNAs. In addition, we also identified a large number of non-canonical miRNA-mRNA interactions. Furthermore, through comparison the miRNA-target interaction maps across three different time points, we find that both the miRNAs and their targets are highly dynamic, demonstrating that a rapidly changing gene regulatory network composed of hundreds of miRNAs and protein genes controls heart development.

**Conclusion** We here describe the first comprehensive identification of miRNA-targets interaction maps in heart development. Our work provides a targetome resource that enables high-throughput analyses of the in vivo targets of miRNAs in the heart.

## The expression of CXCL9 is elevated in congenital pulmonary hypertension

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**Background and purpose** CXC-chemokine ligand 9 (CXCL9) is one of chemokines involving in both physiological and pathological processes of inflammation, and the CXC group of chemokines is gaining importance in various diseases for being angiostatic and angiogenic in function. Abnormal angiogenesis participate in the pathobiology of pulmonary arterial hypertension (PAH). We investigated the serum level of CXCL9 in patients of congenital pulmonary hypertension and lung tissue of PAH rats. Experimental approach Rat model of PAH was induced by monocrotaline (50 mg/kg, subcutaneous injection). The

expression level of CXCL9 and its receptor (CXCR3) was measured by RT-PCR. Serum CXCL9 level was measured by protein affinity microarray. CXCL9 level of patients of congenital heart disease with severe PAH or without PAH was compared.

**Key Result** Compared with control, CXCL9 expression level in lung tissue of rat was elevated about 3 times after monocrotaline injection 1 week, and then declined gradually. The expression level of CXCR3, receptor of CXCL9, also increased after monocrotaline injection, and reached the top (about 1.4 times) in week 3. The mean serum CXCL9 level of congenital heart disease patients with severe PAH was  $11\,500 \pm 410$  pg/ml, about 4 times of congenital heart disease patients without PAH.

**Conclusion and implication** Our preliminary Result showed the serum CXCL9 level is elevated in congenital pulmonary hypertension. This study augments the probability of serum CXCL9 being a new biomarker of PAH.

## Novel desmoglein-2 mutations in arrhythmogenic right ventricular cardiomyopathy

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**Background and purpose** Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/ARVD) is an inherited heart muscle disorder associated with ventricular arrhythmia, heart failure, and sudden death. Genes coding for desmosome have been identified as disease-causing factors. Mutations in the desmoglein-2 (DSG2) gene have been reported in patients with ARVC/D. We sought to discover new mutations of DSG2 causing ARVC by Next Generation Sequencing.

**Methods** Twenty-seven consecutive ARVC/D index cases who fulfilled the International Task Force diagnostic criteria were screened for mutations in genes of each targeted exome by Next Generation Sequencing. We evaluated the pathogenesis of mutated DSG2 protein by bioinformatic analysis.

**Result** Two recognized DSG2 mutations, Y198C and F531C were identified in two cases. Sanger sequencing confirmed the presence of DSG2 mutations in two cases with ARVC. Bioinformatic analysis showed DSG2 Y198C and F531C was not found in dbSNP135 and 1000 genome. And functional predictive analysis (SIFT and PloyPhen2) suggested that the two mutation were damaging.

**Conclusion** Our Result detected two novel mutations of DSG2 causing ARVC. Moreover, the study provided further evidence for a role for DSG2 in the pathogenesis of ARVC and strengthened the view that ARVC is a disease of the desmosome. Moreover, the study illustrated the benefits of genetic testing of ARVC candidate genes.



## Traditional Chinese medicine TongXinLuo protects human cardiac microvascular endothelial cells against hypoxia/reoxygenation injury via inhibition of JAK/STAT pathway

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**Objective** To elucidate the role of JAK/STAT pathway in hypoxia/reoxygenation injury of cardiac microvascular endothelial cells (CMECs), and its activity regulation by traditional Chinese medicine TongXinLuo.

**Methods** CMECs were cultured to passage 3-4 and assigned to different groups: TongXinLuo (TXL) concentration groups (50, 100, 200, 400, 800  $\mu\text{g/ml}$ ) and pathway verification groups: (AG490 50  $\mu\text{M}$  with or without TXL 800  $\mu\text{g/ml}$ ). Cells were subjected to 2 hours' hypoxia then 2 hours' reoxygenation. Flowcytometry was used to analyze cell apoptosis rate via Annexin-V/PI staining method. Western blotting was used to determine the changes of apoptosis related proteins such as Bcl-2, Bax and pathway related proteins JAK2, phosphorylated-JAK2; STAT3, phosphorylated-STAT3.

**Result** Flowcytometric assays showed CMECs apoptosis rate significantly increased after hypoxia/reoxygenation (H/R) ( $23.45 \pm 2.62\%$  in H/R group compared to  $7.54 \pm 1.57\%$  in control group,  $P < 0.05$ ). TXL protected CMECs against H/R injury in a concentration dependent trend, and most significantly in 800  $\mu\text{g/ml}$  group ( $12.83 \pm 1.92\%$ ,  $P < 0.05$ ). CMECs apoptosis rate was decrease by JAK/STAT pathway inhibitor AG490 significantly ( $7.05 \pm 0.97\%$ ,  $P < 0.05$  vs H/R group) and by AG490 with TXL 800  $\mu\text{g/ml}$  in larger extent ( $3.79 \pm 1.04\%$ ). Correspondingly, Bax was increased and Bcl-2 was decreased after hypoxia/reoxygenation, while TXL 800  $\mu\text{g/ml}$ , AG490, and combination groups reversed the trends ( $P < 0.05$ ). AG490, TXL 800  $\mu\text{g/ml}$  and combination groups significantly decreased the phosphorylated-STAT3 in Tyr-705 location.

**Conclusion** TongXinLuo could significantly decrease apoptosis rate of human cardiac microvascular endothelial cells after hypoxia/reoxygenation in 800  $\mu\text{g/ml}$ , and JAK/STAT pathway inhibition is one of mechanisms in its protection roles.

## Involvement of vascular peroxidase 1 in the endothelial dysfunction in hypertension

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**Objective** Vascular peroxidase 1 (VPO1) is a new heme-containing peroxidase, which can utilize hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) generated from co-expressed NADPH oxidase (NOX) to produce hypochlorous acid (HOCl) and catalyze peroxidative reactions. Considering the key role of the interaction between oxidative stress and endothelial dysfunction in causal mechanisms in hypertension. The aims of this study were to determine the potential role of VPO1 in endothelial dysfunction in hypertension.

**Methods** 20 weeks old Spontaneous hypertension rats (SHR) and Wistar-Kyoto rats were selected. The concentration-relaxation curve of aortic ring and the expression of VPO1 and endothelial nitric oxide synthase (eNOS) in arterial tissues were assessed; the nitric oxide (NO) level in plasma was measured. Human umbilical vein endothelial cells (HUVECs) were cultured and treated with angiotensin II, the eNOS expression and NO level were assessed while the expression of VPO1 and generation of  $\text{H}_2\text{O}_2$  and HOCl were measured. Moreover, the effects of NOX inhibitor, the  $\text{H}_2\text{O}_2$  scavenger, and the VPO1 inhibitor on the VPO1 expression,  $\text{H}_2\text{O}_2$  and HOCl production were measured. Moreover, the direct effects of HOCl on eNOS expression and NO generation were also examined.

**Result** The VPO1 expression was significantly increased concomitantly with definite endothelial dysfunction in SHRs assessed by the substantial right shift of the concentration-relaxation curve, the decreased expression of eNOS in aortic ring and the decreased NO level in plasma. In cultured HUVECs we found that the angiotensin II-mediated down-regulation of eNOS expression and NO level was inhibited by knockdown of VPO1 using small hairpin RNA or the VPO1 specific inhibitor 4-aminobenzoic acid hydrazide. Moreover, the NADPH oxidase inhibitor and the hydrogen peroxide scavenger attenuated the angiotensin II-mediated up-regulation of VPO1 and HOCl generation. Furthermore, treatment with HOCl markedly decreased the eNOS expression and NO production.

**Conclusion** VPO1 is a novel regulator of endothelial dysfunction via NOX- $\text{H}_2\text{O}_2$ -VPO1-HOCl-eNOS/NO pathways, which may contribute to the pathogenesis and/or development of hypertension.

## Involvement of Vascular peroxidase 1 in angiotensin II-induced H9c2 cells hypertrophy

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**Objective** Oxidative stress induces hypertrophic gene expression and collagen deposition that mediates cardiac hypertrophy and myocardial fibrosis. Vascular peroxidase 1 (VPO1) is a new heme-containing peroxidase, which can utilize hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) generated from co-expressed NADPH oxidase (NOX) to produce hypochlorous acid (HOCl) and catalyze peroxidative reactions. Our previous studies had found that NOX/VPO1 pathway-mediated oxidative stress plays an important role in myocardial ischemia-reperfusion injury. This study was aim to investigate whether VPO1 mediate angiotensin II induced cardiac hypertrophy in H9c2 cells and to explore the underlying mechanism.

**Methods** Cultured H9c2 cells were treated with angiotensin II, cell hypertrophy were measured by cellular surface size, brain natriuretic peptide (BNP) and atrial natriuretic factor (ANF) gene expression. The effects of NADPH oxidase inhibitor, diphenyleneiodonium (DPI), hydrogen peroxide scavenger, catalase, VPO1 inhibitor 4-aminobenzoic acid hydrazide (ABAH) on cell hypertrophy, VPO1 expression,  $\text{H}_2\text{O}_2$  and HOCl production were measured. And the effect of ABAH on the mitogen-activated protein kinase pathway including p-38, p-JNK and p-ERK were determined.

**Result** Angiotensin II treatment significantly increased the cellular size and the gene expression of BNP, ANF while up-regulated the VPO1 expression and HOCl production. These effects were inhibited

by pretreatment with DPI, catalase and ABAH. Moreover, pretreatment with ABAH abolished the angiotensin II-induced up-regulation of p-ERK activity, not p-38, p-JNK expression.

**Conclusion** These Result indicated that VPO1 play a role in anngitotensin II induced cell hyperthrophy via NOX-H<sub>2</sub>O<sub>2</sub>-VPO1-HOCl-ERK1/2 pathway.

### Traditional Chinese medicine banxiao capsule inhibits the development of atherosclerosis plaques in a rabbit model

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**Objective** Banxiao capsule is a compound prescription formulated according to the Gualou Xieba Decoctio originated from jinguiyaolue, which has been used for the treatment of coronary heart disease and angina pectoris for several hundred years and got very eminent effects in modern clinic. The novelty of Banxiao capsule is that we add Radix Notoginseng to treat CHD more effectively based on the treatment of statin combined with antiplatelet agent. The object is to investigate the protective effect of Banxiao capsule on lowering serum lipid levels and inhibiting the development of atherosclerosis in a rabbit model.

**Methods** Fifty male New Zealand white rabbits were randomly divided into five groups (n = 10 each). The rabbits in the normal group were fed with normal diet, while rabbits in model group and drug treatment groups were fed with high cholesterol diet, then underwent the injury of the left carotid artery adventitia with digestion and blunt dissection, meanwhile the contralateral one obtained sham operation. After the atherosclerotic rabbit model was successfully established, each group was treated with Atorvastatin or different dosage of Banxiao for 16 weeks. At the end, serum lipid, pathologic, immunohistochemical, and gene expression studies were performed.

**Result** After treatment for 16 weeks Banxiao dose-dependently reduced the level of triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and raised the level of high-density lipoprotein cholesterol in blood than model groups. Compared with model group, Banxiao decreased the content of many infla mmatory cytokines in plasm and plaques dose-dependently. Morphological analysis of carotid artery showed that Banxiao increased fibrous cap thickness and smooth muscle cells, reduced lipid core area and macrophages, and contributed to inhibit matrix degradation and infla mmatory response as well as atorvastatin.

**Conclusion** Our study show that Banxiao capsule may lower serum lipid level and inhibit the development of atherosclerosis in rabbit model, indicating that this medicine was a reasonable drug for treating cardiovascular atherosclerosis diseases in clinical.

### Delivery of AAV9 cyclin-A2 via hyaluronic acid hydrogel induces cardiac regeneration as well as improves cardiac function in vivo post MI

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**Objective** To assess the effects of exogenous AAV9 Cyclin-A2 in

vivo post MI.

**Methods** Forty-eight male Sprague Dawley rat were randomly divided into four groups: MI+PBS (n = 12); MI+AAV9 Cyclin-A2 (n = 12); MI+HA (n = 12); MI+HA+AAV-9 Cyclin-A2 (n = 12). The recombinant was constructed, and  $2 \times 10^{11}$  genome copies constructs were injected into the infarcted myocardium at three different points. Echocardiography was performed done to assess the left ventricular function. The hearts of each group were excised post MI four weeks to evaluate gene expression, apoptosis, vascular density, infarct area by Western Blot, immunohistochemistry, and Masson Triple Stain techniques.

**Result** There was a significant statistical difference in expression of Cyclin-A2 and PCNA between HA+AAV9 Cyclin-A2 and two other control groups (MI + PBS and MI + HA) after four weeks. However, mitosis specific protein, H3P, had no statistical difference in expression among four groups (P > 0.05). Strikingly, sequential delivery of AAV9 Cyclin-A2 increased EF compared with PBS alone (P < 0.01) or HA blank (P < 0.01), but no significant difference in the LVESD was observed between the groups. The values of LVESD at four weeks were: PBS alone  $1.18 \pm 0.06$ ; HA alone  $1.11 \pm 0.04$ ; AAV9 Cyclin-A2  $1.18 \pm 0.05$ ; and HA+AAV9 Cyclin-A  $21.26 \pm 0.05$  respectively. Meanwhile, the values of EF were: PBS alone  $0.82 \pm 0.03$ ; HA blank  $1.02 \pm 0.12$ ; AAV9 Cyclin-A2  $0.94 \pm 0.05$ , and HA+AAV9 Cyclin-A2  $1.12 \pm 0.06$  respectively.

**Conclusion** HA can be used as a vehicle for gene delivery. AAV9 Cyclin-A2 serves as a new approach in cardiac remodeling as well as promoting cardiomyocytes regeneration.

### Study the influence of different size balloon on the degree of injury of rabbit abdominal aorta

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**Objective** To study the influence of different size balloon on the degree of injury of rabbit abdominal aortic.

**Methods** Twenty five New Zealand White rabbits were randomly divided into normal control group (5 rabbits) and operated groups (20 rabbits), averagely divided into (Group A, Group B, Group C, Group D), matching to four types of balloon diameters. Intima-media ratio and intimal proliferation were observed to evaluate the degree of injury with high-frequence ultrasonography and pathology examination after balloon-injury 28 days.

**Result** Stenosis ratio of Group A, Group B and Group C were higher than the normal control group and Group D (Neointimal area and intimal-media ratio increased in the operated groups at 4 weeks after injury compared with the normal control group (The degree of vessel expansion in Group D was the highest, but neointimal area and intimal-media ratio of Group D were smaller than those of Group C (P < 0.05).

**Conclusion** Rabbit model of abdominal aortic stenosis could be founded successfully and efficiently with balloon/vessel ratio of 1.5-1.75 with balloon catheter technique. If exceeding the ratio, the degree of injury of intima could not be increased with the size of balloon, even

occurred the rupture of blood vessels.

### Cyclin-A2 promotes cardiac regenerates via the recruitment of cardiac stem cells after myocardium infarction.

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**Objective** To determine whether or not exogenous Cyclin-A2 promotes cardiac regenerate and restart cardiomyocytes cycle in vivo after MI.

**Methods** Mice were randomly divided into two groups; MI + saline (n = 30) and MI+rAAV9-CMV-Cyclin-A2 (n = 30).  $2 \times 10^{11}$  genome copies in 200  $\mu$ l saline were delivered into the mice myocardium through the caudal vein one week before MI. The control group was injected with saline at same volume and time. Post MI observation was one week and three weeks respectively. Echocardiography was performed to measure LVEDD, LVESD, and EF. Western Blot and immunohistochemical analysis were used to detect the expression and location of Cyclin-A2. PCNA and phosphohistone-H3 were used to confirm DNA synthesis and mitosis respectively. C-Kit and connexin 43, which were defined as cardiac stem cells markers, were also measured.

**Result** Western Blot showed that expression of Cyclin-A2 started at two weeks and peaked at four weeks after injection. Expression of Cyclin-A2 in two groups had a significant statistical difference with  $p < 0.01$ . PCNA was specific in S phase and exhibited higher expression in Cyclin-A2 treated group than control group ( $0.75 \pm 0.03$  vs  $0.43 \pm 0.02$ ,  $P = 0.036$ ). However, mitosis specific protein H3P had no statistical difference between the two groups ( $P > 0.05$ ). C-Kit and connexin 43 showed an increase in Cyclin-A2 treated group, but no change in control group ( $P = 0.029$ ) by Masson Triple Stain. There was significant difference in LVEDD, LVESD, and EF between the two groups.

**Conclusion** Cyclin-A2 promotes cardiac self-repair via the recruitment of cardiac stem cells and restart cardiomyocytes cycle after myocardial infarction.

### The angiogenic effect of saponin extract from root and biennial flower of panax notoginseng in zebrafish

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**Objective** To evaluate the angiogenic effect of saponin extract from root and biennial flower of Panax Notoginseng in zebrafish.

**Methods** Healthy transgenic zebrafish embryos at 24 hours post fertilization (hpf) were treated with embryo medium containing 25, 50, 100  $\mu$ g/ml of PNS and Sanqi F for 48 h. In the other treatment plan, zebrafish embryos at 21 hpf were pre-treated with VEGF receptor kinase inhibitor II (VRI) for 3 h then VRI was washed out and subsequently post-treated with the indicated concentrations of 25, 50, 100  $\mu$ g/ml PNS and Sanqi F for 48 h. The subintestinal vessels (SIVs) and intersegmental vessels (ISVs) in zebrafish were assessed for the pro-

angiogenic/protective blood vessels effect of PNS and Sanqi F on vascular change at 72 hpf.

**Result** In healthy zebrafish, Sanqi F stimulated angiogenesis in the SIVs and reflected in increasing the number of sprouting vessels from SIVs basket and frequency of ectopic SIVs embryos in dose-dependent manner. Quantitative analysis confirmed that Sanqi F had been showed more effective angiogenesis than PNS in healthy zebrafish. And in VRI-induced blood vessels loss model, PNS and Sanqi F both could rescue the SIVs and ISVs respectively. It was clear that Sanqi F showed more remarkable potency and efficacy than PNS on recovery rate in VRI-induced blood injury zebrafish.

**Conclusion** The present study demonstrated that PNS and Sanqi F both exhibited pro-angiogenic effect in healthy zebrafish and restorative effect in VRI-induced blood vessels loss model in zebrafish. Intriguingly, our findings also shed light on that Sanqi F showed more powerful and significant angiogenic/restorative effect than PNS.

### Proarrhythmic risk window exists in drugs that block multiple ion channels in the heart

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**Objective** The proarrhythmic risk of QT prolonging drugs varies significantly. However, the mechanisms responsible for the high or low risk of drug-induced arrhythmias remain unknown. In this study, we tested our hypothesis that a proarrhythmic window exists for drugs that block multiple ion channels, which may be a cause of drugs with a high or low risk of proarrhythmia. Based on data from single cell research, tolterodine (a bladder inotropic drug), amiodarone and ranolazine are used as multiple channel inhibitors.

**Methods** Hearts from New Zealand White female rabbits weighing 2.5 – 3.5 kg were isolated, perfused in a Langendorff mode with modified Krebs-Henseleit solution. The atrioventricular nodal area was thermally ablated to produce complete atrioventricular block, and then heart was paced at a frequency of 1 Hz. Multiple channel monophasic action potentials (MAP) and pseudo 12-lead electrocardiograms (ECGs) were recorded. MAPD<sub>90</sub> and transmural dispersion of repolarization (TDR) were measured.

**Result** In the absence of a drug (control), MAPD<sub>90s</sub> recorded from epicardium and endocardium of left ventricle were  $186.5 \pm 5.5$  and  $206.5 \pm 5.1$  ms (n = 8), respectively. Administration of tolterodine from 10 nM to 600 nM, MAPD<sub>90</sub> was increased, in concentration dependent manners, from  $196.70 \pm 4.9$  to  $281.7 \pm 26.8$  ms, and  $220.0 \pm 4.6$  ms to  $350.6 \pm 18.7$  ms (n = 8,  $p < 0.001$  vs control), respectively. However, when the concentration of tolterodine increased to 10  $\mu$ M from 600 nM, MAPD<sub>90</sub> was decreased to  $224.2 \pm 5.9$  and  $252.5 \pm 5.9$  ms (n = 8), respectively. In addition, the incidence of TdP was correlated with the biphasic changes of MAPD<sub>90</sub>. Polymorphic ventricular tachycardias (PVT) were recorded at concentrations of 0.1 – 1  $\mu$ M. There was no arrhythmia in the presence of 100 – 600 nM and 3 – 10  $\mu$ M tolterodine. In contrast, amiodarone caused PVT only at 0.03 – 0.3  $\mu$ M in the presence of late INa enhancer ATX-II. Ranolazine prolonged MAPD<sub>90</sub> in absence, but not in the presence of ATX-II and caused no PVT.

**Conclusion** The biphasic pattern of MAPD induced by tolterodine, as well as by amiodarone and ranolazine, suggests that a proarrhythmic window exists in multiple ion channel blockers, which may be a determinant of the risk of drug-induced proarrhythmias. The mechanism of the biphasic change may be attributed to the relative selectivity of drug on IK and late INa.



## Isolation and culture of SD rats aortic valve interstitial cells

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**Objective** Aortic valve interstitial cells (AVICs) play an vital role in the development of aortic valve stenosis. However, little progress is reported in isolation and culture of AVICs in rats, which is a wide used animal model for human diseases. The aim of this study is to isolate and culture AVICs from SD rats using an improved method.

**Methods** Aortic valves were isolated from the SD rats and techniques were developed with an improved explant method. The myofibroblast markers,  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA) and vimentin, were analyzed using immunofluorescence. Ultrastructural characterization of cells was examined with transmission electron microscope (TEM).

**Result** 1. The time of primary culture were sharply cut down by shorten the contact time of aortic valve with culture media and increasing the density of fetal bovine serum in culture media. 2. Isolated cells exhibited an elongated morphology at low densities and cobblestone morphology at confluence. Cells from SD rats aortic valves were positive for  $\alpha$ -SMA and vimentin. TEM analysis showed ultrastructural features of cells with abundant mitochondria, prominent rough endoplasmic reticulum, and plentiful myofilaments.

**Conclusion** This study provides a reliable and efficient explant method to isolate and culture AVICs from SD rats, which maybe helpful to the mechanism study of aortic valve stenosis and heart valves tissue engineering.

## Relationship between ischemia duration and expression of heat shock protein 70 in ischemia-reperfusion canine hearts

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**Background** Heat shock protein 70 (HSP70) has been shown to exert a protective effect in hearts subjected to ischemia-reperfusion and alleviate adverse effects of myocardial ischemia-reperfusion injury (MIRI). However, little is known about the influence of ischemia time on HSP70 expression. The effects of ischemic duration on the content of HSP70 transcripts in ischemia-reperfusion myocardium were investigated in this article.

**Methods** Male mongrel dogs underwent a 15- or 60-min occlusion of the left anterior descending coronary artery, followed by a 120-min reperfusion. Additionally, a sham-operation group was assigned. The animals were killed after 120-min reperfusion and the heart was quickly removed. The myocardium was examined pathologically by electron microscopy. HSP70 mRNA expression both in intact and ischemic myocardium was measured by a semiquantitative reverse transcriptase-polymerase chain reaction (RT-PCR) method using complementary DNA normalized against the housekeeping gene  $\beta$ -actin.

**Result** (1) No ultrastructural changes of microvessels and myocardial cells except a slight loss of mitochondrial granules were noted in reperfusion myocardium from dogs of 15-min ischemia group.

In 60-min ischemia group, endothelial cells of capillaries were slightly swelling, and the intercellular linking gaps of endothelial cells slightly widened. As for myocardial cells, intercellular, intermyofibrillar, and intermyofibrillar edema were present. Besides, the fractures of a few myofilaments, the granule loss and swelling of mitochondrias were also seen. (2) HSP70 mRNA expression level in both ischemia-reperfusion zone and intact myocardium in 15-min ischemia group was markedly higher than in sham-operation group ( $36.2 \pm 6.5$  vs  $22.0 \pm 4.0$ ,  $P = 0.005$ ;  $29.8 \pm 4.5$  vs  $22.2 \pm 4.7$ ,  $P = 0.050$ ). Compared with sham-operation group, however, no changes in mRNA HSP70 levels in 60min ischemia group ( $25.7 \pm 7.5$  vs  $22.0 \pm 4.0$ ,  $P = 0.681$ ;  $28.5 \pm 4.7$  vs  $22.2 \pm 4.7$ ,  $P = 0.118$ ) were seen. The ratio of HSP70 mRNA expression content in ischemia-reperfusion zone to that in intact myocardium in 15-min ischemia group was not significantly different from sham-operation group ( $1.22 \pm 0.16$  vs  $1.01 \pm 0.22$ ,  $P = 0.233$ ), but remarkably higher than 60-min ischemia group ( $1.22 \pm 0.16$  vs  $0.89 \pm 0.17$ ,  $P = 0.019$ ).

**Conclusion** The change of HSP70 expression in ischemia-reperfusion myocardium is associated with ischemia time, that is, short duration ischemia promotes HSP70 expression, whereas long time ischemia does not. Furthermore, the HSP 70 expression changes consist with the protective extent of myocardial ultrastructures.

## Animal survival experiments for ventricular assist device of “TongXin Demo4”

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**Objective** Ventricular assist devices are of great clinical value in treating end-stage heart failure, but they need preclinical animal experiments to evaluate their hemocompatibility and reliability in order to reduce potential complications such as bleeding, thrombus, infection and multiple organ dysfunction syndrome. “TongXin Demo 4”, a third generation electromagnetic bearingless blood pump manufactured by ChinaHeart Biomedical Inc. at the basis of previous prototype, has an advanced structure design resulting in smaller size and lighter weight. CFD analysis shows a considerable blood compatibility. This study intends to implant “TongXin Demo 4” into animals for mid-and-long term auxiliary circulation, and then assess its hemocompatibility, reliability and effects on end-organs.

**Methods** First, “TongXin Demo 4” was connected into a mock circulatory loop, and generated ( $4.6 \pm 0.1$ ) L/min outflow against a head pressure of ( $100 \pm 3$ ) mm Hg by adjusting thermistor and pump rate. Blood samples were drawn from the reservoir before pumping and at every hour of pumping for measurement of plasma free hemoglobin (FHB) and hematocrit (Hct). The normalized index of hemolysis (NIH) was evaluated. Then pumps were implanted into 2 healthy male sheep (weight  $44.25 \pm 0.25$  kg) via the fifth rib after anesthesia, with inflow inserted into the left ventricular apex and outflow graft anastomosed to the descending aorta, thus building a bypass for blood of “left ventricular  $\rightarrow$  VADs  $\rightarrow$  descending aorta”. Routine hematologic and biochemical tests were performed preoperatively and postoperatively. Pump operating parameters were monitored continuously. At the termination, the sheep were humanely killed for observing pumps, and the end-organs were examined macroscopically and histopathologically.

**Result** We obtained NIH for “TongXin Demo 4” as ( $0.0012 \pm 0.0008$ ) g/100L; both sheep stood up after pulling out breathing cannula

in 2 hours. Hematologic and biomedical data were within the normal range and showed no evidence of organ dysfunction; the animals survived without bleeding and infection; the pumps worked on without mechanical failure; 36 days after surgery, no thrombosis were observed in the pump, inlet and outlet; histopathological examinations showed no lesions for end-organs.

**Conclusion** The “TongXin Demo 4” has excellent blood compatibility and reliability; it basically has no structural and functional effects on major organs; the specific performance needs to be tested through more samples.

### The expression of CXCL10 is elevated in congenital pulmonary hypertension

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**Background and Purpose** CXC-chemokine ligand 10 (CXCL10) inhibits angiogenesis and attracts activated T lymphocytes. Abnormal angiogenesis and lymphocytic infiltration participate in the pathobiology of pulmonary arterial hypertension (PAH). Serum CXCL10 is reported elevated in idiopathic PAH and is associated with clinical outcomes. We investigated the serum level of CXCL10 inpatients of congenital pulmonary hypertension and lung tissue of PAH rats.

**Experimental Approach** Rat model of PAH was induced by monocrotaline (60 mg/kg, subcutaneous injection). Human pulmonary arterial smooth muscle cell (HPASMC) proliferation was induced by fetal bovine serum (10%) after starvation for 24 hours. The expression level of CXCL10 and its receptor (CXCR3) was measured by RT-PCR. Serum CXCL10 level was measured by protein affinity microarray. CXCL10 level of patients of congenital heart disease with severe PAH or without PAH was compared.

**Result** Compared with control, CXCL10 expression level in lung tissue of rat was elevated about 2 times after monocrotaline injection 1 week, and then declined gradually. The expression level of CXCR3, receptor of CXCL10, also increased after monocrotaline injection, and reached the top (about 1.4 times) in week 3. FBS can induce HPASMC expression CXCL10, the expression level was elevated about  $1.91 \pm 0.17$  times after 24 hours compared with control. The expression level of CXCR3 inHPASMC changed insignificantly. The mean serum CXCL10 level of congenital heart disease patients with severe PAH was  $2163 \pm 560$  pg/ml, about 2 times of congenital heart disease patients without PAH.

**Conclusion and Implications** Serum CXCL10 is reported elevated in idiopathic PAH and is associated with clinical outcomes. Our preliminary Result showed it is also elevated in congenital pulmonary hypertension. This study augments the probability of serum CXCL10 being a new biomarker of PAH.

### The expression of CCL4 is elevated in congenital pulmonary hypertension

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**Background and Purpose** Inflammatory processes are prominent in various types of human and experimental pulmonary hypertension (PH) and are increasingly recognized as major pathogenic components of pulmonary vascular remodeling. Macrophages, T and B lymphocytes, and dendritic cells are present in the vascular lesions of PH. CCL4 is an important chemoattractant for macrophages and T lymphocytes. We investigated the serum level of CXCL10 inpatients of congenital pulmonary hypertension and lung tissue of PAH rats.

**Experimental Approach** Rat model of PAH was induced by monocrotaline (60 mg/kg, subcutaneous injection). The expression level of CCL4 and its receptor (CCR5) was measured by RT-PCR. Serum CCL4 level was measured by protein affinity microarray. Circulating CCL4 level of patients of congenital heart disease with severe PAH or without PAH was compared.

**Result** CCL4 expression level in lung tissue of rat was elevated rapidly after monocrotaline injection and maintained with high level. The top level was reached at week 2, about 6.8 times compared with control. The expression level of CCR5, receptor of CCL4, increased slightly after monocrotaline injection and has no significant compared with control. The mean serum CCL4 level of congenital heart disease patients with severe PAH was  $277 \pm 18$ , significantly higher than patients without PAH (about 9 times).

**Conclusion and Implications** Our preliminary result showed serum CCL4 level is elevated in rat PAH model and congenital pulmonary hypertension patients. This study emerged the probability of serum CCL4 being a new biomarker of PAH.

### Comparative myocardial protection between HTK solution and cold blood cardioplegia in immature heart during cardiopulmonary bypass

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**Objective** The optimal myocardial protection strategy for newborns/infants undergoing prolonged cardiac arrest during congenital heart surgery remains controversial. Which is the better option between HTK or blood cardioplegia during neonatal cardiopulmonary bypass is unclear. The purpose of this study was to compare myocardial protection using HTK and cold blood cardioplegia in a neonatal piglet model.

**Materials and Methods** Fifteen piglets were randomized to three groups: the control group (C group,  $n = 5$ ), a single dose of HTK group (HTK group,  $n = 5$ ) and multi-dose cold blood cardioplegia group (cardioplegia : blood = 1 : 1, CBC group,  $n = 5$ ). Animals in the two experimental groups were placed on hypothermic CPB, after which the ascending aorta was clamped for 2 h. The control animals underwent normothermic CPB without cardiac arrest. Serum troponin-T, troponin-I, CK-MB levels were measured before CPB and 2 h after weaning from

CPB. eNOS and VEGF content in coronary vessels and iNOS, TNF- $\alpha$ , IL-1 $\beta$  and ATP content in myocardium were assayed. TUNEL positive myocytes were counted. Myocardial histopathology was examined by light microscopy. Mitochondrial structural damages were assessed by electronic microscopy.

**Result** Transfusion requirement in the CBC group was significantly more than that in the HTK group ( $P < 0.01$ ). Immediately after declamping, both the difference between arterial and coronary sinus blood lactate concentrations and the oxygen extraction did not differ between the two experimental groups ( $P > 0.05$ ). At 2 h after weaning from CPB, rise in serum TnT, TnI and CK-MB levels showed no significant differences between the three groups ( $P > 0.05$ ). There were no differences in eNOS, VEGF, iNOS, TNF- $\alpha$  and IL-1 $\beta$  content in myocardium as well as histopathological score between the HTK group and the CBC group ( $P > 0.05$ ). However, mitochondrial score under electronic microscopy in HTK group was higher than that in the CBC group ( $P = 0.045$ ), and myocardial ATP content in the HTK group was lower than that in the control group ( $P = 0.017$ ). Moreover, TUNEL positive cells in the HTK group increased compared to the CBC group ( $P = 0.037$ ).

**Conclusion** Compared with cold blood cardioplegia, there are no differences in myocardial metabolism, biochemical markers, endothelial activation and early inflammatory reaction and histopathological injury between the HTK group and the CBC group. However, mitochondrial injury in the HTK group shows more damages than that in the CBC group, and there are increased apoptotic cells and trend of reduced ATP content in myocardium in the HTK group. Less transfusion requirement is needed in the HTK group than that in the CBC group. HTK solution can be used as a good alternative cardioplegia to CBC for the neonatal heart within 2 hours of cardiac arrest.

### The cardioprotective effect of an improved cardioplegia

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**Objective** The heart preservation solution is indispensable for the donor-heart preservation during transplantation. We combined "the cardiac protection and the coronary protection" together to intensify the isolated heart preservation effects. We used the isolated rat heart perfusion model to assess the hypothermic preservation effects of the newly designed solution.

**Methods** We randomly divided the male Wistar rats ( $n = 15$ ) to 3 groups as follow: Control, FW and HTK. The hearts, except the control group, were preserved by simply immersion them for 8 hours at 4°C in each solution. At the end of the storage period, the hearts were perfused immediately in the Langend off model. Some indices of myocardial function were measured, every kind of myocardial enzymes were measured in the coronary effluent. Myocardium was reserved to observe the changes of myocardial ultra-structure to assess the quality of heart preservation.

**Result** The heart function of the experimental group decreased to a different degree. Group FW and HTK had a lower mean left ventricular developed pressure (LVDP), dp/dtmax, dp/dtmin compared with the Control group ( $P < 0.01$ ). Group HTK showed better coronary flow (CF) compared to group FW ( $P < 0.05$ ). Group FW showed remarkably decreased release of every kind myocardial enzymes compared to group

HTK ( $P < 0.01$ , respectively) in cTnI, GOT and CK.

**Conclusion** After the preservation in the three kind of profound hypothermia cardioplegia solution for 8 hour, the heart function decrease. Cardioprotection effects of FW solution is better than the HTK solution in the isolated rat heart model during hypothermic preservation.

### The protective effect of FW organ preservation solution on endothelial function

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**Objective** To assess the effect of Fuwai organ preservation solution on endotheliorelaxation and morphology in isolated rat thoracic aortic arteries.

**Methods** After rat thoracic aortic artery rings were incubated in FW (nicorandil 0.1 mmol/L), HTK, UW and Krebs solution at 4 °C for 4 hours, the structural change of endothelium was evaluated by light and electron microscopy, meanwhile pre-contraction induced by prostaglandin F2a (U46619 30 nmol/L) and endothelium-dependent relaxation induced by calcium ionophore (A23187  $10^{-10} - 10^{-6}$  mol/L) were measured in the presence of indomethacin (7  $\mu$ mol/L) and LNNA (300  $\mu$ mol/L) in organ chamber.

**Result** Under light microscopy observation, there was no significant damage of endothelium among the FW group, the HTK group, the UW group and the control (KH) group. Under electron microscopy observation, the of endothelium damages of the group HTK and the FW group were lighter than the UW group. The maximal relaxation response induced by A23187 in group FW ( $65.89\% \pm 10.42\%$ ) and in group HTK ( $63.92\% \pm 11.31\%$ ) was higher than that in group KH ( $42.57\% \pm 12.04\%$ ), whereas the maximal relaxation in group UW ( $32.06\% \pm 12.43\%$ ) was lower than that in group KH ( $P < 0.05$ ).

**Conclusion** Under deep hypothermia condition, the FW solution is superior to the UW solution in the endothelium preservation in the isolated rat thoracic aortic arteries.

### Effect of FW solution on sodium channel in ischemia-reperfusion newborn rat myocytes

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**Objective** To study the effect of the FW solution on sodium channel (INa) in ischemia-reperfusion (I/R) neonatal rat myocytes.

**Methods** Myocytes were primary cultured for 18-48 h before using in the experiment. Cells were treated with I/R in the I/R group and with I/R plus Histidine-tryptophan-ketoglutarat (HTK) solution or FW solution in the HTK and the FW group, respectively. Whole cell patch clamp was used to record the current and gating.

**Result** The peak current density in the FW group decreased significantly than the I/R and the HTK group ( $-305.9 \pm 64.1$  pA/pF vs  $-617.2 \pm 74.2$  pA/pF and  $-547.3 \pm 20.8$ ,  $P < 0.05$ ), the I-V curve of the FW group up-shifted. The peak current in the HTK group decreased than the I/R group, however no significant difference was observed. Compared with the I/R and the FW group, the activation and inactivation



curves of the HTK group left-shifted.

**Conclusion** FW solution could inhibit the INa current after I/R injury in neonatal rat myocytes without affecting the gating characteristics of the channel. This could help alleviating intracellular Na<sup>+</sup> and calcium (Ca<sup>2+</sup>) overload.

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### Effects of bushen jiangya decoction on the CPT-1 gene regulation mechanisms in insulin resistance of spontaneous hypertensive rats

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**Objective** To investigate mitochondrial fatty acid oxidation enzymes carnitine palmitoyl transferase (CPT-1) gene regulation mechanisms in insulin resistance of spontaneous hypertensive rats (SHR), and to observe the effects of Bushen Jiangya Decoction (BJD) on the blood pressure, insulin resistance and the myocardial energy metabolism of adult spontaneous hypertensive rats (SHR).

**Methods** 60 SHRs, 12 weeks old, were randomly divided into five groups.

**Result** After 8 week-treatment, the blood pressure in all rats were recorded; The level of fasting blood glucose (FPG) was determined with enzyme colorimetric and the insulin sensitivity index (ISI) was calculated.

**Conclusion** Bushen Jiangya Decoction can increase CPT-1 gene expression in cardiac tissue, promote myocardial fatty acid metabolism, thereby improve insulin resistance in SHR, and the mechanism may be related to increase the serum level of adiponectin, and improve myocardial tissue adiponectin signaling pathway.

## Cardiovascular Imaging and Laboratory medicine

### Protective effect of Shen Yuan Dan, a traditional Chinese medicine, against myocardial ischemia/reperfusion injury in vivo and vitro

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**Objective** The myocardial ischemia/reperfusion injury is a major problem in myocardial ischemia/reperfusion injury and pharmacological postconditioning could alleviate the injury. The purpose of this study was to investigate the effects and mechanisms of Shen-Yuan-Dan (SYD), which is a widely used traditional Chinese medicine prescription, pharmacological postconditioning on myocardial ischemia/reperfusion injury.

**Methods** The rat ischemia/reperfusion model was established by ligation of left anterior descending coronary artery for 30 min and reperfusion for 3 h and the I/R model in vitro was performed on cultured neonatal cardiomyocytes subjected to simulated hypoxia/reoxygenation. Myocardial injury markers and histopathology staining were examined in rat model. In vitro experiment, cell viability was detected by 3- (4, 5-dimethylthazol-2-yl)-2, 5-diphenyl tetrazolium bromide assays. Cellular apoptosis was determined by hoechst 33342 staining. The protein expressions of Bcl-2 and Bax in different groups were determined by immunocytochemistry assay.

**Result** Both low dose of SYD reduced lactic dehydrogenase and creatine kinase-MB activity and malondialdehyde content, increasing superoxide dismutase activity and attenuating histopathology injury. Meanwhile, SYD promoted cell viability and inhibited the cardiomyocyte apoptosis. The expressions of Bcl-2 and Bax were restored to the normal level by SYD pharmacological postconditioning. These effects of SYD were reversed by LY294002, the inhibitor of the phosphatidylinositol 3-kinase/Akt pathway.

**Conclusion** Our data suggested that SYD pharmacological postconditioning showed cardioprotection against myocardial ischemia/reperfusion injury via activating the phosphatidylinositol 3-kinase/Akt pathway.

### The association between SAA in HDL and coronary heart disease

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**Objective** Serum amyloid A protein (SAA), majorly combining

with high density lipoprotein (HDL) in circulation, plays a role in the atherosclerosis. Whether there was an association between SAA in HDL and CHD was unclear. The present study was to explore the association between SAA in HDL and coronary heart disease (CHD).

**Methods** Stable CHD patients and age and gender matched control subjects were enrolled in this case-control study. Fast plasma was collected before coronary angiography. Potassium bromide (KBr) density gradient ultracentrifugation was used to isolate HDL from plasma. The levels of SAA in the HDL samples were detected by enzyme-linked immunosorbent assay kits. Logistic regression analysis was used to study the association between SAA in HDL and CHD.

**Result** Overall, 67 patients with confirmed stable CHD and 67 control subjects matched in age and gender were enrolled. Compared with controls, patients with CHD had a significant increase in the level of log (SAA) ( $1.39 \pm 0.58$  vs  $1.15 \pm 0.46$ ,  $P = 0.011$ ) independently from age, BMI, HDL cholesterol (HDL-C), etc. Logistic regression analysis showed the level of SAA in HDL was independent determinant of CHD (OR = 5.685, 95% CI: 1.371 – 23.581), which meant when log (SAA) increase 1 unit, the incidence of CHD increase 4.685 times.

**Conclusion** The composition of HDL altered in HDL isolated from CHD patients. The level of SAA in HDL may be associated with the incidence of CHD.

### Two autopsied cases of sudden death in young people with severe coronary atherosclerotic heart disease

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**Objective** To explore the tendency of the incidence of the sudden coronary death in young by analyzing the 2 cases of sudden death in young with severe coronary heart disease.

**Methods** Two cases of sudden death in young with severe coronary heart disease were selected from the autopsied cases in the Department of Forensic Pathology.

**Result** The two cases were both male with the age being 24 and 27 years old. Both of them had no history of heart disease and died without an hour after onset. Autopsy found that there were severest atherosclerotic lesions (in the fourth degree) in the three main branches of coronary arteries in the 24 years old man, of which 2 main branches were up to 90% and 95% respectively. The 27 years old man was found severe atherosclerotic lesions in the fourth degree in LAD and in the third level in RCA.

**Conclusion** Although both the severity degree of the coronary lesion and the incidence of SCD were lower in China than that in the European and American countries, SCD tended to be younger. People should pay more attention to prevention CHD and SCD and that rescue should be done in time and further resuscitation can become possible in order to get survival opportunity for them.

## The electrophysiological changes of inward rectifier potassium channel in ischemia postconditioning of cardiomyocyte

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**Background** Previous study suggested that adjusting the inward rectifier potassium channel in the process of ischemia postconditioning can affect the result of the myocardial protection against the ischemia reperfusion injury, but it is unclear the extent of change of the current density in the myocardial ischemia postconditioning. We observed the difference of inward rectifier potassium channel currents density between the groups with different procedure after a 45 min sustained hypoxia in cultured myocytes of neonatal rat in order to reveal its role in the postconditioning.

**Method** A 105 min continuous oxygenation (CON group), 45 min sustained hypoxia preceded with 60 min reoxygenation (I/R group), 45 min sustained hypoxia, preceded with  $3 \times 5$  min hypoxia/reoxygenation (IPO group) and after 45 min sustained hypoxia, added  $1 \mu\text{mol/L}$  zacopride at the onset of reoxygenation (PZ group) on cultured neonatal rat myocardial cells. Patch clamp recorded the inward rectifier potassium channel current density, cell death rate was observed by using typan blue staining.

**Result** Compared to the I/R group, inward and outward current density of the inward rectifier potassium channel in IPO group and PZ group were significantly increased (at  $-120 \text{ mV}$   $-22.34 \pm 3.14$ ,  $-16.67 \pm 4.27$  vs  $-10.34 \pm 0.82 \text{ pA/pF}$ ,  $P < 0.05$ , at  $-10 \text{ mV}$   $2.35 \pm 0.18$ ,  $2.48 \pm 0.11$  vs  $0.41 \pm 0.29 \text{ pA/pF}$ ,  $P < 0.05$ ). The myocytes mortality of IPO group and PZ group was significantly lower than that of the I/R group ( $49 \pm 7\%$ ,  $53 \pm 6\%$  vs  $69 \pm 5\%$   $\text{pA/pF}$ ,  $P < 0.05$ ).

**Conclusion** Hypoxia postconditioning increased inward rectifier potassium channel current density which may be an important mechanism to against the hypoxia-reperfusion injury by myocardial hypoxia postconditioning.

## Reversal effect of Dahuang Zhechong Pill combined with Jiawei Xiaoyao Pill on atherosclerosis and evaluation of MRI

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**Objective** To observe the atherosclerotic plaque reversal effect with our drugs treatment by MRI.

**Methods** To establish rabbit model of atherosclerosis by abdominal aorta injury operation and high fat diet for 2 month. After the MRI detection of modeling in experiment 1, drug treatment was administered, and MRI detection was administered 1 month and 3 months after. In experiment 2, the rabbits were divided into high dose group, low dose drug group, positive control group and blank control group. The drug groups were treated for 2 months.

**Result** In the three phases of experiment 1, the white development become from annular thick to thin annular and punctuate, finally to disappear. In experiment 2, the plaque of low dose group was significantly reduced, and the plaque of high dose group completely disappeared, while the plaque volume of positive control group remained

constant.

**Conclusion** The plaques decreased to disappear completely. To cure coronary heart disease is possible.

## Preclinical study of the iValve™ transcatheter valve and delivery system: early result of successful TAVI by transapical approach in 18 consecutive miniature pigs

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**Objective** Transcatheter aortic valve implantation (TAVI) is an emerging technology developed for treating patients with severe aortic stenosis who are considered inoperable or at high risk for traditional surgery. In this study, an innovative aortic prosthesis valve - the iValve™ transapical system (JieCheng Medical Technologies, Suzhou, China) that has unique navigation element specifically designed for accurate positioning and alignment of the prosthesis is being introduced for the first time. The purpose of this study is to perform preclinical evaluation for the feasibility and safety of fast transapical implantation of this valve, as well as its early stage hemodynamic performance after implantation, in eighteen Chinese miniature pigs.

**Methods** Self-positioning nitinol stent valve: The iValve™ prosthetic aortic valve (Jie Cheng Medical Technologies, Suzhou, China) contains two relatively independent components, the valve body and the navigation element, both self-expandable and are moveably attached. The valve body consists of a porcine aortic valve sewn to a cylindrical nitinol stent, which is covered with a polyester skirt to prevent periprosthetic regurgitation. The navigation elements are composed of three highly elastic recumbent nitinol filaments joined by three vertical slide tracks at the upper borders. This specific configuration ensures the flexibility and deformability of the navigation elements such that easy yet firm anchor at the bottom of native aortic cusps could be achieved. So the navigation elements are capable of achieving accurate self-positioning and alignment and providing operators with tactile feedbacks in the process that they capture and anchor into the aortic cusps. The connecting elements are placed at the bottom of the valve body where corresponding to the commissure of the leaflets on one end, and within the slide tracks on the other end. They can slide along the tracks during implantation.

The iValve™ TA-VTM delivery system is composed of a cambered delivery catheter at the distal end and a control handle at the proximal end. During implantation, the valve body lies above the navigation elements with the connection elements attached at the upper-end of the slide tracks when the prosthetic valve is to be compressed and loaded in the delivery catheter in vitro. However, the valve body will be pulled downwards to the native annulus after the navigation elements have opened and accurately positioned in the aortic cusps. The valve body descends until to the designed position which is relatively to the level



of navigation elements. At this point, the valve body has automatically aligned within the aortic root. Then the valve body is deployed and released. All the above steps can be finished easily by rotating four corresponding knobs in the control handle.

**Implantation procedure:** Experimental evaluation was performed on eighteen Chinese miniature pigs with a weigh between 40 and 62 kg ( $49.0 \pm 6.8$  kg). An inferior partial median sternotomy and longitudinal incision of the pericardium was adopted to access the left ventricular apex. After pre-operational angiogram of aortic root, the 24F delivery catheter was introduced into the left ventricle and the ascending aorta. Then the prosthetic valve was positioned and released by a standardizable delivery procedure described above. Finally, the delivery catheter and guidewire were retraced from the heart and the apex was closed with the purse string suture.

**Result Valve implantation:** One 21 mm-size, six 23 mm-size and eleven 25 mm-size valves were implanted with fluoroscopic guidance, all valves were successfully deployed after accurate positioning of the navigation elements in the aortic cusps in consecutive 18 miniature pigs except one. In one procedure, a second positioning was processed because one of the navigation ears failed to capture the native valve in the first attempt. Valve position was confirmed by angiography right after release, one valve showed moderate obliqueness to the mitral valve, and the animal dead 6 h after implantation because of valve failure. Another one showed slight obliqueness with no effect on valve's function. No coronary obstruction, valve migration or other serious adverse event was observed during the implantation processes, no conduction block or other type of arrhythmia was recorded either. Benefiting from the navigation ears, valve release procedures only took an average time of  $7.3 \pm 2.5$  minutes. No angiography was needed during the release procedure and no more than three times of angiography were achieved during the whole implantation process. **Hemodynamic performance:** Hemodynamic performance of the prosthetic valves was evaluated immediately after valve implantation and on the seventh day after implantation. Cardiac output was measured by Swan-Ganz catheter before and after valve deployment during implantation, no significant difference was observed ( $2.98 \pm 1.03$  vs  $3.42 \pm 1.50$ ,  $P = 0.088$ ). Mean transvalvular pressure gradient was  $3.33 \pm 1.54$  mm Hg at the baseline, and was slightly elevated after the implantation ( $11.07 \pm 4.35$  mm Hg). But this value remained stable at 7 days follow-up ( $11.85 \pm 5.30$  vs  $11.07 \pm 4.35$  mm Hg,  $P = 0.821$ ). Of the 17 animals lived to a week, only five ones showed trace paraprosthetic leak after implantation which remained the same at 7 days follow-up. Mitral valve regurgitation occurred in five cases after valve deployment, all of them were trace and three of them disappeared at 7 days follow-up.

**Conclusion** In this study we demonstrated feasibility and safety of the iValve<sup>TM</sup> transapical system which has novel navigation elements. This unique design enabled the iValve<sup>TM</sup> prosthesis valve to get anatomically correct self-positioning and alignment automatically within the native aortic annulus during a fast deployment procedure. The valve also showed optimal hemodynamic performance right after implantation, which was unchanged at 7 days follow-up.

## The effect of inward rectifier potassium channel in ischemia postconditioning of isolated ratheart

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**Background** Numerous studies discovered that inward rectifier

potassium channel is changed in ischemia-reperfusion injury, but its effect on myocardial ischemia postconditioning is unclear. The objective of this study is to observe the effect of inward rectifier potassium channels in the protection of myocardial ischemia postconditioning against the ischemia reperfusion injury.

**Method** 32 isolated rat hearts ( $n = 8$ ) suffered a 45 min sustained ischemia, followed by the process of sustained reperfusion (I/R group), ischemic postconditioning (IPO group), ischemic postconditioning + inward rectifier potassium channel antagonist  $20 \mu\text{mol/L}$  BaCl<sub>2</sub> (PB group), and post-processing + inward rectifier potassium channel agonist  $1 \mu\text{mol/L}$  Zaccopride (PZ group). Recorded the hear rate (HR), left ventricular developed pressure (LVDP),  $\pm dp/dt_{\text{max}}$ , coronary flow (CF), cardiac troponin I (cTnI), malondialdehyde (MDA) and total superoxide Dismutase (T-SOD), myocardial infarct size.

**Result** PZ group had better performance in cardiac function and coronary flow than IPO group had after the reperfusion; PZ group also reduced the release of cTnI, MDA and increased the synthesis of T-SOD. The infarct size was significantly reduced in PZ group than in IPO group ( $18.5 \pm 5.2\%$  vs  $29.0 \pm 4.2\%$ ,  $P < 0.05$ ). PB group were declined in the performance of cardiac function and CF, increased in the release of cTnI, MDA, but T-SOD synthesis was decreased comparing with the IPO group.

**Conclusion**  $20 \mu\text{mol/L}$  BaCl<sub>2</sub> partly eliminated, but  $1 \mu\text{mol/L}$  Zaccopride enhanced the protection of ischemia postconditioning against the myocardial ischemia reperfusion injury.

## Dyslipidemia in rat fed with high-fat diet is not associated with PCSK9-LDL-receptor pathway but ageing

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**Background** Obesity is associated with unfavorable alternations in plasma lipid profile and a broad spectrum of cardio-metabolic disorders. Proprotein Convastase Subtilisin Kexin type 9 (PCSK9) is a novel circulating protein that promotes hypercholesterolemia by decreasing hepatic low lipoprotein density receptor (LDLR) protein. However, the relationship between PCSK9 concentration and lipid profile in an obesity condition has less been investigated.

**Objective** In this study, we aimed to examine the changes of plasma PCSK9 concentration in a rat model fed with high fat diet (HFD) and its correlation to lipid profile, body weight and ageing.

**Method** Twenty male Sprague Dawley rats were divided the two groups: the control group (fed with normal pellet for 4 weeks), and high-fat diet group (fed with 3% cholesterol enrich diet for 4 weeks). Blood samples of rats were obtained before and at days 14, 21, and 28 in both groups. The body weight, plasma metabolic parameters (glucose, lipid profile) and PCSK9 were determined at indicated time points.

**Result** The body weights were significantly increased in rats fed with HFD compared to that in rats with normal pellet at day 28. Additionally, total cholesterol (TC), Triglyceride (TG), and low density lipoprotein cholesterol (LDL-C) levels in rat fed with HFD were also higher than that in rat fed with control diet while a decreased high density lipoprotein cholesterol (HDL-C) levels were found in rats with HFD at day 28. More interesting, there were no differences of plasma PCSK9 concentrations as well as hepatic expression of LDLR between the two

groups at day 28.

**Conclusion** Although the body weight and LDL-C were significantly increased in rats fed with HFD at 4 weeks there were no differences of changes in plasma PCSK9 concentration and LDLR expression of liver tissue in both groups at baseline and day 28, suggesting that dyslipidemia in rat model with HFD appears not associated with PCSK9-LDLR pathway but ageing.

### Atrial vagal-selective denervation using cell-penetrating (cp)-G $\alpha$ i1/2 C-terminal peptide via ultrasound-targeted microbubble destruction

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**Objective** The parasympathetic nervous system plays a critical role in the pathogenesis of atrial fibrillation (AF). The parasympathetic signalling is primarily mediated by the heterotrimeric G-protein, G $\alpha$ i $\beta$  $\gamma$ . We hypothesized that targeted inhibition of G $\alpha$ i interactions in the left atrium would suppress vagal-induced AF via ultrasound-targeted microbubble, which can carry peptide and release it by ultrasound with site-specific release pattern.

**Methods** By stimulating vagus nerve trunk and rapid right atrial pacing, we established paroxysmal atrial fibrillation model in canine. Rhodamine-labeled cell-penetrating (cp)-G $\alpha$ i1/2 C-terminal peptide combined with ultrasound-targeted microbubble using a direct connection method. The fluorescent intensity and binding rates were measured and analyzed using the fluorescence microscope observation and flow cytometry detection. A total of 12 canines were divided into 2 groups (n = 6): the experimental group using ultrasound plus targeted microbubbles with cp-G $\alpha$ i1/2 peptide, while in control group using ultrasound plus targeted microbubbles only. Confocal fluorescence microscopy was used to verify the expression of cp-G $\alpha$ i1/2 peptide. G $\alpha$ i1/2 subunit mRNA and protein expression were assessed by real-time PCR and western blot respectively. The amounts of cAMP in left atrium (LA) homogenates were assessed via competitive enzyme immunoassay.

**Result** Microbubbles and cp-G $\alpha$ i1/2 peptide were combined successfully. Fluorescence microscope observation showed that the microbubble's surface emitted orange-red fluorescence before and after washing; Result of flow cytometry detection showed that the binding rates of cp-G $\alpha$ i1/2 peptide were 93.4%  $\pm$  11.0% and 90.2%  $\pm$  9.4% before and after washing respectively. Cp-G $\alpha$ i1/2 peptide was confirmed existing in experimental group LA. There was no significant difference in the mRNA and protein expression of G $\alpha$ i1/2 subunit between the two groups, while cAMP levels in experimental group LAs were found to be significantly higher than that in control group (P < 0.01). Electrophysiological mapping of canine left atrial pulmonary veins (PVs), left atrial appendage (LAA) and coronary sinus (CS) indicated that the delivery of cp-G $\alpha$ i1/2 peptide into the LA prolonged effective refractory periods (ERP) and the dERP of different sites (P < 0.05).

**Conclusion** These Result demonstrate that specific G $\alpha$ i C-terminal peptide can be used to achieve selective disruption of parasympathetic-mediated M2R/Gi-protein coupled signalling by the inhibition of AC/cAMP/PKA pathway, thus decreases vagal-induced atrial fibrillation.

### The protective effects of a Non-depolarizing cardioplegia and its electrophysiological mechanisms

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**Objective** 1. To investigate the cardioprotective effects of St. Thomas (ST) solution, Histidine-Tryptophan-Ketoglutarate (HTK) solution and Non-depolarizing (NDP) solution after preservation in the three solutions at room temperature and 4 °C, separately. 2. To investigate the effects of ST solution, HTK solution and NDP solution on the electrophysiological characteristics of action potential (AP), fast sodium current (INa), L-type calcium current (ICa-L) and transient outward potassium current (Ito) from new-born rat cardiomyocytes. 3. To investigate the effects of ST solution, HTK solution and NDP solution on the cytoplasmic and mitochondrial calcium metabolism and their membrane potential migration. 4. Compare the cardioprotective and electrophysiological effects of ST solution, HTK solution and NDP solution.

**Methods** 1. Sixty-four isolated SD rat hearts were perfused with 37 °C oxygen-saturated KH solution for 15 min and then divided into 8 groups, 8 for each group. (1) for the hearts preserved under room temperature: we used 24 – 26 °C calcium-free KH solution, ST solution, HTK solution and NDP solution for cardiac arrest and the 1 hour-preservation for the Con group, the ST group, the HTK group and the NDP group separately. After preservation, hearts were reperfused with 37 °C oxygen-saturated KH solution for 1 h; (2) for the hearts preserved under icy temperature: we used 4 °C calcium-free KH solution, ST solution, HTK solution and NDP solution for cardiac arrest and the 8 hour-preservation for the Con group, the ST group, the HTK group and the NDP group separately. After preservation, hearts were rewarmed with each solution and reperfused with 37°C oxygen-saturated KH solution for 1 h Heart function recovery, Cardiac troponin I (cTnI) level, myocardial infarction area, ATP and lactic acid (LA) content and morphology variations were compared between each group. 2. We cultured the new-born rat cardiomyocytes. Cells after 36 hours' culturation were used for whole-cell patch clamp detection. Five groups were included: (1) the Control (Con) group: normal cardiomyocytes; (2) the ischemia/reperfusion (I/R) group: cells were treated with 3-hour ischemia and 1-hour-reperfusion; (3) the ST group, the HTK group and the NDP group: during the ischemia-reperfusion (I-R) treatment, ST solution, HTK solution and NDP solution were added in the culture medium separately. The characteristics of the AP, INa, ICa-L and Ito were compared between each group. 3. We cultured the new-born rat cardiomyocytes. Cells after 5 days' culturation were used for laser confocal microscopy scanning. Cells were incubated with four different fluorochromes. Under each condition, four groups were included: the Con group were scanned for 35 min continuously; after 5 min scanning, the ST group, the HTK group and the NDP group were treated with ST solution, HTK solution and NDP solution separately, and then followed with 30 min continuous scanning.

**Result** 1. Under the 1-hour-room temperature condition: the heart function recovery in the HTK group and the NDP group were superior to the ST group (P < 0.05); the coronary flow in the NDP group increased compared with the ST group and the HTK group (P < 0.05); the infarction percentage and cTnI level in the HTK group were lower than the ST and NDP groups (P < 0.05); there was no significant difference in the ATP and LA content among the three groups. 2. Under the 8-hour-icy temperature condition: the heart function of the ST group could not effectively recover; the heart function of the NDP group could recover

to the level of 90% of the preischemic value; the cTnI levels of the HTK and NDP groups were lower than the ST group. Compared with the ST group and the HTK group, the infarction area of the NDP group decreased, and the ATP content increased. There was no significant difference in the LA content among the three groups. 3. The electrophysiological changes of each group were as follows. (1) AP: the action potential amplified (APA) and action potential duration (APD) of the I/R group decreased and the resting membrane potential (RMP) depolarized compared with the Con group. The RMP, APA, APD of the NDP group recovered almost to the normal level. (2) INa: the peak current density of the I/R group decreased significantly than the Con group ( $P < 0.05$ ), the activation curve right-shifted and the inactivation curve left-shifted. Compared with the I/R, ST and the HTK groups, the peak current density increased ( $P < 0.05$ ), and the inactivation curve right-shifted. (3) ICa-L: the peak current density of the I/R group decreased significantly than the Con group ( $P < 0.05$ ), the activation curve right-shifted and the inactivation curve left-shifted. Compared with the I/R, ST and the HTK groups, the peak current density increased ( $P < 0.05$ ), and the inactivation curve right-shifted. (4) Ito: the peak current density of the I/R group decreased significantly than the Con group ( $P < 0.05$ ), the activation curve right-shifted and the inactivation curve left-shifted. Compared with the I/R, ST and the HTK groups, the peak current density of the NDP group increased ( $P < 0.05$ ), and the inactivation curve left-shifted. 4. The calcium and membrane potential variations of each group were as follows. After the addition of each cardioplegia: (1) cytoplasmic calcium: the fluorescent intensity baseline in the NDP group kept staying at a lower level compared with the ST and the HTK groups. (2) Cell membrane potential: the potential of the NDP group maintained at a hyperpolarization level, while of the ST and the HTK groups, the membrane potential kept at a depolarization level. (3) Mitochondrial calcium: the fluorescent intensity in the ST group increased than the Con and the HTK groups, while the NDP group decreased. (4) Mitochondrial membrane potential: the depolarization level of the ST group increased gradually, while the NDP and the Con groups tended to be more hyperpolarized.

**Conclusion** 1. Under the 1-hour-room temperature condition, the NDP solution could effectively protect the coronary function. The HTK solution and the NDP solution could improve the I-R heart function recovery, while there was no significant difference between the two groups. The result suggested that the application advantage of NDP solution in the regular cardiac surgery needed further studies. 2. Under the 8-hour-icy temperature condition, the NDP solution could improve the heart function to an almost normal level. This result suggested, compared with the HTK solution, that the NDP solution was a more ideal preservation solution during the organ transference process in heart transplantation. 3. The NDP solution could superiorly recover the electrophysiological characteristic changes caused by I-R injury. 4. The NDP solution could maintain the cytoplasm and the mitochondria calcium concentration at a continuous low level. These Result indicated that the NDP solution could effectively reduce the risk of the intracellular calcium overload, and was beneficial for the mitochondrial calcium absorption function, which could intensify the myocardial anti-I-R effects. 5. The NDP solution tended to induce the cell and the mitochondria membrane potential at hyperpolarization level, which could help maintain the cell calcium homeostatic and prevent the heart against oxidative damages during the I-R procedure.

## Median nerve stimulation reduces ventricular arrhythmia induced by isoproterenol infusion in normal dogs

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**Background** Spinal cord and vagus nerve stimulation were demonstrated to reduce the incidence of ventricular arrhythmias (VAs), somatic nerve stimulation was reported to improve myocardial ischemia and showed a salutary effect on arrhythmias, we hypothesized that median nerve stimulation (MNS) decreases the incidence of VAs induced by isoproterenol (ISO) infusion.

**Methods** 12 anesthetized dogs were instrumented to measure heart rate (HR) and arterial blood pressure (BP). Stimulating electrodes were positioned in right ventricular and bilateral median nerves. Each animal underwent two same episodes of VAs induction, during the second episode, animals received MNS. VAs were induced by intravenous ISO (0.6  $\mu\text{g}/\text{kg}/\text{min}$ , 5 minutes), if no VAs induced, ISO (0.6  $\mu\text{g}/\text{kg}/\text{min}$ ) with programmed stimulation (PS) was used to induce VAs again. The dogs with successfully induced VAs solely by ISO were used to testify the effect of vagus nerve.

**Result** HR and BP were reduced by MNS but without significant difference compared with baseline ( $P > 0.05$ ), HR was increased and decreased abruptly after infusion and cessation of ISO, MNS prevented this suddenly change ( $P < 0.05$ ), and delayed the occurrence of maximum HR ( $155.0 \pm 66.1$  s vs  $225.0 \pm 87.0$  s,  $P < 0.05$ ). No VAs was induced in baseline during MNS. VAs were successfully induced in 8 dogs with ISO infusion (4 with PS); the number of arrhythmic beats was significantly reduced ( $58.4 \pm 80.5$  vs  $11.4 \pm 7.7$   $P < 0.05$ ), and the time of first arrhythmic beat occurrence was significantly delayed ( $224.1 \pm 178.7$  s vs  $424.4 \pm 277.3$  s,  $P < 0.05$ ) by simultaneous ISO infusion and MNS. The inhibitory effect of MNS on VAs was not affected after bilateral vagotomy.

**Conclusion** Concurrent MNS reduced the magnitude responses of HR to ISO infusion. MNS decreased the occurrence of ISO-induced VAs in normal dogs, and this inhibitory effect had no relationship with the vagus nerve.

## The role of $\alpha\text{B}$ -Crystallin in the mTOR activation-induced cardiomyopathy

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**Objective** Dilated cardiomyopathy (DCM)'s and hypertrophic cardiomyopathy (HCM)'s underlying mechanisms remain poorly understood, and there is no effective treatment for them. The mammalian target of rapamycin (mTOR) is critical in maintaining the hemostasis of cardiomyocytes. Hyperactivation of mTOR can lead to cardiac hypertrophy and dilation in mice.  $\alpha\text{B}$ -crystallin is a member of the small heat shock protein (HSP) family. The missense mutation and the deletion mutation of  $\alpha\text{B}$ -crystallin can cause various forms of myocardial



disorders, including HCM, DCM and heart failure. Our recent studies demonstrate that  $\alpha$ B-crystallin is a downstream target protein of mTOR signaling and one of the central controllers of cell growth, proliferation and cancer development.

We hypothesized that the activation of mTOR could induce cardiac hypertrophy and dilation through upregulation of  $\alpha$ B-crystallin, so inhibition of  $\alpha$ B-crystallin might abolish mTOR activation-induced cardiac hypertrophy and dilation.

We investigated the role of  $\alpha$ B-crystallin in the mTOR activation-induced cardiac hypertrophy and dilation in this study. And the completion of this project can expand our understanding of the pathogenesis of cardiomyopathy, which may provide a better therapeutic strategy for the treatment of HCM and DCM.

**Methods** To test this hypothesis, we generated an mTOR activation-induced cardiac hypertrophy and dilation mouse model through inducible tuberous sclerosis complex 1 (Tsc1) knockout in cardiomyocytes (Tsc1-cKO). These mice then are crossmated to  $\alpha$ B-crystallin knockout mice to check whether the hypertrophy and dilation phenotype of Tsc1-cKO mice could be ameliorated or even disappears. Cardiac morphology and function were quantified using echocardiography at different time points. The heart size, heart weight and the thickness of left ventricular wall were determined by heart weight to body weight ratio (HW/BW) and HE staining. The protein levels of mTOR signaling were measured using Western Blot. The re-expression of cardiac fetal genes, such as ANF, BNP,  $\beta$ -MyHC and Sk.Actin, were assessed using real-time PCR. Meanwhile, the mortality was observed.

**Result** ① Within two weeks of inducible cardiac Tsc1 knockout, the mice had a higher mortality (50% vs 0%,  $P < 0.001$ ). The hearts exhibited a significant left ventricular dilation (left ventricular internal diameter in diastole (LVID, d)  $3.68 \pm 0.21$  mm vs  $3.40 \pm 0.29$  mm,  $P < 0.05$ ; left ventricular internal diameter in systole (LVID, s)  $2.46 \pm 0.24$  mm vs  $1.90 \pm 0.41$  mm,  $P < 0.05$ ) concomitant with decreased systolic and diastolic function (EF  $37.8 \pm 4.3\%$  vs  $70.6 \pm 8.6\%$ ,  $P < 0.001$ ; FS  $18.1 \pm 2.3\%$  vs  $39.9 \pm 7.2\%$ ,  $P < 0.01$ ). Besides that, the movement of ventricular wall was worse. In a word, cardiac dilation happened. ② At four weeks after Tsc1 knockout, the mice developed cardiac hypertrophy. The heart weight of Tsc1-cKO mice was significantly increased (HW/BW  $0.0066 \pm 0.0009$  vs  $0.0049 \pm 0.0007$ ,  $P < 0.05$ ; LV Mass (AW) Corrected  $110.6 \pm 15.3$  mg vs  $83.8 \pm 12.5$  mg,  $P < 0.01$ ) accompanied with an increased heart size when compared with controls. Moreover, the thickness of ventricular wall was increased (left ventricular anterior wall thickness in diastole (LVAW, d)  $1.02 \pm 0.10$  mm vs  $0.88 \pm 0.08$  mm,  $P < 0.05$ ; left ventricular posterior wall thickness in diastole (LVPW, d)  $1.01 \pm 0.11$  mm vs  $0.74 \pm 0.08$  mm,  $P < 0.05$ ). ③ After Tsc1 knockout in cardiomyocytes, mTOR signaling was hyperactivated, and cardiac function deteriorated rapidly afterward, which resulted in the significantly elevation of cardiac fetal genes re-expression, including ANF ( $P < 0.05$ ), BNP,  $\beta$ -MyHC and Sk.Actin ( $P < 0.01$ ), as assessed using real-time PCR. ④ As Western Blot showed,  $\alpha$ B-crystallin was the downstream target protein of mTOR signaling. When mTOR activated, it upregulated the expression level of  $\alpha$ B-crystallin. ⑤ Cardiac-specific Tsc1 and  $\alpha$ B-crystallin double knockout resulted in an improvement in cardiac morphology and function, as well as a decreased mortality.

**Conclusion** ① This study showed that after cardiac-specific Tsc1 knockout, hyperactivation of mTOR signaling was induced, which upregulated the expression of  $\alpha$ B-crystallin, then cardiac hypertrophy and dilation happened. ② Inhibition the expression of  $\alpha$ B-crystallin may attenuate mTOR signaling activation induced-cardiac hypertrophy and dilation, which provides therapeutic potential for HCM and DCM.

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### Effects of renal sympathetic denervation on the development of atrial fibrillation Substrates in dogs with pacing-induced heart failure

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**Objective** We examined the role of renal denervation on the inducibility of AF in dogs with pacing-induced HF.

**Background** Atrial fibrillation (AF) and heart failure (HF) are common interrelated conditions that are associated with renin-angiotensin-aldosterone system activity.

**Methods and Result** Nineteen dogs were randomized into sham-operated (7 dogs), HF (6 dogs) and HF+renal artery ablation (RAA, 6 dogs) groups. Sham-operated dogs were implanted with transvenous cardiac pacemakers without pacing. Dogs in the HF group were implanted with pacemakers and underwent right ventricular pacing for 3 weeks at 240 bpm to induce HF. The dogs in the HF+RAA group received double renal artery ablation. The dogs recovered for 8 weeks and underwent the same HF-inducing procedure. Compared to the baseline, the atrial dimensions increased and the right atrial ERP ( $131 \pm 14$  ms to  $112 \pm 12$  ms,  $P = 0.02$ ) decreased significantly after 3 weeks in the HF dogs but not the HF+RAA dogs. A greater number of AFs were induced in the HF dogs than the HF+RAA dogs ( $2.2 \pm 0.6$  vs  $0.3 \pm 0.3$ ,  $P = 0.03$ ). The atrium from HF hearts revealed a large amount of fibrosis, whereas control and HF+RAA dogs showed minimal fibrous tissue. The levels of BNP, Ang II, TNF- $\alpha$  and expression of TGF- $\beta$  and Cx43 in atrial tissue were increased in the HF dogs compared to the sham-operated and HF+RAA dogs.

**Conclusion** RAA suppressed the atrial substrate remodeling and the AF vulnerability that was induced by long-term rapid ventricular pacing.

### Membrane trafficking dysfunction plays an important role in the pathogenesis and progression of pulmonary hypertension

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**Background** Pulmonary hypertension is a pathophysiologic syndrome with high mortality and disability. Pulmonary hypertension is associated with intracellular membrane trafficking in which the protein Snap-23 is crucial. The aim of this study is to investigate the role of membrane trafficking dysfunction in the pathogenesis of pulmonary hypertension.

**Methods** We create a membrane trafficking model in human pulmonary artery endothelial cells by down regulation of Snap-23 gene expression. The mRNA and protein level of Snap-23, endothelial nitric oxide synthase, caveolin-1, bone morphogenic protein receptor II were

tested by reverse transcription-real time PCR and Western Blot.

**Result** In our cell model, compared to the control group, the expression of endothelial nitric oxide synthase, caveolin-1, bone morphogenic protein receptor II were decreased.

**Conclusion** Membrane trafficking dysfunction plays an important role in the pathogenesis and progression of pulmonary hypertension.

### A study of the effect on collagen and TGF- $\beta$ 1, AT1, CYP11B2 of dilated cardiomyopathy by transplantation of bone marrow mesenchymal stem cells

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**Objective** To investigate transplantation of MSCs in treatment of DCM on the feasibility of TGF- $\beta$ 1, AT1, CYP11B2 and myocardial collagen expression.

**Method** 1. Rats were injected ADR to build DCM model. 2. Through injecting of MSCs to treat the DCM rats.

**Result** 1. After ADR injection, Cardiac Ultrasound examination showed that the heart function was better than the DCM rats. HE staining and Masson staining were better than before. CVF was higher than the normal rats ( $P < 0.05$ ). RT-PCR: I collagen, I/III collagen gray scale, TGF- $\beta$ 1, AT1, CYP11B2 are all higher than normal ( $P < 0.05$ ), but lower than DCM rats ( $P < 0.05$ ). III collagen is higher than normal and DCM rats ( $P < 0.05$ ).

**Conclusion** 1. Through ADR injection we can establish classic DCM animal model of heart failure. 2. Through injecting of MSCs, DCM rats, cardiac function can be improved. 3. One of the mechanisms of MSCs transplantation for treatment of rats with DCM, may be the inhibition of myocardial collagen network remodeling.

### Neuregulin-1 protects against doxorubicin-induced apoptosis in cardiomyocytes through an Akt-dependent pathway

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**Purpose** In previous studies, it has been shown that recombinant human neuregulin-1 (rhNRG-1) is capable of improving the survival rate in animal models of doxorubicin (DOX)-induced cardiomyopathy

**Methods and Result** Neonatal rat ventricular myocytes (NRVMs) were subjected to various treatments. Activation of apoptosis was determined by observing increases in the protein levels of classic apoptosis markers (including cleaved caspase-3, cytochrome c, Bcl-2, BAX and terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick-end labeling (TUNEL) staining). All of these effects of DOX were markedly antagonized by pretreatment with rhNRG-1. It was then further demonstrated that the effects of rhNRG-1 could be blocked by the phosphoinositole-3-kinase inhibitor LY294002, indicating the involvement of the Akt process in mediating the process.

**Conclusion** RhNRG-1 is a potent inhibitor of doxorubicin-induced apoptosis, which acts through the PI3K-Akt pathway.

### Neuregulin-1 attenuates doxorubicin-induced autophagy in neonatal rat cardiomyocytes

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Recombinant human neuregulin-1 (rhNRG-1) improves cardiac function in animal models of doxorubicin (DOX)-induced cardiomyopathy, but the underlying mechanism remains largely unknown. Here, we confirm a role for rhNRG-1 in attenuating DOX-induced autophagy and define the signaling pathways through which it mediates some of its effects. Neonatal rat ventricular myocytes were subjected to different treatments in order to both induce autophagy and to determine the effects of rhNRG-1 on the process. rhNRG-1 is a potent inhibitor of DOX-induced autophagy and multiple signaling pathways, including Akt and activation of ROS, play important roles in the anti-autophagy effect. rhNRG-1 is a novel drug that may be effectively therapeutically in protecting further damage in DOX-induced damaged myocardium.

### The effect of sildenafil on the pathology progress and mechanism research on pulmonary arterial hypertension induced by monocrotaline in pneumonectomized rats

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**Objective** To investigate the effects of sildenafil on the remodeling of pulmonary arterial and TNF-alpha expression in model induced by monocrotaline in pneumonectomized rats.

**Methods** Male 24 SD rats were randomly divided into sham group ( $n = 8$ ), PAH group ( $n = 8$ ) and sildenafil group ( $n = 8$ ). The rats in group PAH and sildenafil were treated with monocrotaline (MCT) after pneumonectomy (PE); The sildenafil group was given sildenafil 50 mg/kg/day while others the saline. The rats were sacrificed at the 35<sup>th</sup> day and hemodynamic measurements and study on the morphological were performed. The expression of TNF-alpha was detected by the RT-PCR and WB.

**Result** Compared with the control, the PAH group had higher mPAP, sRVP, RV/(LV+S) ratio, RMT (all  $P < 0.05$ ), and the TNF-alpha expression ( $P < 0.05$ ). Between the control and the sildenafil group, no differences were found (all  $P > 0.05$ ).

**Conclusion** Sildenafil inhibits the remodeling of the PAH perhaps relying on the down-regulation of the TNF-alpha.

## The impact and the mechanism of Captopril on the pulmonary arterial hypertension model induced by chronic hypoxia in rats

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**Objective** To investigate the effects of Captopril on the hemodynamic, the pulmonary arterial remodeling and PI3K/AKT expression in pulmonary arterial hypertension (PAH) induced by chronic hypoxia in rats.

**Methods** Male 30 SD rats were randomly divided into control (n = 10), PAH group (n = 10) and Captopril group (n = 10). The rats in group PAH and Captopril were treated with chronic hypoxia; the Captopril group was given Captopril 100 mg/kg/day while others the saline. The rats were sacrificed at the 28<sup>th</sup> day. The hemodynamic and morphological study was performed. The expressions of PI3K/AKT were detected by the RT-PCR and WB.

**Result** Compared with the control, the PAH group had higher mPAP, sRVP, RV/(LV+S) ratio, RMT (all P < 0.05), and PI3K/AKT expression (P < 0.05). Between the control and the Captopril group, these parameters were found no difference (all P > 0.05).

**Conclusion** Captopril inhibits the pathology progress of the PAH and may rely on the inhibition of expression of the PI3K/AKT.

## Effects and mechanism of Danlou tablets on lipid metabolism and progression of atherosclerosis

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**Objective** We choose the Danlou tablet which is the only SFDA approved representative of removing both phlegm and blood stasis, through chronic hyperlipidemia and AS rabbits model, to explore the specific curative effect and mechanism of cure phlegm first, as well as the size of atherosclerotic lesions in vascular system.

**Methods** 44 healthy adult male New Zealand White rabbits were randomly divided into 4 groups: blank control group, model control group, Danlou tablet group, atorvastatin group. After carotid artery adventitial injury, the latter 3 groups rabbits were fed with an atherogenic diet for 28 weeks, which respectively feeding with Danlou tablets (2 g/kg), atorvastatin tablets (1 mg/kg), and vehicle as model controls. Every 4 weeks after intervention, testing blood lipid and plasma lipoprotein oxidation level, unit LDL-C content and its degree of oxidation back to normal, then all the rabbit were killed and their carotid artery, thoracic aorta, liver, ileum were taken out to undergo pathological examination. High pressure liquid chromatography combined with fluorescence detection, immunohistochemistry and real-time RT-PCR were performed to determine MDA content, expressions on high density lipoprotein receptor (SR-BI) and lectin sample oxidized low density lipoprotein receptor (LOX-1) in plaques and expressions of liver HMG CoA reductase, 7-hydroxylase, acetyl-CoA carboxylase, cholesterol transport protein, glucose-6-phosphatase and ileal bile acid transporter.

**Result** Comparison of model control group can be found after 4 weeks intervention, serum TC TG, LDL - C content has a significant decrease in Danlou tablet (2 g/kg) group (P < 0.05), lipid-lowering effect reach to the peak in 12 weeks; detection of serum lipoprotein oxidation degree show that, to 12 weekends, LDL oxidation degree in Danlou tablet group is significantly lower than the model control group (P < 0.05); after 20 weeks of continuous intervention, compared with model control group, Danlou tablet group animal carotid plaques in load area decreased to 10% significantly (P < 0.05), from local plaques and systemic atherosclerosis disease in comprehensive analysis, the progression of AS disease in Danlou tablet group was obviously lighter than model control group (P < 0.05), and is superior to the conventional dose of atorvastatin. And liver cholesterol and triglyceride levels in Danlou tablet group were significantly lower 30% than the model control group (P < 0.05); Compared to the statin group, liver expression of HMG CoA reductase, 7 - hydroxylase (CYP7A1) in Danlou tablet group have no obvious inhibition (P < 0.05); the expression of liver glucose 6 phosphatase (G - 6 - P) and acetyl CoA carboxylase (ACC) reduced 50% both significantly (P < 0.05); Compared with model control group, ileal bile acid transporter expression in Danlou tablet group reduced 20% significantly (P < 0.05), and the expression of lectin oxidized low density lipoprotein receptor (LOX - 1) significantly reduced, HDL receptor (SR - BI) expression significantly elevated (P < 0.05) and MDA plaques were significantly reduced 50% (P < 0.05) in Danlou tablet group.

**Conclusion** After long-term intervention, Danlou tablets have significantly lower liver cholesterol and triglyceride levels, serum-lipid lowering effect does not cause liver lipid deposition and does not affect the sugar and lipid normal metabolism, may be related to inhibiting the intestine bile acid transporter gene expression. And it not only reduces carotid atherosclerotic lesions significantly, also can delay systemic atherosclerosis progress.

## Cyclin-A2 promotes cardiac regenerate via the recruitment of cardiac stem cells after myocardium infarction

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**Objective** To determine whether or not exogenous Cyclin-A2 promotes cardiac regenerate and restart cardiomyocytes cycle in vivo after MI.

**Methods** Mice were randomly divided into two groups; MI+saline (n = 30) and MI+rAAV9-CMV-Cyclin-A2 (n = 30).  $2 \times 10^{11}$  genome copies in 200  $\mu$ l saline were delivered into the mice myocardium through the caudal vein one week before MI. The control group was injected with saline at same volume and time. Post MI observation was one week and three weeks respectively. Echocardiography was performed to measure LVEDD, LVESD, and EF. Western Blot and immunohistochemical analysis were used to detect the expression and location of Cyclin-A2. PCNA and phosphohistone-H3 were used to confirm DNA synthesis and mitosis respectively. C-Kit and connexin 43, which were defined as cardiac stem cells markers, were also measured.

**Result** Western Blot showed that expression of Cyclin-A2 started at two weeks and peaked at four weeks after injection. Expression of Cyclin-A2 in two groups had a significant statistical difference with P < 0.01. PCNA was specific in S phase and exhibited higher expression in Cyclin-A2 treated group than control group ( $0.75 \pm 0.03$  vs  $0.43 \pm 0.02$ , P = 0.036). However, mitosis specific protein H3P had no statistical



difference between the two groups ( $P > 0.05$ ). C-Kit and connexin 43 showed an increase in Cyclin-A2 treated group, but no change in control group ( $P < 0.05$ ). Immunohistochemistry showed that Cyclin-A2 after transfection was located in cytoplasm but not in nucleus. A decreased level of collagen I and III was observed in Cyclin-A2 treated group than control group ( $P = 0.029$ ) by Masson Triple Stain. There was significant difference in LVEDD, LVESD, and EF between the two groups ( $0.31 \pm 0.02$  cm vs  $0.44 \pm 0.01$  cm,  $0.21 \pm 0.02$  cm vs  $0.34 \pm 0.01$  cm and  $55 \pm 2.3\%$  vs  $40 \pm 1.7\%$ ).

**Conclusion** Cyclin-A2 promotes cardiac self-repair via the recruitment of cardiac stem cells and restart cardiomyocytes cycle after myocardial infarction.

### The expression of lox-1 and upar with oxldl on normal human peripheral blood mononuclear cells

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**Objective** Investigate the effect of oxLDL in different concentrations on uPAR and LOX-1 protein expression in human peripheral mononuclear cell in different times.

**Methods** PBMC were isolated from peripheral blood of healthy people. Then the mononuclear cells were allowed to culture in RPMI1640 medium with 20% autologous serum. Western blot was used to detect the effect of oxLDL of different concentration and time on protein expression of uPAR and LOX-1.

**Result** in 24 hours, as the concentrations increase, the expression of uPAR and LOX-1 protein level raised, the 50  $\mu\text{g/ml}$  was peaked, and high concentrations (100  $\mu\text{g/ml}$ ) were inhibited both of them. At 72 h, low concentrations (10, 20  $\mu\text{g/ml}$ ) can not effectively increase the expression of uPAR, higher concentrations (50, 100  $\mu\text{g/ml}$ ) can be more effective in increasing the expression of uPAR.

**Conclusion** In this study, oxLDL had different effects on the body in different times, 72 hours, showing more than 24 hours of injury.

### Relationship between ischemia duration and expression of heat shock protein 70 in ischemia-reperfusion canine hearts

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**Background** Heat shock protein 70 (HSP70) has been shown to exert a protective effect in hearts subjected to ischemia-reperfusion and alleviate adverse effects of myocardial ischemia-reperfusion injury (MIRI). However, little is known about the influence of ischemia time on HSP70 expression. The effects of ischemic duration on the content of HSP70 transcripts in ischemia-reperfusion myocardium were investigated in this article.

**Methods** Male mongrel dogs underwent a 15- or 60-min occlusion of the left anterior descending coronary artery, followed by a 120-min reperfusion. Additionally, a sham-operation group was assigned. The animals were killed after 120-min reperfusion and the heart was quickly

removed. The myocardium was examined pathologically by electron microscopy. HSP70 mRNA expression both in intact and ischemic myocardium was measured by a semiquantitative reverse transcriptase-polymerase chain reaction (RT-PCR) method using complementary DNA normalized against the housekeeping gene  $\beta$ -actin.

**Result** (1) No ultrastructural changes of microvessels and myocardial cells except a slight loss of mitochondrial granules were noted in reperfusion myocardium from dogs of 15-min ischemia group. In 60-min ischemia group, endothelial cells of capillaries were slightly swelling, and the intercellular linking gaps of endothelial cells slightly widened. As for myocardial cells, intercellular, intermyofibrillar, and intermyofibrillar edema were present. Besides, the fractures of a few myofilaments, the granule loss and swelling of mitochondria were also seen. (2) HSP70 mRNA expression level in both ischemia-reperfusion zone and intact myocardium in 15-min ischemia group was markedly higher than in sham-operation group ( $36.2 \pm 6.5$  vs  $22.0 \pm 4.0$ ,  $P = 0.005$ ;  $29.8 \pm 4.5$  vs  $22.2 \pm 4.7$ ,  $P = 0.050$ ). Compared with sham-operation group, however, no changes in mRNA HSP70 levels in 60 min ischemia group ( $25.7 \pm 7.5$  vs  $22.0 \pm 4.0$ ,  $P = 0.681$ ;  $28.5 \pm 4.7$  vs  $22.2 \pm 4.7$ ,  $P = 0.118$ ) were seen. The ratio of HSP70 mRNA expression content in ischemia-reperfusion zone to that in intact myocardium in 15-min ischemia group was not significantly different from sham-operation group ( $1.22 \pm 0.16$  vs  $1.01 \pm 0.22$ ,  $P = 0.233$ ), but remarkably higher than 60-min ischemia group ( $1.22 \pm 0.16$  vs  $0.89 \pm 0.17$ ,  $P = 0.019$ ).

**Conclusion** The change of HSP70 expression in ischemia-reperfusion myocardium is associated with ischemia time, that is, short duration ischemia promotes HSP70 expression, whereas long time ischemia does not. Furthermore, the HSP 70 expression changes consist with the protective extent of myocardial ultrastructures.

### Effects of Visfatin on the function of endothelial progenitor cells and the possible mechanisms

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**Objective** We explore the effect and related mechanism of Visfatin on proinflammatory role of EPCs.

**Method** 1. EPCs were isolated and cultured in vitro. 2. EPCs stimulated with Visfatin. 3. PDTC on the stimulation of EPCs to Visfatin.

**Results** 1. ICAM-1 and VCAM-1 mRNA increased in Visfatin group. 2. The expression of ICAM-1 in 4 groups were  $18.25 \pm 3.77\%$ ,  $25.40 \pm 4.25\%$ ,  $38.88 \pm 4.02\%$  and  $48.83 \pm 5.12\%$ , respectively ( $P < 0.05$ ). The expression of VCAM-1 were  $6.75 \pm 2.07\%$ ,  $10.65 \pm 2.33\%$ ,  $17.11 \pm 2.37\%$  and  $24.82 \pm 3.19\%$ , respectively ( $P < 0.05$ ). 3. ICAM-1 and VCAM-1 mRNA of PV group decreased. 4. The ICAM-1 and VCAM-1 expression of PV group was lower than that of Visfatin group.

**Conclusion** 1. It is feasible to obtain EPCs from cord blood in vitro. 2. ICAM-1 and VCAM-1 mRNA and protein expression increased in Visfatin group in a dose-and effect-relationship. 3. PDTC inhibits the mRNA and protein expression of ICAM-1 and VCAM-1 on EPCs surface, which suggested the inflammatory effect of Visfatin to EPCs may be mediated by NF- $\kappa$ B signaling pathway.

### Study the influence of different size balloon on the degree of injury of rabbit abdominal aorta

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**Objective** To study the influence of different size balloon on the degree of injury of rabbit abdominal aortic.

**Methods** Twenty five New Zealand White rabbits were randomly divided into normal control group (5 rabbits) and operated groups (20 rabbits), averagely divided into (Group A, Group B, Group C, Group D), matching to four types of balloon diameters. Intima-media ratio and intimal proliferation were observed to evaluate the degree of injury with high-frequency ultrasonography and pathology examination after balloon-injury 28 days.

**Result** Stenosis ratio of Group A, Group B and Group C were higher than the normal control group and Group D ( $P < 0.05$ ). Neointimal area and intimal-media ratio increased in the operated groups at 4 weeks after injury compared with the normal control group ( $P < 0.01$ ). The degree of vessel expansion in Group D was the highest, but neointimal area and intimal-media ratio of Group D were smaller than those of Group C ( $P < 0.05$ ).

**Conclusion** Rabbit model of abdominal aortic stenosis could be founded successfully and efficiently with balloon/vessel ratio of 1.5-1.75 with balloon catheter technique. If exceeding the ratio, the degree of injury of intima could not be increased with the size of balloon, even occurred the rupture of blood vessels.

### Effect of salvianolic acid B on ICAM-1 and E-selectin expression after cerebral ischemia reperfusion injury in rats

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**Objective** To research ICAM-1, E-selectin expression in rats following focal cerebral ischemia-reperfusion and the intervention effects of salvianolic acid B (SalB).

**Methods** Wistar rats were randomly divided into sham operation group, model group and SalB group. A rat cerebral middle artery occlusion model was established. At 4 time points (6 h, 24 h, 48 h, 72 h), the neurological deficit scores were evaluated, RT-PCR detection for brain tissue ICAM-1, E-selectin mRNA expression.

**Result** The neurological behavior scores were higher in SalB group than in model group at 4 time points ( $P < 0.001$ ). The expression of ICAM-1 mRNA in model group was increased at 6 h, reached peak at 24 h; the expression of E-selectin mRNA was increased at 6 h, reached peak at 48 h. The expression of ICAM-1 in SalB group was lower than in model group at 4 time points ( $P < 0.001$ ,  $P < 0.005$ ); the expression of

E-selectin at 6 h, 24 h, 48 h ( $P < 0.001$ ).

**Conclusion** SalB could improve MCAO rat neurological function and depress ICAM-1, E-selectin expression.

### Study of low-frequency focused ultrasound associated with microbubbles to open the blood brain barrier of mice

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**Objective** The aim of our study is to explore the safety and effectiveness of low-frequency focused ultrasound associated with microbubbles to open the blood brain barrier (BBB).

**Methods** The right basal ganglia of the mice were sonicated by the high-MI therapeutic impulses, through their intact skin and skull, after continuous intravenous injection of microbubbles and Evans blue (EB). The degree of BBB opening was evaluated quantitatively based on the extravasation of EB and qualitatively under the fluorescence microscope. The safety was inspected by observation of cell morphology under hematoxylin eosin (HE) staining.

**Result** After sonicated by the high-MI therapeutic impulses and microbubbles, in the sonicated area, we can see significantly red fluorescence of Evans blue under fluorescence microscope. The concentration of EB in the sonicated side is much higher than the normal side. The cellular morphology and structural integrity were normal.

**Conclusion** The BBB of mice can be opened targeted and noninvasively by low-frequency focused ultrasound with continuous intravenous injection of microbubbles.

### Clinical application of left ventricular systolic function in patients with rheumatic disease by three-dimensional ultrasound speckle tracking imaging

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**Objective** The aim of our study is to assess left ventricular global and regional systolic function in patients with pure mild to moderate rheumatic mitral stenosis (MS) by 3-dimensional ultrasound speckle tracking imaging (3D-STI).

**Methods** Fifty patients with pure mild to moderate rheumatic MS were enrolled in this study, 40 normal subjects matched with age and sex were selected as control groups. LV 3D-global longitudinal peak systolic strain (GLS), 3D-regional peak systolic strain in 16 segments of left ventricular mitral annular level, papillary muscle level and apical level were measured in all subjects by 3D-STI from the apical full-volume image and compared between groups. LV ejection fraction (LVEF) was acquired from 3DSTI.

**Result** Despite normal LV systolic function as assessed by LVEF, LV GLS was significantly reduced in patients with isolated MS ( $P < 0.05$ ). Regional analysis demonstrated that patients with MS had a significantly reduced 3D-regional peak strain in all basal, and some mid (inferior, anteroseptal, posteroseptal) segments of the left ventricle. 3D-regional peak strain values were similar in other segments between the groups. A Pearson correlate revealed that LV GLS corresponded with LVEF ( $r =$

0.601,  $P < 0.001$ ) in patients with isolated MS, and LV GLS correlated with LVEF in normal subjects ( $r = 0.709$ ,  $P < 0.001$ ).

**Conclusion** LVglobal 3D strain decreases in patients with pure mild to moderate rheumatic MS in the Subclinical period. 3D-STI identified early abnormalities in MS patients who had apparently normal systolic function by traditional echocardiography.

### Assessment of regional left ventricular systolic function in patients with hypertrophic cardiomyopathy by real-time three-dimensional echocardiography

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**Objective** The aim of our study is to assess left ventricular regional systolic function in patients with hypertrophic cardiomyopathy (HCM) using real-time three-dimensional echocardiography (RT-3DE).

**Methods** RT-3DE was performed in 25 HCM patients and 20 healthy subjects. The left ventricular volume-time curves were analyzed quantitatively with Tomtec 4DLV-Analysis 3.0, and regional left ventricular end diastolic/systolic volume (rEDV/rESV), the time to minimum systolic volume (rESVT), regional stroke volume (rSV), regional ejection fraction (rEF), regional-global ejection fraction (rgEF) and the parameters of left ventricular dyssynchrony were measured.

**Result** In HCM group, Tmsv16-Dif, Tmsv16-SD, Tmsv16-Dif%, Tmsv16-SD% were significantly reduced than those of normal group ( $P < 0.01$ ), and rEDV, rSV, rEF and rgEF in hypertrophic segments were lower than those in non-thickening and mild-thickening segments ( $P < 0.05$ ). In normal group, there were no significant difference in those parameters among all segments ( $P > 0.05$ ). Compared with normal group, rEDV, rSV and rgEF in hypertrophic segments were decreased in HCM group ( $P < 0.05$ ). rEF in hypertrophic segments were decreased at basal level but increased at apical level, however, no difference was found at midventricular level; rEF and rgEF in non-thickening and mild-thickening segments were increased ( $P < 0.05$ ).

**Conclusion** RT-3DE could sensitively detect left ventricular dyssynchrony and accurately assess regional left ventricular volume and function of different segments.

### Correlation between intima-media inhomogeneity and carotid artery elasticity in patients with type 2 diabetes mellitus

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**Objective** The aim of our study is to explore the correlation between intima-media inhomogeneity (IMI) and carotid artery elasticity in patients with type 2 diabetes mellitus (T2 DM).

**Methods** Patients with T2 DM ( $n = 39$ ) and normal control subjects ( $n = 31$ ) were studied. IMI and IMTmean of carotid artery were measured by an automatic measuring system. Elastic indexes ( $\beta$ mean, Ep, AC, PWV $\beta$ mean) of carotid artery were measured by Echo-Tracking. The relationship between the IMI and elastic index and cardiovascular risk factors were analyzed.

**Result** ① IMTmean, IMTmax and IMI were higher in patients

with T2DM than in normal subjects ( $P < 0.05$ ). ②  $\beta$ mean was higher in patients with T2DM than in normal subjects ( $P < 0.05$ ). ③ IMI was positive correlated with  $\beta$ mean, Ep, PWV $\beta$ mean, age, TG, HDL, FPG and IMTmean ( $r = -0.372 - 0.657$ ,  $P < 0.05 - 0.01$ ).

**Conclusions** The IMI is thought as a new index to reflect the atherosclerotic wall process.

### Evaluation of arterial alterations and associated factors of chronic kidney disease by ultrasonography

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**Objective** The aim of our study is to evaluate the changes in the structural and elastic of the arteries in chronic kidney disease (CKD) patients with predialysis by echo-tracking technique (ET).

**Methods** Thirty-nine CKD patients with predialysis were enrolled in the study and were subdivided into CKD stage 2 – 3 group ( $n = 19$ ) and stage 4 – 5 group ( $n = 20$ ). Forty healthy subjects were selected as the control group. The parameters of arterial structural and stiffness measured by echo-tracking technique were compared among groups: Intima-media thickness (IMT), stiffness parameter ( $\beta$ ), pressure strain elastic modulus (Ep), arterial compliance (AC), augmentation index (AI), carotid pulse wave velocity (PWV $\beta$ ), carotid-femoral pulse-wave velocity (PWVcf), carotid diameter (D). Furthermore, we explored the associated factors of arterial stiffness.

**Result** Compared with healthy group, PWVcf and D in stage 2 – 3 group were significantly increased ( $P < 0.05$ ,  $P < 0.001$ ), while PWV $\beta$  significantly were significantly increased in stage 4 – 5 ( $P < 0.05$ ); compared with CKD 2 – 3 group, PWVcf and D were significantly increased in stage 4 – 5 ( $P < 0.05$ ,  $P < 0.001$ ). Stepwise multiple regression analysis demonstrated that age, estimated glomerular filtration rate (eGFR) per  $1.73 \text{ m}^2$  were independent impact factors of PWVcf.

**Conclusion** Echo-tracking technique can assess the changes in vascular structure and elasticity in patients with chronic renal insufficiency in the early stage; it can provide valuable information for clinical treatment and prevention of cardiovascular complication.

### Assessment of the ventricular-arterial coupling in the patients with systemic lupus erythematosus by ultrasound

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**Objective** The aim of our study is to assess the ventricular-arterial coupling in the patients with systemic lupus erythematosus (SLE) by ultrasound.

**Methods** Twenty-Five patients with SLE and twenty age and gender matched healthy subjects were studied. Left ventricular mass index (LVMI), relative wall thickness end-diastolic (RWT), carotid-femoral pulse wave velocity (CFPWV), effective arterial elastance (Ea) and Ea/Ees were measured.

**Result** Ed in the patients SLE were significantly higher than those in control group ( $P < 0.05$ ), there was no significant difference in Ees and Ea/Ees between two groups ( $P > 0.05$ ). Ed was correlated positively with



Ea ( $r = 0.472$ ,  $P < 0.01$ ). RWT was correlated positively with Ed and Ea ( $r = 0.388$ ,  $P = 0.016$ ;  $r = 0.336$ ,  $P = 0.026$ ). Ed was correlated positively with E/e ( $r = 0.939$ ,  $P < 0.01$ ). CFPWV was correlated positively with Ed and E/e and LVMI ( $r = 0.349$ ,  $P < 0.05$ ;  $r = 0.376$ ,  $P < 0.05$ ;  $r = 0.323$ ,  $P < 0.05$ ). diffD% was correlated negatively with E/e and LVMI ( $r = -0.328$ ,  $P < 0.05$ ;  $r = -0.428$ ,  $P < 0.01$ ).

**Conclusion** The structure and function of left ventricle is associated with arterial elastance. Their matching relation can be applied to evaluate ventricular-arterial coupling.

### The value of real-time three-dimensional echocardiography in diagnosis of cardiac mass

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**Objective** To study the value of real-time three-dimensional echocardiography (RT3DE) in diagnosis of cardiac tumor.

**Methods** Sixty-five patients with primary cardiac mass were retrospective studied. All cases were diagnosed using two-dimensional and RT3DE by Philips Sonos 7500 and iE33. The operative and pathological findings were collected.

**Result** Of these patients, 24 cases were left atrial mass, 13 cases were right atrial mass, 9 cases were left ventricular mass, 11 cases were right ventricular mass, 1 case was right ventricular and atrial mass, 1 case was right atrial and pericardial mass, 5 cases were pericardial mass, 1 case was pulmonary artery mass. Thirteen patients undertook the surgery.

**Conclusion** Echocardiography is a preferred method in the diagnosis of cardiac mass. Real-time dimensional echocardiography appeared advantages in showing the whole modality and adjacent tissue.

### The prognostic role of myocardial fibrosis detected by cardiac magnetic resonance in hypertrophic cardiomyopathy

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**Background** Hypertrophic cardiomyopathy is the most common inherited genetic cardiovascular disease and the main cause of sudden cardiac death (SCD) in the young, it can also cause other hard end points such as heart failure death and stroke. The mechanism is believed due to malignant ventricular and/or left ventricular outflow tract obstruction (LVOTO), and myocardial fibrosis and scar were thought to be the pathological substrate, which is reported as an independent determinant of adverse cardiac events. This study is aimed to evaluate the prognostic role of myocardial fibrosis detected by cardiac magnetic resonance late gadolinium enhancement (LGE-CMR) in the mid-term follow up of HCM.

**Methods** From Apr. 2010 to May 2012, we followed up all HCM patients come to our hospital every 3 to 6 month intervals, with exclusion of those who had prior gradient reduction therapy. Only new events occurred during the follow up were regarded as end points, which primary end points included cardiovascular death, heart transplantation, SCD /

aborted SCD, sustained ventricular tachycardia, ventricular fibrillation and appropriate implantable cardiac defibrillator (ICD) discharge; and secondary end point included progressive heart failure, unplanned cardiovascular hospitalization and non-sustained ventricular tachycardia (NSVT). The extent of LGE was divided into three groups: mild (1% – 25%/LV), moderate (25% – 50%/LV) and severe (> 50%/LV). Kaplan-Meier curves and log-rank test were used to estimate the events free survival distributions and compare the difference among different LGE groups. A multivariable Cox proportional hazard model was constructed with a forward selection procedure to estimate the hazard ratio (HR) for the presence or absence of fibrosis and to estimate the effect on the outcomes of increased amounts of fibrosis. Hypertrophic obstructive cardiomyopathy (HOCM) patients were also compared with non-obstructive patients for the events free survival curves, and patients received gradient reduction therapy were compared with those HOCM who didn't receive any surgical procedure.

**Result** Totally 392 patients were followed up, including 80 patients received gradient reduction therapy during the follow-up. Among the 312 natural procession patients, LGE was observed in 218 patients (70%). There were statistical significance on NYHA cardiac class, left ventricular mass, average wall thickness, extreme hypertrophy (> 30 mm), prevalence of atrial fibrillation and NSVT between patients with and without LGE. 35 patients reached the primary end points, including 5 in the LGE negative and 30 in the LGE positive group (5.3% vs 13.8%,  $p < 0.05$ ); while 3 cardiac deaths, 1 heart transplantation and 9 sustained ventricular tachycardia / ventricular fibrillation were all happened in the fibrosis group. 77 patients reached the secondary end points, including 10 in the LGE negative and 67 in the LGE positive (10.6% vs 30.7,  $P < 0.05$ ). There was statistical significance among Kaplan-Meier survival curves among different LGE groups, no matter regarding to primary or secondary end points. The left ventricular outflow tract obstruction (LVOTO) and LGE positive were the independent determinants for the primary end points after Cox proportional hazard regression, while only LGE was the risk factor for the secondary end points. There were statistical significance among the events free survival among HOCM, non-obstructive and apical HCM patients, and patients received gradient reduction therapy had better prognosis than those HOCM patients who didn't received intervention.

**Conclusion** Myocardial fibrosis detected by CMR can play an important prognostic role in HCM. The prognosis of HOCM was worse than the non-obstructive HCM patients, while receive gradient reduction therapy would benefit the mid-term survival.

### The application of transthoracic echocardiography for the diagnosis of congenital coronary artery fistula

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**Objective** The purpose of our study is to evaluate the application of transthoracic echocardiography for the diagnosis of congenital coronary artery fistula (CAFs).

**Methods** The echocardiographic appearances of 74 patients with CAFs were analyzed retrospectively, and the Result were compared with findings of surgery and coronary artery angiography.

**Result** Right CAFs were detected in forty-one patients (55.4%). Left CAFs were detected in thirty-three patients (44.6%). Most of the entry point was a single orifice (93.2%), rarely, it was multiple

(6.8%). Simplex coronary fistulas were diagnosed in fifty-four patients (73.0%). Twenty patients had other congenital cardiac malformations (27.0%). Thirty-two patients had also undergone conventional coronary angiography (CAG) before surgery. The ultrasonographic diagnosis of 67 patients was in line with surgical findings. The accurate rate for the diagnosis of CAFs was 90.5%. 7 patients were not found by transthoracic echocardiography. The missed diagnosis rate was 9.5%.

**Conclusion** Transthoracic echocardiography could be a primary method for diagnosis of CAFs.

### Application of echocardiography in minimal-invasive surgical device closure of primemembranous ventricular septal defects

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**Background** This study focused on the exploratory development of the safety and feasibility of minimal-invasive surgical device closure of types of perimembranous ventricular septal defects (PMVs Ds) in children and the clinical criteria in assessment and guidance by echocardiography.

**Methods** We enrolled 730 children diagnosed as PMVs Ds from Apr. 2010 to Nov. 2012. All children underwent full evaluation by transthoracic echocardiography (TTE) and multiplane transesophageal echocardiography (MTEE), such as the sizes, types, spatial positions of defects and the relationship with the adjacent tissues. The chosen domestic device was inserted to occlude the PMVs Ds under the guidance of MTEE.

**Result** 690 (94.55%) of the 730 children underwent successful closure. Symmetric devices were used in 575 children (including 33 A4B2 occluders) and asymmetric in other 115. All patients received follow-ups at regular intervals after successful occlusion. The occluders had stayed firmly. No noticeable residual shunt or valve regurgitation were discovered except for 1 child, whose original mild aortic regurgitation aggravated to nearly moderate in the follow-up of 18th month. Also, there were no significant arrhythmia detected except two children had sudden attack with Adame-Stokes syndrome 2 and 6 days after operation respectively.

**Conclusion** Minimal-invasive surgical device closure of PMVs Ds is mostly safe and feasible. Echocardiography plays a vital role and provides relatively reliable basis in all stages of closure. MTEE is more accurate in evaluating the defects, such as the shape and size which is important in determining the right occluder.

### Increases in CO<sub>2</sub> levels enhance late sodium current and promote polymorphic ventricular tachycardia

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**Objective** Increased CO<sub>2</sub> levels in the myocardium may be global

due to inadequate ventilation/circulation or local due to myocardial ischemia/infarction (by 4 times higher than the normal), and are associated with ventricular arrhythmias. We hypothesized that the increase in CO<sub>2</sub> levels augment late sodium current (INa) and is an independent factor to induce polymorphic ventricular tachycardia.

**Methods** Female rabbit isolated hearts were paced at 1 Hz and exposed to solutions gassed with 5, 10 and 20% CO<sub>2</sub>. A pH value was kept at 7.4 for all solution and osmolarity was adjusted. Rabbit ventricular myocytes were isolated and exposed to solutions with different CO<sub>2</sub> levels (pH = 7.4). Monophasic action potential duration (MAPD) and ion currents were recorded using MAP electrodes and whole-cell patch clamp, respectively.

**Result** When the pH value in solutions was kept at 7.4 and CO<sub>2</sub> levels were increased from 5 (Physiological) to 10 (respiratory failure) and 20% (CO<sub>2</sub> intoxication), the amplitude of late sodium current in ventricular myocytes was increased from  $-0.406 \pm 0.009$  to  $-0.827 \pm 0.029$  and  $-1.253 \pm 0.043$  pA/pF ( $n = 7$ ,  $p < 0.01$ , compared to 5% CO<sub>2</sub>) in a concentration-dependent manner. These increases in late INa were completely reversed by 2  $\mu$ M TTX in the presence of either 10 or 20% CO<sub>2</sub>. MAPD<sub>90</sub> from the whole heart was increased significantly by  $20 \pm 3$  and  $63 \pm 6$  ms from a baseline of  $189 \pm 4$  to  $208 \pm 4$  and  $252 \pm 8$  ms ( $n = 11$ ,  $P < 0.01$ ), respectively. At CO<sub>2</sub> level of 5%, E-4031 (10 nM,  $n = 11$ ) and ATX-II (1 nM,  $n = 8$ ) prolonged MAPD<sub>90</sub> by  $27 \pm 5$  and  $31 \pm 3$  ms, respectively, and caused no TdP. In the presence of either E-4031 or ATX-II, increases of CO<sub>2</sub> to 10 and 20% cause greater increase in MAPD<sub>90</sub> by  $52 \pm 8$  and  $42 \pm 5$ , and  $105 \pm 15$  and  $133 \pm 11$  ms ( $n = 11$  and  $8$ ,  $P < 0.01$  compared to the values at 5% of CO<sub>2</sub>). In hearts treated with either E-4031 or ATX-II, a high concentration (20%) of CO<sub>2</sub> caused polymorphic ventricular tachycardia in 8/11 (73%) and 7/8 (87.5%) of hearts studied, respectively.

**Conclusion** Increased CO<sub>2</sub> levels is an independent factor (to acidosis) to enhance late sodium current and cause APD prolongation. These effects are expected to reduce repolarization reserve in the heart and therefore are proarrhythmic, which may explain the clinical arrhythmias in patients with obstructive sleep apnea, sudden infant death syndrome and ischemia.

### Electrocardiographic abnormalities in asymptomatic or mildly symptomatic patients with hypertrophic cardiomyopathy: A cardiovascular magnetic resonance study

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**Background** A spectrum of alterations in the 12-lead electrocardiogram (ECG) has been described in hypertrophic cardiomyopathy (HCM). However, although most individuals with HCM are asymptomatic or mildly symptomatic, data from previous studies (mostly echocardiography) that concerned this subgroup were limited.

**Aims** We sought to investigate the prevalence and diagnostic value of ECG abnormalities in asymptomatic or mildly symptomatic patients with HCM, and relate these ECG patterns to the magnitude and distribution of left ventricular (LV) segmental hypertrophy and myocardial fibrosis, in an attempt to clarify the mechanisms of ECG changes in HCM.

**Methods** 118 patients with asymptomatic or minimally symptomatic HCM were examined with late gadolinium enhancement (LGE) CMR. The distribution and magnitude of LV segmental hypertrophy and LGE were assessed and analyzed in relation to ECG abnormalities.

**Result** Abnormal electrocardiograms were found in 113 of 118 (95%) patients. Patients without LV outflow obstruction (when compared to patients with) had significantly lower frequencies of abnormal electrocardiograms ( $P = 0.02$ ), repolarization abnormalities ( $P = 0.01$ ), left ventricular hypertrophy ( $P = 0.02$ ) and abnormal Q waves ( $P = 0.01$ ). T-wave inversions were associated with greater apical septal thickness ( $P = 0.009$ ) and increased ratio of LV septum to free wall thickness ( $P = 0.01$ ). Giant negative T waves (GNT) were found in 19 patients (16%), and were associated with the type of apical HCM ( $P < 0.001$ ), greater apical thickness ( $P = 0.004$ ) and increased ratio of LV apical to basal wall thickness ( $P < 0.001$ ). However, no significant association was demonstrated between GNT and apical LGE ( $P = 0.71$ ). Left ventricular hypertrophy was related to greater LV mass ( $P = 0.002$ ), LVEDV ( $P = 0.002$ ), mean LV thickness ( $P = 0.03$ ), maximal LV thickness ( $P = 0.04$ ), and LV septal thickness ( $P = 0.04$ ). Abnormal Q waves were associated with greater basal anteroapical thickness ( $P = 0.001$ ) and more segments with transmural LGE ( $P = 0.001$ ).

**Conclusion** The distribution and magnitude of LV hypertrophy and LGE show significant association with various ECG changes. This finding adds pathophysiological insight into understanding ECG changes in HCM, and may suggest a potential role of these ECG patterns in the risk stratification of HCM patients, since the magnitude of LV hypertrophy and myocardial fibrosis have been proved to be indicators of adverse outcomes.

### Characteristics of intravascular ultrasound image of target borderline lesion in the proximal left anterior descending artery

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**Background** To investigate the characteristics of intravascular ultrasound (IVUS) image of target borderline lesion in the proximal anterior descending artery (LAD) for finding the basement to treating these patients with the lesions.

**Methods** The borderline lesions with 30% – 70% dimension stenosis in the proximal LAD were found in 10 patients from Jun. 2010 to Oct. 2011. All the 10 patients had some discomfort in the precordium, including 7 males, 1 with diabetes, 3 with hypertension, 2 smokers and 2 with infarct history. The intervention was done in the patient with the typical syndrome after IVUS. For the atypical patients, the exercise test was done. The intervention was done in the positive patient after IVUS.

**Result** The discomfort in the precordium disappeared in all the 10 patients. The minimal lumen area (MLA) of them in the proximal LAD was  $4.85 \pm 1.49 \text{ mm}^2$ . MLA in the 7 patients was more than  $4 \text{ mm}^2$ . The area stenosis (AS) of them in the proximal LAD was  $69.99\% \pm 7.07\%$ . AS in the 4 patients was less than 70%.

**Conclusion** It is questionable that the  $4 \text{ mm}^2$  of MLA or 70% of AS was considered to be the cut-off value for the intervention therapy. The suitable strategy to the patients with borderline lesion in the proximal LAD should come from the combination of IVUS and clinical condition.

### Correlations between right ventricular function and increased $^{18}\text{F}$ -fluorodeoxyglucose uptake of the right ventricle in patients with pulmonary hypertension in fasting and glucose loading conditions

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**Purpose** This study was designed to measure glucose uptake of right ventricle (RV) in PH patients by  $^{18}\text{F}$ -fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging in fasting and glucose condition, and attempted to investigate the correlations between FDG uptakes and right ventricular function as well as hemodynamics.

**Methods** Thirty eight patients with PH were observed prospectively.  $^{18}\text{F}$ -FDG PET scanning was performed in fasting and glucose loading conditions in all the patients, and the standardized uptake value (SUV) of RV was measured after corrected for partial volume effect. The ratio of RV to left ventricle (LV) SUV (RV/LV-SUV) was calculated. Right heart catheterization, echocardiography and cardiac magnetic resonance (CMR) were performed in all patients within 1 week.

**Result** RVs UV and LVs UV were higher in glucose loading than in fasting condition. RVs UV and RV/LVs UV in fasting condition showed significant relations with right ventricular ejection fraction (RVEF) derived from CMR ( $r = -0.341$ ,  $P = 0.036$  and  $r = -0.345$ ,  $P = 0.034$ ), and in glucose loading condition ( $r = -0.362$ ,  $P = 0.028$  and  $r = -0.512$ ,  $P = 0.001$ ). RV/LVs UV in glucose loading condition also correlated significantly with TAPSE ( $r = -0.347$ ,  $P = 0.035$ ), IVA ( $r = -0.417$ ,  $P = 0.011$ ) and RVFAC ( $r = -0.326$ ,  $P = 0.049$ ).

**Conclusion** The glucose uptake of right ventricle increases with right ventricular systolic function decrease in PH patients, which is more significant in glucose loading than in fasting condition.

### Echocardiographic parameters in patients with pulmonary arterial hypertension: correlations with right ventricular ejection fraction and hemodynamics

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**Background** As the most common and convenient method used to evaluate RV function and hemodynamics of pulmonary circulation; several echocardiographic parameters are studied in previous studies. But the value of these parameters to assess the severity and RV function in patients with pulmonary arterial hypertension (PAH) is not well defined.

**Methods** Patients with PAH were observed prospectively. Right heart catheterization, echocardiograph and cardiac magnetic resonance (CMR) were performed in all patients within 1 week interval. The correlations between echocardiographic parameters and right ventricular



ejection fraction (RVEF) derived from CMR as well as hemodynamics were analyzed.

**Result** Thirty patients were enrolled including 24 patients with idiopathic pulmonary hypertension, 5 patients with pulmonary hypertension associated with connective tissue diseases and 1 patient with hereditary pulmonary arterial hypertension. All echocardiographic parameters except RVMPI correlated significantly with RVEF measured by CMR (TAPSE,  $r = 0.426$ ,  $P < 0.001$ ; S',  $r = 0.452$ ,  $P = 0.004$ ; IVA,  $r = 0.485$ ,  $P = 0.002$ ; RVFAC,  $r = 0.563$ ,  $P < 0.001$ ; RVETD/LVETD,  $r = -0.616$ ,  $P < 0.001$ ; RVMPI,  $r = -0.208$ ,  $P = 0.204$ ). After adjusted for mRAP, mPAP and PVR, only IVA and RVETD/LVETD could independently predict RVEF. Four echocardiographic parameters displayed a significant correlation with PVR (TAPSE,  $r = -0.615$ ,  $P < 0.001$ ; S',  $r = -0.557$ ,  $P = 0.002$ ; RVFAC,  $r = -0.454$ ,  $P = 0.012$ ; RVETD/LVETD,  $r = 0.543$ ,  $P = 0.002$ ).

**Conclusion** Among the echocardiographic parameters, IVA and RVETD/LVETD can reflect RVEF independently regardless of hemodynamics, and TAPSE, S', RVFAC and RVETD/LVETD can also reflect PVR in PAH patients.

### Value of myocardial scar identified by magnetic resonance imaging in predicting left ventricular functional improvement after surgical revascularization

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**Objective** Information on the relative merits of myocardial scar to predict functional recovery in patients with left ventricular (LV) dysfunction who underwent coronary artery bypass grafting (CABG) is lacking. This study assessed the prognostic value of myocardial scar determined by late gadolinium-enhanced cardiovascular magnetic resonance imaging (LGE-CMR) in predicting LV functional improvement after surgical revascularization.

**Methods** Between Nov. 2009 and Nov. 2011, 34 patients with reduced left ventricular ejection fraction (LVEF) referred for isolated CABG were prospectively enrolled, 31 were included in final analysis (3 excluded because of graft failure). LV functional parameters and scar tissue was assessed by LGE-CMR at baseline and 6 months after CABG. Patency of grafts was evaluated by computed tomography angiography (CTA) scan 6 months post-surgery. Predictors for global functional improvement were analyzed.

**Result** The baseline LVEF was  $34.6 \pm 10.1\%$ , which improved to  $44.6 \pm 12.0\%$  6 months later and 22/31 patient's improved LVEF by  $\geq 5\%$ . Multivariate logistic regression analysis showed that the only independent predictor for global functional recovery was the number of scar segments (Odds ratio 3.292, 95% Confidence Interval 1.374 – 7.887,  $P = 0.008$ ). Receiver-Operator-Characteristic (ROC) analysis demonstrated  $\leq 4$  scar segments predicted global functional recovery with a sensitivity and specificity of 88.9% and 95.5%, respectively (AUC = 0.92,  $P < 0.001$ ). Comparison of ROC curves also indicated that scar tissue (AUC = 0.922) was better than viable myocardium (AUC = 0.720) in predicting cardiac functional recovery ( $P < 0.001$ ).

**Conclusion** Our study suggests that based on the American Heart Association (AHA) 17-segment format, patients with  $\leq 4$  scar segments on LGE-CMR could improve global LV function after CABG, while patients with more such segments did not. These observations might be useful to determine which patients with LV dysfunction are most likely to benefit from surgical revascularization.

### Prolonged QRS duration: A new predictor of adverse outcome in idiopathic pulmonary arterial hypertension

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**Objective** To investigate whether a prolonged electrocardiographic (ECG) QRS duration is an independent predictor of clinical severity and mortality in patients with idiopathic pulmonary arterial hypertension (IPAH).

**Methods** The initial 12-lead ECG was analyzed for QRS duration in 212 consecutive IPAH patients seen at our center between 2006 and 2009. Patients were subgrouped according to QRS duration  $\geq 120$  ms. The baseline characteristics and survival of the two groups were compared.

**Result** Thirty-five IPAH patients (16.5%) had a QRS duration  $\geq 120$  ms, including 21 (9.9%) with right bundle-branch block (RBBB) and 14 (6.6%) with nonspecific intraventricular conduction delay (IVCD). Prolongation of the QRS duration was associated with a worse WHO functional class and 6-minute walk test distance, and higher serum uric acid (UA) and brain natriuretic peptide (BNP) concentrations when compared with patients with normal QRS duration ( $P < 0.05$ ). Prolonged QRS duration was an independent predictor of mortality and was associated with a 2.4-fold increased risk of death ( $P < 0.05$ ).

**Conclusion** Prolongation of the QRS duration is associated with both clinical severity and survival in patients with IPAH. Therefore, interventions such as cardiac resynchronization therapy or an implantable cardioverter-defibrillator could potentially improve clinical outcomes for IPAH patients with prolonged QRS duration.

### The value of color doppler echocardiography in the elderly during the procedure of patent ductus arteriosus occlusion

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**Background** To investigate the value of color Doppler echocardiography (CDE) in the closure of patent ductus arteriosus (PDA) in the elderly.

**Methods** Before the occlusion, screening the indications for twenty-five elderly patients with PDA by CDE. Using the shunt flow signal of color Doppler flow imaging (CDFI) to estimate the pulmonary side diameter of PDA, compare with the angiography and determine its accuracy through statistics. Using the continuous wave

Doppler (CW) to measure peak velocity of tricuspid regurgitation and estimate cross-tricuspid pressure gradient according to the simplified Bernoulli equation  $\Delta P = 4V^2$ , together with the inherent right atrial pressure to estimate pulmonary artery pressure. Then compare cross-tricuspid pressure gradient and pulmonary artery pressure with cardiac catheterization. Determine its accuracy through statistics. All patients underwent interventional therapy and determine the efficacy of occlusion by CDE.

**Result** All the occlusion of the elderly patients with PDA was successful through the examination by CDE. The diameter of the PDA pulmonary side estimated by the shunt flow signal had a positive correlation with angiocardiology ( $r = 0.71$ ,  $P < 0.001$ ). Pulmonary artery pressure estimated by the CW had a positive correlation with cardiac catheterization contrast ( $r = 0.63$ ,  $P < 0.001$ ).

**Conclusion** CDE has an important value in the elderly during the procedure of patent ductus arteriosus occlusion. Using CDFI to estimate PDA pulmonary side diameter and CW to estimate pulmonary artery pressure before the occlusion is the key to screen the indication of occlusion. And it is also important for using CDFI to observe whether there was a residual PDA shunt after transcatheter closure.

### The value of color Doppler echocardiography in occlusion of elderly with atrial septal defect

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**Background** To investigate the value of color Doppler echocardiography (CDE) in occlusion of elderly with atrial septal defect (ASD).

**Methods** In total of 64 cases of elderly ASD, observe the location, size and residual edge using two-dimensional echocardiography (2DE), observe the atrial septal colorful shunt bunch flow signal and the heart valve colorful regurgitation bunch flow signal using color Doppler flow imaging (CDFI) and measure the pulmonary artery pressure using continuous Doppler (CW) before the occlusion. If the patient had atrial fibrillation or multiple ASDs, transesophageal echocardiography (TEE) examination should be used to screen the patients according to the indication of ASD occlusion. During the procedure of occlusion of ASD, 2DE was used to monitor the position of occluder, CDFI was used to monitor residual shunt through the atrial septum and CDE was used to determine the efficacy of occlusion.

**Result** According to the Result of CDE, we selected 64 cases of elderly ASD, the implementation of all ASD occlusion were successful and the efficacy was satisfactory.

**Conclusion** CDE plays a important role in ASD occlusion. Before ASD occlusion, 2DE is recommended to observe the location, size and residual edge, CW is recommended to measure the pulmonary artery pressure. TEE is the key to screen according to the indications of ASD occlusion for the patients with atrial fibrillation or multiple ASDs. All elderly patients with ASD should undergo coronary angiography before the occlusion to exclude the patients with coronary artery disease who can't treat by stenting.

### Value of color Doppler echocardiography in occlusion of rupture of aortic sinus aneurysm

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**Background** To evaluate the value of color Doppler echocardiography (CDE) in occlusion of rupture of aortic sinus aneurysm (RASA).

**Methods** Fifteen patients with RASA were indicated for interventional occlusion by CDE. CDE take part in all the process as monitoring in the occlusion operation, judging the effect after occlusion and follow-up.

**Result** According to the characteristics images of CDE, we correctly confirmed the ruptured sinus and the chamber it ruptured into, any complications, and successfully occluded the ruptures in all 15 cases.

**Conclusion** CDE plays very important roles in case of RASA occlusion. It can defined the ruptured sinus of aorta and the ruptured-into chamber, the diameter of the rupture, and rule out complications as ventricular septal defect before operation which is the most essential for the success of the occlusion. CDE can be used to monitor the correct implantation of the occluder, evaluate the residual shunt signals and the impingement on the aortic valve during the procedure and follow-up.

### Transthoracic echocardiographic study in transcatheter closure of ventricular septal defects in children

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**Background** To evaluate the value of transthoracic echocardiographic (TTE) in transcatheter closure of ventricular septal defects (VSD) in Children.

**Methods** 855 patients aged 3 – 14 years (average 6.8 years) with VSD were occluded, including 828 patients with membranous or perimembranous VSD, 9 patients with muscular VSD and 18 patients with intracristal VSD. TTE was performed before catheterization to examine the VSD and the rims, to evaluate the occluder device, and to evaluate the efficacy of the device occlusion on parasternal long axis of left ventricle, short axis of aorta and five chamber views.

**Result** The size of VSD measured with TTE were 3.0 – 7.0 mm (average 4.8 mm). Mild residual shunt was revealed in 38 patients, which disappeared in 24 – 48 h after the procedure. At follow-up in 1 m – 1 y, TTE revealed 1 patient residual shunt.

**Conclusion** TTE is a useful approach for the preliminary selectable of VSD in children, for decision of the procedure and enables determination of device size, correct placement of the device, assessment of the closure procedure and result evaluation at follow-up.

## The usefulness of echocardiogram in predicting post-procedural pulmonary artery pressure in patients with patent ductus arteriosus and severe pulmonary arterial hypertension

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**Background** Patent ductus arteriosus (PDA) is one of the commonest congenital heart defects which are prone to be complicated with pulmonary arterial hypertension (PAH). The present study aims to assess the usefulness of echocardiogram in predicting post-procedural pulmonary artery pressure after transcatheter closure of PDA with severe PAH.

**Methods** A cohort of patients with PDA and severe PAH undergoing transcatheter closure of PDA were included in this study. Patients with isolated PDA, cardiac function  $\leq$  NYHA class II, systolic pulmonary arterial pressure (sPAP)  $\geq$  70 mm Hg and pulmonary capillary wedge pressure  $\leq$  15 mm Hg and those who underwent cardiac catheterization under local anesthesia were included in this study. After PDA was completely closed, pulmonary arterial pressure and aortic pressure were re-measured. According to post-closure sPAP, patients were divided into three groups: patients with sPAP  $<$  40 mm Hg (group A), from 40 to 70 mm Hg (group B) and  $>$  70 mm Hg (group C) after PDA closure. Differences in baseline parameters of echocardiogram and the correlations between these parameters and the decrease (%) in mean PAP were analyzed.

**Result** A total of 63 patients (49 females) aged from 10 to 60 years were recruited into this study. There was no significant differences in the age ( $P > 0.05$ ) and the size of PDA ( $P > 0.05$ ) between groups. The left atrium diameter indexes ( $35.96 \pm 6.60$  vs  $31.17 \pm 6.85$  vs  $22.24 \pm 3.47$  mm/m<sup>2</sup>;  $P < 0.05$ ) and the left ventricular end diastolic volume indexes ( $279.45 \pm 89.42$  vs  $162.88 \pm 54.13$  vs  $60.94 \pm 9.87$  ml/m<sup>2</sup>;  $P < 0.05$ ) decreased significantly from group A to group C. The left ventricular diameter/right ventricular diameter ratio in group C ( $1.86 \pm 0.38$ ) was less than that in group A ( $4.29 \pm 1.85$ ;  $P < 0.05$ ) and group B ( $3.18 \pm 1.21$ ;  $P < 0.05$ ) but had no significant difference between group A and group B. Linear regression analysis showed a significant correlation between the decrease in pulmonary artery mean pressure and the baseline of left ventricular end diastolic volume index ( $P < 0.05$ ).

**Conclusion** In patients with PDA and severe PAH, the baseline echocardiographic parameters are capable of predicting the outcome of transcatheter PDA closure. The decrease in pulmonary artery mean pressure after device closure is well correlated with the baseline left ventricular end diastolic volume index.

## Percutaneous transcatheter closure of congenital heart septal defect with real-time three-dimensional echocardiography

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**Objective** To evaluate the value of percutaneous transcatheter closure of congenital heart septal defects with real-time three-dimensional echocardiography (RT-3DE).

**Methods** During the catheter-based interventional procedures, thirty-four patients (aged  $6.9 \pm 4.6$  years) were examined and guided by Philips RT-3DE system including Live-3D, Full Volume and 3D Color, etc. Their offline qualitative and quantitative analyses were made and compared with those of two-dimensional Doppler echocardiography (2DE).

**Result** By objectively demonstrating dynamic detailed cardiovascular normal anatomy and abnormal pathology, RT-3DE was more helpful and informative to the qualitative diagnoses than 2DE. Before transcatheter closure, Live-3D and full volume showed the anatomic position, spatial morphology and size of the septal defect and its relationship to other surrounding cardiac structures from en face view of left and right atrial/ventricular side. 3D Color also showed left-to-right shunt. Furthermore, the whole course of interventional procedure was guided and monitored online by RT-3DE, providing pushed location of guide-wire and catheter sheath, spatial morphology of device and its relation with contiguous cardiac structures, etc. After the device was first released, there were the incorrect spatial location of occluder in 2 cases and the smaller size of device in 1 case displayed by Live-3D and full volume. There was some residue left-to-right shunt with 3D Color. Under the guidance and monitoring of RT-3DE, the second released were correctly completed through replacing the larger device and relocating the position of the delivery sheath and device. There was no residual defect and no residual left-to-right shunt displayed by RT-3DE and also confirmed by Angiography. In addition, the diameter of septal defect measured ( $1.15 \pm 0.67$  cm) by RT-3DE was well correlated with that measured ( $1.01 \pm 0.96$  cm) by 2DE ( $r = 0.96$ ), but the measurement of RT-3DE was correlated with the size of its device ( $r = 0.97$ ) better than that of 2DE ( $r = 0.92$ ). Thus, RT-3DE played an important role in the process of occluder selection and closure by guiding the measurement of the balloon stretched diameter and validating the position of the delivery sheath and the Amplatzer occluder in the atria/ventricles, etc. **Conclusion** With instant visualization of cardiovascular structures and online guidance of percutaneous transcatheter closure, RT-3DE will be a safe and valuable imaging technique for selecting preoperative patient, choosing suitable device, performing optimal interventional manipulation and making postoperative effect assessment.

## Quantitative myocardial CT perfusion with rapid kV switching dual energy CT: a microspheres validation study

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**Purpose** We validated the usefulness of beam hardening (BH) reduction with a rapid kV switching dual energy CT (DECT) protocol in quantitative myocardial perfusion (MP) imaging against microspheres measurement of MP.

**Methods** Normal pigs were scanned using a Discovery 750 HD scanner (GE Healthcare, GE) with a DECT protocol: 140/80 kilovolts



(kV) alternating at 0.2 ms intervals, 640 mA and 0.35 s gantry period. In each study, 22 axial scans covering 40 mm of the heart were triggered under normal physiologic conditions every 1-2 heart beat at mid-diastole together with contrast injection at 4 ml/s. Single energy CT (SECT) and DECT monochromatic 70 keV images were reconstructed with 140 kV and both 80 and 140 kV projections respectively. The SECT images were also corrected for BH using an image-based correction algorithm (iBHC). Each image set was analyzed using CT Perfusion (GE) to derive MP functional maps. Fluorescent microspheres were injected into the left atrial appendage of the heart after the CT perfusion studies to measure MP. Mean MP in the lateral, apical and septal segments over 4 to 6 consecutive 5-mm-thick slices measured by microspheres and from the three CT image sets were compared using linear regression and Bland-Altman analysis. A total of 57 segments in 19 slices in four pigs were analyzed in this study.

**Result** DECT exhibited the highest correlation with microspheres ( $R = 0.77$ ) compared to SECT with ( $R = 0.56$ ) and without ( $R = 0.49$ ) iBHC. DECT also had the smallest difference in mean MP from microspheres (2.2 ml/min/100 g) compared to SECT without iBHC (29.2). Despite a comparable mean difference from microspheres (-2.0), SECT with iBHC showed a wider limits of agreement (-45.0 to 41.0 ml/min/100 g) than DECT (-30.7 to 35.2).

**Conclusion** In SECT MP imaging, BH induced significant shifts in CT number in different myocardial segments lead to spatially inconsistent overestimation of MP. While such BH errors are reduced after iBHC is applied, DECT provides better BH correction and more accurate MP measurements that are better correlated with and have smaller differences from the gold standard microspheres measurements of MP. DECT minimizes beam hardening in contrast-enhanced cardiac images which leads to a more accurate MP measurement with CT Perfusion to facilitate reliable assessment of ischemic heart disease.

### Low dose quantitative myocardial CT perfusion with adaptive statistical iterative reconstruction: a microspheres validation study

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**Purpose** We validated the effectiveness of adaptive statistical iterative reconstruction (ASIR, GE Healthcare, GE) for minimizing image noise in low dose quantitative myocardial perfusion (MP) imaging against microspheres MP measurement.

**Methods** Iodinated contrast (Iovue 370, 0.7 mgI/kg) was injected at 3 to 4 ml/s into 68 ± 25 kg normal pigs via an ear vein and the heart was scanned using a GE Discovery 750HD scanner with a prospectively ECG triggered dynamic protocol (Snapshot Pulse (SSP), GE): axial scan every 1-2 heart beats for 22 scans using 140 kV, 0.35 s gantry period and 80 mA (normal dose). MP measurement was repeated with the x-ray tube current reduced to 20 mA (low dose). The normal- and low-dose SSP images were reconstructed using filtered back projection (FBP) (SSP80) and both FBP (SSP20<sub>FBP</sub>) and ASIR (SSP20<sub>ASIR</sub>) respectively.

All images were corrected for beam hardening from which MP maps were generated using CT Perfusion (GE). After the CT perfusion studies, fluorescent microspheres were injected into the left atrial appendage of the heart to measure MP. Mean MP measured with microspheres and the three CT image sets in 45 segments from the lateral, apical and septal wall in 15 slices from three pigs were compared using linear regression and Bland-Altman analysis. Effective dose (ED) of each SSP protocol was estimated from the dose-length product provided by the scanner.

**Result** SSP80 images exhibited the highest correlation with microspheres ( $R = 0.69$ ) compared to SSP20<sub>ASIR</sub> ( $R = 0.60$ ) and SSP20<sub>FBP</sub> ( $R = 0.57$ ). SSP80 images also showed the smallest difference in mean MP from microspheres and narrowest limits of agreement with microspheres [7.0 and -32.9 to 46.8 ml/min×100/g (80)] compared to SSP20<sub>ASIR</sub> (11.3 and -35.3 to 57.8 (93)) and SSP20<sub>FBP</sub> [15.7 and -32.8 to 64.1 (97)]. ED of the SSP80 and SSP20 protocols were 4.5 and 1.1 mSv respectively.

**Conclusion** Noise in low dose SSP images reconstructed with FBP was excessive which led to less accurate and reproducible MP estimation with CT Perfusion but such errors could be reduced with ASIR. With the proposed image acquisition and reconstruction approaches, MP measurement with low dose CT Perfusion is a feasible alternative to MRI and SPECT for studying ischemic heart disease.

### Evaluation of functional significance of coronary artery stenosis with baseline myocardial mean transit time

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**Purpose** Mean transit time (MTT) is inversely related to perfusion pressure. We herein investigated the relationship between baseline myocardial MTT measured by dynamic contrast-enhanced (DCE) CT imaging and the degree and hemodynamic significance of coronary stenosis in patients with coronary artery disease (CAD).

**Methods** Thirteen CAD patients underwent invasive coronary angiography and CT myocardial perfusion (MP) imaging within 2 weeks. Degree of stenosis in each coronary artery and its branches was qualitatively classified from angiogram as non-significantly stenosed (NS, normal, mildly irregular or = 70% narrowed). For the CT MP study, 8.5 mm of the heart was scanned for 30 s using a GE Healthcare Discovery VCT scanner with 140 kV, 50 mA and 0.4 s gantry period after a bolus injection of contrast (Omnipaque 300, 0.7 mgI/mL) at 4 mL/s. The study was repeated at 3 min after a 4-min infusion of dipyridamole (Persantine, 0.56 mg/kg). DCE cardiac images from each scan were corrected for beam hardening using an image-based correction algorithm before analyzed using a model-based deconvolution algorithm (CT Perfusion, GE Healthcare) to generate functional maps of MP and MTT. In each map, myocardium in horizontal long-axis was divided into six segments and assigned to a supply coronary artery according to the AHA schema. Myocardial perfusion reserve (MPR) in each segment was calculated as the ratio of MP at stress to that at rest. Baseline MTT and MPR in segments perfused by NS and SS coronary arteries were averaged over all slices and compared using paired t-tests.

**Result** Mean baseline MTT in NS myocardial segment was  $5.20 \pm 0.61$  s and was significantly lower than that in SS segment ( $5.56 \pm 0.69$  s,  $P < 0.05$ ). By contrast, the corresponding mean MPR in NS segment was significantly higher than that in SS segment ( $2.19 \pm 0.45$  vs  $1.85 \pm 0.49$ ,  $P < 0.05$ ).

**Conclusion** Flow pressure across SS lesions in coronary arteries was much reduced leading to decrease in the downstream perfusion pressure hence prolonged baseline myocardial MTT and attenuated MPR compared to those in remote NS segments. A single DCE CT protocol acquired at rest without stressing the heart with pharmacologic stimuli is sufficient for assessing the functional significance of coronary artery stenosis.

### Differences in the prognostic mortality value of red cell distribution width in patients with heart failure due to various heart diseases

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**Background** Increased red blood cell distribution width (RDW) has been associated with adverse outcomes in patients with heart failure. The objective of this study was to compare differences in the predictive value of RDW in patients with heart failure of different causes.

**Methods and Result** We studied prospectively 1 021 patients with heart failure from Oct. 2009 to Dec. 2011. The RDW and patients' clinical information were obtained at baseline. The median RDW in patients who died was 14.8%, significantly higher than that (13.3%) of survivors ( $P < 0.001$ ). After adjustment for other prognostic factors in a multivariable Cox proportional hazards model, RDW remained a significant predictor [hazard ratio (HR) 1.182, 95% confidence interval (CI) 1.083 – 1.291],  $P < 0.001$ ]. Patients with coronary heart disease, dilated cardiomyopathy and valvular heart disease, three major causes of heart failure, were selected for investigation. The RDW, mortality and survival time were significantly different among the three groups. Receiver operating characteristic curve (ROC) curve analysis showed that RDW had predictive value for death in patients with heart failure caused by coronary heart disease and dilated cardiomyopathy; the area under the curve (AUC) was 0.704 ( $P < 0.001$ , 95% CI 0.609 – 0.799) and 0.753 ( $P < 0.001$ , 95% CI 0.647 – 0.860), respectively. In a multivariable model, RDW was an independent predictor for coronary heart disease mortality ( $P < 0.001$ , HR 1.315, 95% CI 1.122 – 1.543). Kaplan – Meier analysis showed that cumulative survival was significantly lower in patients with coronary heart disease and dilated cardiomyopathy in the higher quartiles of RDW, but cumulative survival was not significantly different in those with valvular heart disease.

**Conclusion** The RDW can be used as a prognostic indicator in patients with heart failure. In patients with heart disease of different etiologies, the predictive values of RDW are different. RDW can be used as a prognostic indicator for patients with heart failure caused by coronary heart disease and dilated cardiomyopathy, but not in those with valvular heart disease. These findings may provide the basis for the use of RDW in specific clinical applications.

### Clinical significance of coronary CT angiography in asymptomatic patients with type 2 diabetes mellitus

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**Objective** Diabetic patients with coronary artery disease are often asymptomatic, making appropriate care of such patients difficult. The purpose of this study was to investigate the prevalence of coronary lesions in asymptomatic diabetic patients.

**Methods** Coronary computed tomography (CT) angiography was performed in 240 consecutive diabetic patients. Images from patients whose coronary artery calcium scores (CAC scores) were less than 400 were subjected to stenosis and plaque analysis. Significant stenosis was defined as coronary artery stenosis  $> 70\%$ . High-risk plaque was defined as plaque having both a CT density  $< 30$  Hounsfield Units (HU) and showing positive remodeling.

**Result** Significant stenoses were identified in 30.5% of the patients. High-risk plaques were identified in 17.1% of the patients. Less than half of the high-risk plaques were obstructive plaques. There was a statistically significant association between significant stenosis and high-risk plaque by chi-square test ( $P = 0.013$ ). We found significant stenosis even in patients whose CAC score = 0 at a rate of 5.0%. Using univariate logistic-regression analysis, we found that coronary risk factors associated with significant stenosis and high-risk plaque were dyslipidemia ( $P = 0.028$ ) and current smoking ( $P = 0.03$ ), respectively.

**Conclusion** We found that the higher prevalence of coronary lesions in asymptomatic diabetic patients. We feel that our method of focusing on remodeling and attenuation in plaque analysis has the potential to lead to true identification of vulnerable plaque. However, to confirm this assumption will need to conduct a prospective study.

### Assessment of coronary non-calcified and mini-calcified mixed plaque progression in coronary computed tomography angiography

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**Objective** Coronary computed tomography angiography (CCTA) can non-invasively visualize the coronary atherosclerotic plaque, especially non-calcified plaques (NCP) and mini-calcified mixed plaque. The changes of those plaques were not clear. We detected NCPs and mini-calcified mixed plaques using original and follow-up CCTAs in order to determine those changes.

**Methods** Patients suspected coronary artery disease with twice CCTAs consecutively from 2009 Sep. to 2012 Dec. were retrospectively included. Those patients were showed in CCTA with an obvious NCPs or mini-calcified mixed plaque in a branch of coronary artery but no evidence of percutaneous coronary intervention and coronary artery bypass grafting. The informations of those patients was collected by medical record and calling back. The length of plaque, minimum lumen diameter, minimum lumen area, total plaque volume, plaque volume and remodeling index were measured at offline workstation. The changes

of plaque in length and stenosis in lumen were calculated and analysed. Interobserver and intraobserver agreement for plaque measurement was analyzed.

**Result** Sixty subjects (45 males, mean age  $52 \pm 8$  years) with NCPs or mini-calcified mixed Plaque by MSCT were divided patients into statins group and non-statins group. The risk factors and the interval time of CCTAs between two groups at baseline have no significant difference, except the lengths of plaques in statins group were longer than no statins group ( $18.88 \pm 10.04$  mm vs  $13.42 \pm 5.37$  mm,  $P = 0.009$ ). The length of plaques have significant difference between twice CCTAs in non-statins group ( $13.43 \pm 5.38$  mm vs  $15.56 \pm 6.24$  mm,  $P = 0.006$ ), while that of statins group without difference ( $18.88 \pm 10.04$  mm vs  $18.50 \pm 10.96$  mm,  $P = 0.56$ ). The length changes of plaques and ratio of length changes in statins group significantly differ from that of no statins group ( $P < 0.05$ ). In multiple linear regression analysis, diabetes mellitus and no statins therapy were independently associated with the length progression of plaque after adjustment for age, sex, and follow-up time interval. Close correlations between the original analysis and re-analysis were found ( $r = 0.92$  for length,  $r = 0.83$  for vessel lumen).

**Conclusion** CCTA can non-invasively assess the progression or regression of coronary atherosclerosis plaque. Diabetes mellitus were independently associated with the length progression of plaque. Lipid-lowering therapy with statins can delay the progression of NCPs or mini-calcified mixed plaque in length.

### Transthoracic echocardiography for diagnosis of right pulmonary artery to left atrial fistula

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**Background** No overview has been published to date of the transthoracic echocardiography (TTE) signs of the rare cardiovascular anomaly of right pulmonary artery (RPA) to left atrial (LA) fistula (RPA-LAF).

**Objective** To summarize the characteristics of the transthoracic echocardiography (TTE) for diagnosing the rare cardiovascular anomaly of right pulmonary artery to left atrial fistula.

**Methods** Three patients were diagnosed with RPA-LAF at Fuwai Hospital from 2000 to 2010. The patients were all male and were aged 14 years, 7 years and 6 months. All patients underwent clinical examination, chest roentgenogram, laboratory testing, electrocardiography, transthoracic echocardiography (TTE), contrast echocardiography, and cardiac catheterization. We undertook a detailed review of their TTE and contrast echocardiography findings to determine the characteristic findings of this condition.

**Results** TTE was performed in all cases, and in two cases contrast echocardiography was also performed. In two cases, the LA was abnormally shaped and enlarged, the RPA was obviously enlarged and aneurysmal, and the fistula was detectable on TTE. In the other case, there was only mild enlargement of the left heart, and contrast echocardiography led to a misdiagnosis of pulmonary arteriovenous fistula. Successful detection of a fistula may be related to the degree of dilatation of the LA and RPA, the location of the fistula, and the type of RPA-LAF. Cases with a dilated LA and with the fistula located at the proximal and posterior RPA and LA may be easier to diagnose by TTE. The shunt from the RPA to the LA can clearly be seen by color Doppler flow imaging. The preferred imaging planes were the pulmonary artery long-axis, aortic short-axis, and apical four-chamber views, and the subxiphoid coronal view of the right ventricular outflow tract.

**Conclusion** Diagnostic guidelines of TTE can help in the detection of RPA-LAF. With the correct views, echocardiography was effectively able to diagnose RPA-LAF, including diagnosis of the complications and malformations which can guide typing.

### Congenital anomalies of coronary arteries in complex congenital heart disease: diagnosis with dual-source computed tomography

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**Objective** Anomalous origins and course of the coronary arteries can affect the effect of surgical operation in complex congenital heart disease. Dual-source CT (DSCT) seems to be a promising tool for detection of coronary arteries prior to surgical operation. The objective of the study is to explore the clinical value of DSCT in the identify of congenital coronary artery anomalies (CAA) in patients with complex congenital heart disease and analysis the incidence of CAA in those patients.

**Methods** 417 patients with complex congenital heart disease at our institution underwent ECG-gated DSCT angiography between the period of Aug. 2009 and Feb. 2012 were involved. The Result were retrospectively analyzed, including the types and proportion of congenital heart disease, incidences of CAA, incidences of abnormal coronary artery crossing right ventricular outflow tract and prognosis. Each subject was analyzed independently by two experienced cardiovascular radiologists. The consensus was achieved by the both when there was a difference in each other's Result. Image quality was assessed by a five-point score. A score of  $< 3$  represents non-diagnostic.

**Result** Thirty-five of 417 patients (8.39%) were non-diagnostic with image quality score  $< 3$ . 63 cases of patients with congenital coronary artery anomalies were detected. The incidence of anomalous anatomical origin and course of the coronary arteries in our study was 16.49%. 6 cases in 108 Tetralogy of Fallot (TOF, 5.56%) had coronary artery anomalies, 18 in 84 double outlet right ventricle (DORV, 21.43%), 11 in 97 pulmonary atresia (PA, 11.34%), 7 in 36 transposition of great arteries (TGA, 22.22%), 15 in 41 single ventricle (SV, 36.59%), 4 in 12 truncus arteriosus/aortopulmonary window (33.33%), 2 in 39 interruption of aortic arch (IAA, 5.13%). Highest incidence (23 cases, 6.02%) is L-coronary artery, which occupy 36.51% of coronary artery anomalies. 13 (20.63%) cases of abnormal coronary artery crossing the right ventricular outflow tract. which including 1 cases of TOF, 9 cases of DORV, 2 cases of PA/Vs D, 1 cases of TGA; 18 cases (4.71%) is R-coronary artery, 18 cases (4.71%) is single coronary artery, 1 cases (0.26%) is coronary arterial dilation, 3 cases (0.79%) is coronary with anomalous termination with pulmonary artery. The mean effective dose was  $1.28 \pm 1.05$  mSv.

**Conclusion** Prospective ECG-triggering DSCT angiography with a very low effective radiation dose allows the accurate diagnosis of coronary arteries and other structural anomalies in patients with complex CHD before surgical operation. It has great promise to become a commonly used second-line technique for complex CHD.



## Prognostic value of myocardial fibrosis in patients with dilated cardiomyopathy detected by contrast-enhanced cardiac magnetic resonance imaging

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**Objective** To investigate the characteristics and prognostic importance of fibrosis detected by contrast-enhanced cardiac magnetic resonance imaging (CE-CMR) in Chinese patients with dilated cardiomyopathy (DCM).

**Methods** 123 hospitalized patients with DCM (age  $45 \pm 12$  years, 98 male) referred for CE-CMR assessment were followed-up for 3 – 79 months (median 29 months). Major adverse cardiac events (MACE) were defined as all-cause death, or ventricular tachycardia. Left ventricular end-diastolic diameter (LVEDD) and left ventricular ejection fraction (LVEF) were calculated from the short axis cine images of CMR, while late gadolinium enhancement (LGE) was used to assess myocardial fibrosis. Ventricular tachycardia was monitored by means of 24-hour dynamic electrocardiogram (24 h-Holter).

**Result** Myocardial fibrosis (LGE) was present in 42.3% of patients, the majority of which was mid-myocardial enhancement (84.6%). Both LVEDD and LVEF were similar in patients with or without LGE (LVEDD:  $70.4 \pm 9.5$  mm vs  $68.4 \pm 8.1$  mm,  $P = 0.200$ ; LVEF:  $22.4 \pm 7.3\%$  vs  $21.8 \pm 7.4\%$ ,  $P = 0.634$ ). Compared with patients without LGE, patients with LGE had a greater occurrence of MACE (42.3% vs 25.4%,  $P = 0.047$ ) after a median follow-up of 29 month. Notably, there was a higher incidence of ventricular tachycardia in patients with LGE (34.6% vs 18.3%,  $P = 0.040$ ), although there was no significance in all-cause mortality between patients with and without LGE ( $P = 0.963$ ). In the multivariate Cox proportional hazard model regression, forward stepwise analysis adjusted by age, gender, duration of symptoms, NYHA functional class, LVEDD and LVEF, indicated that presence of LGE was an independent strong risk factor for MACE (HR = 2.621, 95% CI 1.354 – 5.074,  $P = 0.004$ ).

**Conclusion** Patients with DCM frequently have myocardial fibrosis detected on CE-CMR and the major pattern is mid-myocardial enhancement. Fibrosis, as reflected by the presence of LGE, is associated with worse outcome in the medium term. The information obtained from CE-CMR may be of incremental prognostic value.

## A novel categorization of congenital double-outlet right ventricle diagnosis by echocardiology

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**Objective** The feasibility and reasonability of category methodology for novel and effective DORV echocardiology diagnosis is discussed.

**Methods** According to artery relations (normal relation: AN; abnormal relation: AA), Vs D location (sub-artery ventricular septal

defect A-Vs D; non-co mmitted ventricular septal defect, N-Vs D) pulmonary valve stenosis (Pulmonary valve stenosis PS; pulmonary hypertension PH), the congenital DORV is categorized. After permutation and combination, 8 categories are acquired, that is, type I AN, A-Vs D, PH; type II AN, A-Vs D, PS; type III AN, N-Vs D, PH; type IV AN, N-Vs D, PS; type V AA, A-Vs D, PH; type VI AA, A-Vs D, PS; type VII AA, N-Vs D, PH; Type VIII AA, N-Vs D, PH. Based on this categories, 409 DORV cases are categorized by echocardiology diagnosis, and contrasted with clinic diagnosis Result (cardiac CT cross sectional scanning, cardiac MRI examination, cardiac catheter test, operation), so as to analyze the scientificness of this categorization. Meanwhile, the instructional significance of this categorization to selection of clinic therapy is also summarized. The clinic therapy Result for all the patients who were given operations proved the effectiveness and clinic significance of the categories.

**Result** 409 DORV cases were categorized in this method. Result are listed as follows: I typed 52 cases, accounts for 12.7%, II typed 87 cases, 21.3%, III typed 27 cases, 6.6%, IV typed 24 cases, 5.9%, V typed 59 cases, 14.4%, VI typed 39 cases, 9.5%, VII typed 35 cases, 8.6%, VIII typed 82 cases, 20.1%. The result of echocardiology diagnosis accord completely to those of clinic final diagnosis. Based on this categorization, by precluding special abnormal influence factors that is considered to affect the choice of operation ways, it shows that each type of DORV is corresponding to some type of operation way, which indicates that this novel categorization could instruct the choosing of clinic therapy accurately and effectively.

**Conclusion** A novel categorization by echocardiology diagnosis can accurately diagnose all the DORV cases, which is considered to be scientifically and effectively instructive to the choosing of clinic therapy.

## T1 mapping for detection of left ventricular myocardial fibrosis in hypertrophic cardiomyopathy: a preliminary study

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2. Siemens Healthcare

**Purpose** To investigate the diagnostic value of T1 mapping imaging of evaluating fibrosis in patients with hypertrophic cardiomyopathy (HCM).

**Methods** 21 subjects with HCM and 18 healthy volunteers underwent conventional late gadolinium enhancement (LGE) imaging and T1 mapping imaging. The region of myocardium in HCM is divided into remote area of LGE, peri-LGE, LGE (halo-like LGE and typical patchy LGE). These regions combined with normal volunteers myocardium were calculated by the reduced percent of T1 value (RPTV).

**Result** The RPTV in healthy volunteers was no significant comparing with that in the remote area of LGE in HCM subjects ( $3.98 \pm 3.19$  vs  $3.34 \pm 2.75$ ,  $P > 0.05$ ). There were significant statistical differences in pairwise among the remote area of LGE, peri-LGE, halo-like LGE and typical patchy LGE in the RPTV ( $P < 0.0001$ ). There was no difference in the RPTV between healthy volunteers myocardium and the remote area of LGE in HCM patients, therefore, in the present study we use the RPTV of the healthy volunteers myocardium and the remote area of LGE as the standard of true negative for fibrosis. Figure 6 illustrates the diagnostic performance of T1-mapping compared to the

LGE technique in detecting fibrosis ROC analysis. T1-mapping showed improved detection of fibrosis compared to LGE (T1-mapping area under the curve  $0.975 \pm 0.07$  vs LGE area under the curve  $0.753 \pm 0.26$ ,  $P < 0.0001$ ). According to ROC curve, the best cut-off value for RPTV to detect fibrosis is 7.86% (sensitivity of 90.4% and specificity of 95.3%).

**Conclusion** HCM has a high prevalence of fibrosis and with varying severity. T1 mapping imaging can be a useful method to evaluate the severity of the fibrosis in HCM.

### Fat deposition in idiopathic dilated cardiomyopathy assessed by magnetic resonance imaging

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**Objective** The aim of this study was to prospectively investigate the prevalence of fat deposition in idiopathic dilated cardiomyopathy (DCM) by fat-water separation imaging. An auxiliary aim was to determine the relationship between LV fat deposition and characteristic myocardial fibrosis, as well as cardiac functional parameters.

**Background** Idiopathic DCM remains the most common cause of heart failure in young people referred for cardiac transplantation; little is known about what the clinical value of fat deposition in DCM.

**Methods** One hundred and twenty-four patients with DCM were studied after written informed consents were obtained. The MR scan protocols included a series of short-axis LV cine imaging for functional analysis, fat-water separation imaging, and late gadolinium enhanced (LGE) imaging. Fat deposition and fibrosis location were compared to the scar regions on LGE images using 17-segment model. Statistical comparisons of LV global functional parameters, fibrosis volumes, and fat deposition were carried out using the Pearson correlation, student t test and multiple regressions.

**Result** The patients had a 41.9% (52 of 124) prevalence of positive LGE. And 12.9% (16/124) of fat deposition prevalence was found in this DCM cohort. The patients with fat deposition had larger left ventricular end-diastolic volume (LVEDV) index ( $140.8 \pm 20.2$  ml/m<sup>2</sup> vs  $123.4 \pm 15.8$  ml/m<sup>2</sup>;  $P < 0.01$ ), larger left ventricular end-systolic volume (LVESV) index ( $111.3 \pm 19.2$  ml/m<sup>2</sup> vs  $87.0 \pm 20.3$  ml/m<sup>2</sup>,  $P < 0.01$ ) and decreased left ventricular ejection fraction (LVEF) ( $21.1 \pm 7.1\%$  vs  $30.0 \pm 10.7\%$ ;  $P < 0.01$ ). Higher volume of LGE was found in the group of myocardial fat deposition ( $18.39 \pm 9.0$  ml vs  $13.40 \pm 6.54$  ml,  $P = 0.001$ ), as well as a higher percentage of LGE/LV mass ( $19.11 \pm 7.78\%$  vs  $13.60 \pm 4.58\%$ ,  $P < 0.001$ ). The volume of fat deposition was correlated with scar volume, LVEF, LVEDV index, and LVESV index.

**Conclusion** Fat deposition is quite a common phenomenon in DCM. And it is associated with DCM characteristics such as fibrosis volume and LV function.

### Metal artifact reduction in computed tomography for assessment of lead extraction in patients with implantable cardiac defibrillator

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**Purpose** Patients with implantable cardiac defibrillator (ICD) may require lead extraction if there is presence of lead fibrosis and calcification but such procedure requires specialist equipment and skills and is associated with high mortality. We investigated the effectiveness of several image acquisition, reconstruction and processing Methods for metal artifact reduction in CT to facilitate its use for pre-procedural identification of lead calcification.

**Methods** A dual coil ICD lead (Medtronic Sprint Quattro Secure 6947M) with radiopaque beads attached was inserted into the right ventricle of an excised pig heart. The heart was filled with water and scanned in approximately the same orientation as in patients with a single energy CT (SECT) protocol using 120 kV, 120 mAs and 0.625 mm collimation on a Discovery 750HD scanner (GE Healthcare). The scan was repeated with a dual energy CT (DECT) protocol using 140/80 kV alternating every 0.2 ms and 210 mAs. Three sets of 0.625-mm-thick cardiac images were generated using the DECT scan data: (1) monochromatic 70 keV, (2) 70 keV plus ASIR (Adaptive Statistical Iterative Reconstruction), (3) 70 keV plus MARS (Metal Artifact Reduction Software, GE). Image set (1) to (3) were used to reduce artifacts from beam hardening, projection noise and projection truncation induced by the lead respectively. Artifacts in each image set were compared against those in the 0.625 mm and 10 mm averaged SECT images.

**Result** DECT 70 keV and 70 keV+ASIR images manifested intense shading and streaking artifacts that were minimally different from those of the 0.625 mm SECT image and the lead was not visible in all these images. 70 keV+MARS image exhibited less artifacts but the lead region was invisible. The 10 mm averaged SECT image showed the least artifacts while the lead with the attached beads was clearly seen.

**Conclusion** DECT+MARS showed better artifact removal than DECT without MARS or with ASIR suggesting projection truncation was the dominant cause of the lead artifacts. However, MARS is unable to restore the lead image adequately. The averaging method cancelled out the artifacts while restoring the lead image with minimal compromise of the axial resolution. Lead extraction is complicated and associated with significant mortality and morbidity. The proposed method facilitates the use of CT for assessing lead calcification and the need of lead extraction.

### Transthoracic echocardiography for diagnosis of right pulmonary artery to left atrial fistula: report of three cases and review of the literature

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**Background** No overview has been published to date of the transthoracic echocardiography (TTE) signs of the rare cardiovascular anomaly of right pulmonary artery (RPA) to left atrial (LA) fistula (RPA-LAF).

**Objective** To summarize the characteristics of the transthoracic echocardiography (TTE) for diagnosing the rare cardiovascular anomaly of right pulmonary artery to left atrial fistula.

**Methods** Three patients were diagnosed with RPA-LAF at Fuwai Hospital from 2000 to 2010. The patients were all male and were aged 14 years, 7 years and 6 months. All patients underwent clinical examination, chest roentgenogram, laboratory testing, electrocardiography, transthoracic echocardiography (TTE), contrast echocardiography, and cardiac catheterization. We undertook a detailed review of their TTE and contrast echocardiography findings to determine the characteristic findings of this condition.

**Result** TTE was performed in all cases, and in two cases contrast echocardiography was also performed. In two cases, the LA was abnormally shaped and enlarged, the RPA was obviously enlarged and aneurysmal, and the fistula was detectable on TTE. In the other case, there was only mild enlargement of the left heart, and contrast echocardiography led to a misdiagnosis of pulmonary arteriovenous fistula. Successful detection of a fistula may be related to the degree of dilatation of the LA and RPA, the location of the fistula, and the type of RPA-LAF. Cases with a dilated LA and with the fistula located at the proximal and posterior RPA and LA may be easier to diagnose by TTE. The shunt from the RPA to the LA can clearly be seen by color Doppler flow imaging. The preferred imaging planes were the pulmonary artery long-axis, aortic short-axis, and apical four-chamber views, and the subxiphoid coronal view of the right ventricular outflow tract.

**Conclusion** Diagnostic guidelines of TTE can help in the detection of RPA-LAF. With the correct views, echocardiography was effectively able to diagnose RPA-LAF, including diagnosis of the complications and malformations which can guide typing.

### Evaluation renal function of cardiac transplant patients with glomerular filtration rate imaging

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**Purpose** Evaluation renal function of cardiac transplant patients with glomerular filtration rate imaging

**Methods** We collected patients underwent heart transplantation and had 3 times GFR (before operation, 1 month after operation, 1 year after operation). Renal function analysis indicators include left kidney GFR, right kidney GFR, total GFR, left renal clearance rate, right renal clearance rate, left renal peak time, right renal peak time.

**Result** The GFR indicators 1 month after operation are similar with

the GFR indicators before operation, the differences were not statistically significant. Left GFR ( $30.3 \pm 12.6$ ), right GFR ( $31.1 \pm 13.0$ ), total GFR ( $61.2 \pm 24.7$ ) 1 year after operation decreased comparing with the Left GFR ( $35.8 \pm 13.3$ ), right GFR ( $35.9 \pm 12.7$ ), total GFR ( $71.7 \pm 24.7$ ) before operation, differences were statistically significant (P values were 0.024, 0.038, 0.026); Left renal clearance rate, right renal clearance rate, left renal peak time, right renal peak time was no significant difference (P > 0.05).

**Conclusion** There is no significant difference between renal function 1 month after and before heart transplantation. The renal function 1 year after heart transplantation decreased comparing with the renal function before heart transplantation. Protect kidney function after 1 year heart transplantation, and monitor closely the kidney function.

### Electrophysiological characteristic and ablation of epicardial idiopathic ventricular arrhythmias arising around left fibrous triangle

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**Background** The success rate of radiofrequency catheter ablation of ventricular arrhythmias originating from left fibrous triangle (LFT) is not high. This article was to discuss the characteristics of surface electrocardiogram and the strategy of ablation of ventricular arrhythmias originating from LFT.

**Methods** From Feb. 2002 to Mar. 2012, total 323 patients with outflow ventricular arrhythmias were ablated in our hospital, including 46 patients whose ventricular arrhythmias originated from the LFT. The mean age of the 46 patients was  $44 \pm 13$  years (16 – 87 years), and 24 of them (52.2%) were male. Thirty patients had frequent premature ventricular contractions (PVCs) and 16 patients had both PVCs and nonsustained or sustained ventricular tachycardia (VT). All the patients were examined with ECG, electrophysiology, active mapping and pace mapping. The computer tomography angiogram (CTA) 3D reconstruction of coronary artery, venous was completed in 20 patients.

**Result** Successful ablation was achieved in 41 of the 46 patients (89.1%, 41/46) targeting left coronary cusp (LCC, 30 patients), infra aortic valve (infra AV, 6 patients) and great cardiac vein (GCV, 5 patients). The surface ECG in all the three groups presented with inferior axis and R/S-transition in lead V<sub>1</sub> and V<sub>2</sub>. There were no differences in the total QRS duration in the three groups. Most of the patients presented with right bundle branch block (RBBB) morphology in infra AV group and GCV group compared with LCC group (67%, 80% vs 15%, P = 0.002). Regarding to the classification of the LFT according to CTA, the patterns of distribution were as follows: “closed” in 10 (50%, 10/20) hearts; “completely opened” in 2 (10%, 2/20); “inferiorly opened” in 5 (25%, 5/20) hearts and “superiorly opened” in 1 (5%, 1/20) hearts. In the remaining 2 (10%, 2/20), there were not any distances between GCV and left coronary artery. The closest distance between the corner of the GCV and LCC is  $17.6 \pm 4.2$  mm (9.1 – 26.3 mm).

**Conclusion** Ventricular arrhythmias originating from the LFT can be ablated in the nadir of the LCC, infra AV and the GCV. The success rate may be impacted by the distance from the GCV and the LCC.



## A new algorithm differentiate the septum originated ventricular arrhythmias from the free wall in the right ventricular outflow tract

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**Introduction** Until now, no ventricular arrhythmias QRS axis dominated ECG algorithms was used to differentiate ventricular tachycardia or premature ventricular complexes (VT/PVCs) originating from the free wall or septum in the RVOT. In this study, we designed new ECG criteria and investigated the sensitivity and specificity of them in practice.

**Methods** Consecutive 120 patients with left bundle branch block morphology and precordial transition lead  $\geq V_4$  were successfully underwent mapping and ablation. They were rerolled into the septum group (n = 95) and the free wall group (n = 25) according to VT/PVCs origin. We analyzed the ECG pattern with following criteria. 1) QRS axis  $> 89^\circ$ ; 2) R wave amplitude in lead III  $>$  II, and 3) A2III score included QRS axis  $> 84.5^\circ$  (score = 1), lead III QRS duration  $> 154.5$  ms (score = 1) and AVL QRS duration  $> 156.5$  ms (score = 1).

**Result** Retrospective analysis showed that VT/PVC axis  $> 89^\circ$  or R wave amplitude in lead III  $>$  II predict VT/PVC originating from the septum with 100% sensitivity, 93.94% specificity, and 97.78% positive prediction value. A2III score  $\geq 2$  predicts VT/PVCs originating from the free wall in the RVOT with 80.00% sensitivity, 87.50% specificity and 84.09% positive predictor value. The new algorithms predict VT/PVCs originating from the free wall in the RVOT with the overall sensitivity, specificity, and positive predictor value were 81.48%, 91.30% and 88.76%. Prospective analysis in 20 patients showed that VT/PVCs originating from the free wall in the RVOT with the overall sensitivity, specificity, and positive predictor value were 90%, 89.74% and 95%.

**Conclusion** VT/PVC axis  $> 89^\circ$ , R wave amplitude in lead III  $>$  II and A2III score  $< 2$  with very high sensitivity, specificity and positive prediction value for prediction VT/PVCs originating from the septum origin in the RVOT. A2III score  $\geq 2$  predicts VT/PVCs originating from the free wall in the RVOT.

## Long term outcomes of right ventricular outflow tract ventricular arrhythmias ablation guided by non-contact mapping

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**Background** Limited data exists about long term success rate after ablation of right ventricular outflow tract (RVOT) ventricular arrhythmias (VA) guided by the non-contact mapping system (NCM). In this study, we aim to investigate long term outcomes following NCM guided RVOTVA ablation.

**Methods** From Jun. 2006 to Dec. 2011, consecutive patients with RVOT VA underwent mapping and ablation using NCM (group A, n = 136) or 3-D contact mapping system (control group B, n = 18). Within group A, ablation was randomized to be initiated at either the site of earliest electrical activity (EA site) or the break-out site from which rapid

centrifugal electrical propagation originated from (BO site). Clinic visits, ECGs and 24 hour Holters were conducted monthly for the first three months and then in six months intervals.

**Result** 154 (60 male, mean age  $41.8 \pm 13.5$  years old) consecutive patients were enrolled. With follow up of  $36.2 \pm 17.5$  months, the long term success rate after a single procedure without anti-arrhythmic agents was 86.8% (118/136) in the NCM cohort. Baseline characteristics, acute and long term success rates, complications were similar between Groups A and B. A learning curve of 20 cases was associated with the use of NCM. The initial ablation is more successful when directed at the EA sites rather than the BO sites identified by NCM ( $P < 0.01$ ).

**Conclusion** NCM-guided RVOT VA ablation is highly effective and associated with long term clinical outcomes comparable to ablation guided by 3-D mapping systems. Ablation is more successful when directed at the EA sites identified by the NCM.

## Magnetic vs manual catheter navigation for mapping and ablation of right ventricular outflow tract ventricular arrhythmias: a randomized controlled study

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**Background** There has been no randomized controlled study to prospectively compare the performance and clinical outcomes of remote magnetic control (RMC) vs manual catheter control (MCC) during ablation of right ventricular outflow tract (RVOT) ventricular premature complexes (VPC) or tachycardia (VT). This study prospectively evaluated the efficacy and safety of using either RMC vs MCC for mapping and ablation of RVOT VPC/VT.

**Methods** Thirty consecutive patients with idiopathic RVOT VPC/VT were referred for catheter ablation and randomized into either RMC or MCC group. A non-contact mapping system (NCM) was deployed in the RVOT to identify origins of VPC/VT. Conventional activation and pace-mapping was performed to guide ablation. If ablation performed using one mode of catheter control was acutely unsuccessful, the patient crossed over to the other group. The primary endpoints were patients' and physicians' fluoroscopy exposure and times.

**Result** Mean procedural times were similar between RMC and MCC groups. The fluoroscopy exposure and times for both patients and physicians were much lower in RMC group than in the MCC group. Ablation was acutely successful in 14/15 patients in the MCC group and 10/15 in the RMC group. Following cross-over, acute success was achieved in all patients. No major complications occurred in either group. During 22 months of follow-up, RVOT VPC recurred in 2 RMC patients.

**Conclusion** RMC navigation significantly reduces patients' and physicians' fluoroscopy times by 50.5% and 68.6% respectively when used in conjunction with a NCM to guide ablation of RVOT VPC/VT.

## Catheter ablation of ventricular tachycardia in patients with ischemic cardiomyopathy under the guidance of three-dimensional electroanatomic mapping

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**Objective** To introduce the initial experience of electroanatomic mapping and catheter ablation of VT in patients with ischemic cardiomyopathy (ICM).

**Methods** 7 ICM patients with VT attack were referred for catheter ablation guided by 3-dimensional electroanatomic mapping. The scar area was identified by voltage map. Activation mapping, pace mapping and entrainment mapping were then performed to localize the reentrant circuit, critical isthmus, slow conduction zone and exit sites, which were the targets for ablation.

**Result** Among 7 patients, 13 VTs were induced. Catheter ablation successfully eliminated all 8 VTs in 5 patients, partially succeeded in 1 patient with 2 VTs, and failed in 1 patient with 3 VTs. ICD was implanted into that 2 patients.

**Conclusion** 3-dimensional electroanatomic mapping, combined with activation mapping and pacing maneuvers can help to discover the origin, reentrant circuit, slow conduction zone and the exit of ICM-VT, providing an effective way to eliminate such VTs.

## Cardiovascular Disease Therapeutics

### Uselessness of admission concentrations of D-dimer to predict in-hospital mortality in patients with Stanford type a acute aortic dissection

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**Objective** Concentrations of D-dimer, a degradation product of cross-linked fibrin, were found to be raised in patients with AAD by several studies. Admission concentrations of D-dimer have emerged as a complementary diagnostic marker for acute aortic dissecting (AAD). But its prognostic role with in-hospital mortality in patients with Stanford type A AAD was not well elucidated. To clearly elucidate the prognostic role of D-dimer with in-hospital mortality in patients with Stanford type A AAD, we conducted the present study enrolling relatively larger patients with AAD in a single center with abundant source of patients in China

**Methods** From Feb. 2012 to Jan. 2013, a total of 268 consecutive patients with chest pain admitted to Fuwai hospital (Beijing, China) was confirmed the diagnosis of AAD. Of these 268 patients, 141 patients were Stanford type A and 127 were Stanford type B. The study enrolled 133 consecutive patients with Stanford type A AAD. Routine laboratory tests, chest X-ray, ultrasonic cardiogram and electrocardiogram were performed for each patient. Aorta angiography with multi-detector computed tomography was performed to confirm the diagnosis. Primary outcome was in-hospital mortality. To determine the predictors of in-hospital mortality, baseline clinical characteristics such as sex, age, Stanford type of AAD, whether or not acute intramural hematoma, interval from onset of symptoms to hospital, smoking and drink habits; previous medical histories including hypertension, diabetes mellitus, coronary artery disease, stroke and hyperlipidemia; baseline parameters of physical examination and laboratory tests including platelet counts, C-reactive protein (CRP), D-dimer; imaging examinations and in-hospital managements were well recorded according to pre-designed case report form. Predictors of in-hospital mortality were determined using univariate and multivariate logistic analyses. Considering of dissection related organ ischemia and platelet counts also affecting the concentration of D-dimer, we constructed two multivariate Models. Model1 included age, sex, Debakey type, acute intramural hematoma, interval from symptom onset to hospital, hypertension, diabetes mellitus, coronary artery disease, diastolic blood pressure, D-dimer, aortic diameter, B-receptor blocker, calcium channel blocker and surgery. Model 2 which includes Model 1, organ ischemia and platelet counts.

**Result** Mean age of the entire study population was 52 years. More than 90% AAD was Debakey type I. the morbidity of acute intramural hematoma was around 10%. Among the 133 patients with Stanford type A AAD, death during hospitalization was observed in 19 patients. In-hospital mortality was 14.3%. 6 patients died from dissection related organ ischemia including acute renal failure, visceral or limb ischemia, cerebral ischemia, multiple organ failure. 2 patients

died during perioperative period: one from anesthesia, the other from cardiac arrhythmia. 11 patients died from aortic rupture: one patient with aortic rupture into mediastina, other rupture into pericardial cavity. On univariate analysis, admission concentrations of D-dimer correlated with in-hospital mortality (OR, 1.102; 95% CI, 1.030 – 1.180; P = 0.005). In Model 1, D-dimer still correlated with in-hospital mortality (OR, 1.125; 95% CI, 1.022 – 1.238; P = 0.016). But in Model 2 we found that concentrations of D-dimer did not correlate with in-hospital mortality (OR, 1.026; 95% CI, 0.914 – 1.152; P = 0.659), while platelet counts with OR (95% CI): 0.961 (0.925 – 0.998) and organ ischemia with OR (95% CI): 10.66 (1.43 – 79.68) were independent predictors for in-hospital mortality in Stanford type A AAD.

**Conclusion** Despite rapid progress in the management of Stanford type A AAD, its in-hospital mortality was still high. Plasma concentrations of admission D-dimer did not correlate with in-hospital mortality. Dissection related organ ischemia and admission platelet counts were independent predictors for in-hospital mortality of Stanford type A AAD. This is supplementary to the existing research evidence regarding to predictors of mortality of AAD.

### The effects of cardiopulmonary exercise testing in patients with chronic thromboembolic pulmonary hypertension

Zhihui Zhao

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**Objective** To evaluate the value of cardiopulmonary exercise testing in patients with chronic thromboembolic pulmonary hypertension (CTEPH).

**Methods** One hundred and sixteen consecutive patients admitted to the Cardiology Department of Fu-wai Hospital. The patients were divided into three groups, there were 44 patients in the CTEPH group, 24 patients without pulmonary hypertension in the chronic pulmonary embolism (CPE) group, and 48 patients without pulmonary embolism or pulmonary hypertension in the control group, respectively. All the patients were measured the levels of N-Terminal Pro-Brain Natriuretic Peptide (NT-proBNP) and underwent incremental cardiopulmonary exercise testing and compared the difference of the Result of incremental cardiopulmonary exercise testing among three groups, and evaluate the correlation between the NT-proBNP and the cardiopulmonary exercise test parameters.

**Result** The body mass index (BMI) in the CTEPH group was lower than those in the CPE group and control group [(23.8 ± 3.9) vs (26.1 ± 3.6) and (26.7 ± 3.2) kg/m<sup>2</sup>], both P < 0.05]; the medical history in the CTEPH group was longer than those in the CPE group and control group [(58 ± 48) vs (12 ± 10) and (29 ± 25) months, both P < 0.05] The plasma concentrations of NT-proBNP in the CTEPH group were higher than those in the CPE group and control group [(1678 ± 1255) vs (577 ± 167) and (608 ± 247) pmol/L, both P < 0.05]. All the patients completed the test and there were no severe complications such as syncope or exacerbation of disease. Maximum oxygen consumption (VO<sub>2max</sub>), percentage of the predicted maximum oxygen consumption (VO<sub>2</sub>%), oxygen consumption in relation to body weight (VO<sub>2</sub>/kg), anaerobic threshold and O<sub>2</sub> pulse in the CTEPH group were significantly lower than those in the CPE group and control group (P < 0.05). The ratios of dead space volume (VD) to tidal volume (VT) in the CTEPH group and CPE group were higher than that in the control group (P < 0.05).



The plasma concentrations of NT-proBNP were inversely correlated with right ventricular internal diameter ( $r = -0.690$ ,  $P = 0.000$ ) and  $VO_2/kg$  ( $r = -0.496$ ,  $P = 0.0001$ ). The right ventricular internal diameter ( $\beta = 0.583$ ,  $P = 0.000$ ) and  $VO_2/kg$  ( $\beta = 0.233$ ,  $P = 0.032$ ) were powerful independent determinants of NT-proBNP.

**Conclusion** Cardiopulmonary exercise testing may be used to evaluate the cardiopulmonary function of CTEPH patients objectively and safely, and could response the pathophysiology of CTEPH.

### The relationship between red blood cell distribution width and early warning, risk stratification and short-term prognosis of acute coronary syndrome

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**Objective** The aim is to determine the relationship between the red blood cell distribution width and early warning, risk stratification and in-hospital short term prognosis of acute coronary syndrome.

**Methods** A total of 2651 chest pain patients presenting to the Peking University People's hospital who had undergone coronary artery angiography were recruited for this study between Jan. 2008 and Dec. 2010. Patients were divided into 2 groups according to mean of baseline RDW (13.22%): a high RDW group ( $RDW > 13.22\%$ ;  $n = 1144$ ); and a low RDW group ( $RDW \leq 13.22\%$ ;  $n = 1507$ ). The causes of chest pain were compared between groups. Then, a total of 2213 patients diagnosed ACS were divided into 2 groups according to mean of baseline RDW: the low RDW group ( $RDW < 13.26\%$ ,  $n = 1256$ ) and the high RDW group ( $RDW \geq 13.26\%$ ,  $n = 957$ ). The severity of coronary artery lesion, heart function and in-hospital mortality were compared between groups.

**Result** The cumulative incidence of ACS was significantly higher in the high RDW group than in the low RDW group (89.1% vs 79.2%,  $P < 0.001$ ). The multivariate logistic regression analysis found that a high RDW was an independent factor related to ACS (OR = 2.027, 95% CI 1.597 – 2.573,  $P < 0.001$ ). The difference of the severity of coronary artery lesion between two groups were not statistically significant (all  $P > 0.05$ ). However, patients with high RDW had lower LVEF than patients with low RDW ( $61.65 \pm 11.05\%$  vs  $62.78 \pm 10.59\%$ ,  $P = 0.03$ ). In addition, the in-hospital mortality of the high RDW group was significantly higher than the low RDW group (4.8% vs 1.0%,  $P = 0.0001$ ). All deaths were cardiac death. In multivariate analysis, baseline high RDW level ( $RDW \geq 13.26\%$ ) was an independent predictor of in-hospital mortality of ACS (OR = 3.597, 95% CI 1.720 – 7.522,  $P < 0.001$ ).

**Conclusion** In patients admitted to the hospital because of chest pain, RDW may present as an early warning marker of ACS. Meanwhile, RDW can predict heart function and in-hospital mortality in ACS patients.

### Relationship between acute high altitude response, cardiac function injury and high altitude de-adaptation response after return to lower altitude

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3. The 68303 Troop Hospital of People's Liberation Army, Wu Wei, 733000, China.

**Objective** To assess the relationship between acute high altitude response (AHAR), cardiac function injury and high altitude de-adaptation response (HADAR).

**Methods** Ninety-six military personnel of rapid entering into high altitude (3 700 to 4 800 m) with strong physical work were analyzed, all subjects were male, aged 18 – 35 years. According to the symptomatic scores of AHAR were divided into 3 groups: sever AHAR (group A, 24), mild to moderate AHAR (group B, 47) and non-AHAR (group C, 25) at high altitude. According to the symptomatic scores of HADAR were divided into 3 groups: sever HADAR (group E, 19), mild to moderate HADAR (group F, 40) and non-HADAR (group G, 37) after return to lower altitude (1500 m). Mean pulmonary arterial pressure (mPAP), right ventricular internal dimension (RVID), outflow tract of right ventricle (RVOT), left ventricular internal dimension (LVID), left ventricular ejection fraction (LVEF), cardiac muscle work index (Tei index), creatine kinase isoenzymes-MB (CK-MB), lactic dehydrogenase isoenzyme-1 (LDH-1) were measured at high altitude stayed 50 days and after return to lower altitude 12 h, 15 d, and 30 d. Fifty healthy volunteers (group D) at 1500 m altitude served as control.

**Result** Level of mPAP, RVID, RVOT, RVID/LVID ratio, Tei index, CK-MB, and LDH-1 were higher, and LVEF was lower in group A than those in group B, C and D, there were significantly differences between group B and C, C and D (all  $P < 0.01$ ). AHAR scores was positively correlated with HADAR scores ( $r = 0.863$ ,  $P < 0.001$ ). 12 h after return to lower altitude, level of mPAP, RVID, RVOT, RVID/LVID ratio, Tei index, CK-MB, and LDH-1 were higher, and LVEF was lower in group E than those in group F, G and D, there were significantly differences between group F and G, G and D (all  $P < 0.01$ ). 15 days after return to lower altitude, level of mPAP, RVID, RVOT, RVID/LVID ratio were higher in group E than those in group F, G, and D, there were significantly differences between group F and G, and D ( $P < 0.01$  or  $P < 0.05$ ), there were no significantly differences between group G and D (all  $P > 0.05$ ), LVEF, Tei index, CK-MB, LDH-1 showed no significantly differences among groups (all  $P > 0.05$ ). 30 days after return to lower altitude, these parameters in group E, F, and G showed no significantly differences compared with those of group D (all  $P > 0.05$ ).

**Conclusion** The severity of HADAR is associated with severity of AHAR and cardiac injury, the more serious of AHAR and cardiac injury at high altitude, the more serious of HADAR and cardiac injury after return to lower altitude, the more long of restore of right cardiac structure injury.

## Changes of the cardiac structure and function in Han people returning to lower altitude for at least 3 years after long-term exposure to high altitude

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**Objective** To study the changes of cardiac structure and function in Han people returning to the plain after longterm exposure to high altitude.

**Methods** Echocardiographic examinations were performed in 348 residents who once lived in high altitude and then returned to the plain for at least 3 years (altitude exposure group) and in 86 healthy people without exposure to high altitude (control group). The cardiac function and structure were measured and compared between two groups according to different genders.

**Result** Compared with the control group, the right atrium short diameter (RAD) was longer in altitude exposure group (male  $30.81 \pm 3.89$  vs  $29.39 \pm 3.93$ ; female  $29.05 \pm 3.06$  vs  $27.40 \pm 2.97$ ,  $P$  all  $< 0.05$ ) and left ventricular posterior wall thickness (LPVW) in altitude exposure group was larger than in control group, ( $P < 0.05$ ). The incidence of tricuspid regurgitation (TR) in altitude exposure group was significantly higher than that of the plain control (44.25% vs 8.13%,  $P < 0.001$ ). In altitude exposure group the incidence of TR in female was higher than that in male (50.28% vs 38.15%,  $P = 0.025$ ).

**Conclusion** Long-term exposure to high altitude is associated with the changes of the structure of right atrium and left ventricular (and the increased incidence of TR) which is higher in female than in male. And these changes mentioned above were hard to recover even after returning to the plain for several years.

## Deadaptation change in cardiac function of laborers engaged in physical labor at high altitude after returning to lower altitude

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**Objective** To assess the effects of physical labor on cardiac function of laborers at high altitude and changes in cardiac function after returning to lower altitude.

**Methods** According to symptomatic scores on Chinese acute high altitude reaction (AHAR) 96 male officers and soldiers who rapidly entered high altitude areas (3 700 m altitude), and engaged in

heavy physical work for 50 days were be scored and graded. Levels of creatine kinase isoenzymes-MB (CK-MB) and lactic dehydrogenase isoenzyme-1 (LDH-1) in the serum, Tei index, left ventricular ejection fraction (LVEF) and left ventricular fractional shortening (LVFS) were measured in the 96 servicemen at the 50<sup>th</sup> day of residing at high altitude, and the 2<sup>nd</sup> and 15<sup>th</sup> day after returning to lower altitude (1 500 m altitude), and the result were compared with that of 50 healthy controls residing at 1 500 m.

**Result** Among the 96 male service men, 71 developed AHAR and 24 of them had Severe AHAR, 47 mild to moderate AHAR and the rest 25 had no AHAR. Levels of serum CK-MB, LDH-1 and Tei index were higher in the severe AHAR group than in the mild to moderate AHAR group, higher in the mild to moderate AHAR group than in the no AHAR group, and higher in the no AHAR group than in the healthy group. As far as the values of LVEF and LVFS were concerned, the severe AHAR group  $<$  mild to moderate AHAR group  $<$  no AHAR group  $<$  control group. Significant difference was found in these levels between every two successive groups ( $P < 0.01$ ). Linear correlation analysis showed that levels of CK-MB and LDH-1 of persons staying at 3700 m altitude for 50 days were positively correlated with Tei index ( $r = 0.625, 0.598$ , respectively,  $P < 0.01$ ), and negatively correlated with LVEF ( $r = -0.716, -0.658$ , respectively,  $P < 0.01$ ) and also negatively correlated with LVFS ( $r = -0.639, -0.727$ , respectively,  $P < 0.01$ ). Level of serum CK-MB, LDH-1 and Tei index at 3700 m altitude for 50 days were significantly higher than those 2 days and 15 days after returning to 1 500 m altitude and those in control group ( $P < 0.01$ ) and were significantly higher on the 2<sup>nd</sup> day than on the 15<sup>th</sup> day. Moreover, the values of LVEF and LVFS were significantly lower than those at 2 and 15 days after returning to 1 500 m altitude and those in control group ( $P < 0.01$ ) and significantly lower on the 2<sup>nd</sup> day than on the 1<sup>st</sup> day. All parameters after 15 days returning to low altitude showed no significant difference compared with control group ( $P > 0.05$ ).

**Conclusion** Heavy physical work at high altitude could obviously impair human cardiac function. The impairment may aggravate along with increase in severity of AHAR. However, cardiac function may be improved significantly after returning to low altitude for 2 days, and recover to normal status 15 days later.

## The research of heart rate variability in children with viral myocarditis

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**Objective** The aim of this study was to evaluate autonomic nervous activity in children with VMC by analysis of HRV. Then to discuss the value of HRV analysis regarding to diagnosis, therapy and prognosis in children with VMC.

**Methods** We collected 600 (305 males and 295 females, aged 3 – 14 years, mean age 7.5 years old) children with VMC who were acute period patients as researching objects in our hospital. 590 (300 males and 290 females, aged 3 – 14 years, mean age 7.1 years old) healthy children served as control group. They hadn't caught diseases which can affect autonomic nerve activity, such as cardiac diseases, diabetes mellitus, hyperthyrosis, and infectious diseases. All the children's body weight was in the range of  $X \pm 2SD$ . We monitored all the children by 12 leads dynamic electrocardiogram device which was produced by Kang Tai medical company limited in American. We demanded everyone not take medicine which can affect heart activity. Time domain indexes of HRV were measured, including SDNN: the standard deviation (SD)

of the R-R interval (RR), SDANN: SD of the mean of RR intervals in all 5-minute segments of the 24-hour ECG, SDNN Index: the average of SD of RR intervals in all 5-minute segments of the 24-hour ECG, RMSSD: the root mean square of successive differences in RR intervals, PNN50: the percentage between the pieces of RR intervals' phase difference were above 50 ms and all the RR intervals' pieces in the 24-hour ECG. The recording time included 24 hour-period, waking hours (8: 00 – 21: 00), sleeping hours (21: 00 – 6: 00). The HRV numeric value per hour is made into diagram of curve. We also calculated the abnormal result of SDNN, creatine kinase-MB, action-X, Doppler and dynamic electrocardiogram.

**Result** (1) The HRV indexes during 24-hour period is significantly difference between control group and VMC group. (2) The HRV indexes during waking hours in children with VMC was significantly smaller compared with that in control group. (3) The HRV indexes during sleeping hours in children with VMC was significantly smaller compared with that in control group. (4) The changeable breadth of circadian rhythm in patients with VMC is significantly smaller compared with that in control group, and the PNN50 and R mmSD were the most sensitive indexes. (5) The most highest percentage of abnormal index was SDNN.

**Conclusion** (1) The autonomic nervous system activity in children with VMC is changed, especially the vagus nerve was damaged mostly, so the indexes of HRV was reduced. HRV indexes can become sensitive marker. (2) The circadian rhythm of autonomic nerve was almost disappeared. HRV indexes can become one marker which can predict the prognosis of ventricular arrhythmia in children with VMC. (3) In the future, the medicine of alterate HRV is one of investigate direction.

### Significance of cardio-ankle vascular index in diagnosis of senile aorta atherosclerosis

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**Objective** To investigate the clinical significance of a new indicator for diagnosing aorta atherosclerosis: cardio-ankle vascular index (CAVI) in old patients.

**Methods** CAVI was detected by applying VS -1000 Atherosclerosis Detective System in 115 old patients (male 92 and female 32). The ankle brachial index (ABI), carotid intima-media thickness (IMT) and relevant indexes of biochemistry were determined at the same time.

**Result** The average age of 115 old patients was  $75.6 \pm 4.8$  and their average CAVI was  $10.70 \pm 4.32$ . The abnormal rate of CAVI was 88.1% (CAVI  $\geq 9$  defined as abnormal), which was similar to the detectable rate of senile aorta atherosclerosis (89.7%, when IMT  $\geq 9$  mm). In the group of aorta atherosclerosis accompanied by peripheral artery disease (PAD) CAVI was  $12.0 \pm 19.44$  and that was  $10.38 \pm 1.19$  in the group without PAD. There was a significant difference between two groups ( $P < 0.01$ ). The Correlative Coefficient between CAVI and ABI was  $-0.247$  ( $P < 0.05$ ), There was no significant difference in CAVI between hypertension group and non-hypertension group, diabetes group and non-diabetes group, or smoking group and non-smoking group respectively. CAVI was no correlated to age ( $P > 0.05$ ).

**Conclusion** CAVI can be taken as one of indicators for screening aorta atherosclerosis non-invasively, while which should be combined with multiple noninvasive indicators used in senile patients in order to clinical comprehensive analysis and diagnosis.

### Ischemic preconditioning offers cardioprotection in coronary artery bypass graft: a meta-analysis of 10 randomized controlled trials

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**Background** Result from clinical trials on cardioprotection by ischemic preconditioning (IPC) for patients undergoing coronary artery bypass graft (CABG) are mixed. The aim of this meta-analysis was to evaluate the effect of IPC on the postoperative biomarkers of myocardial injury in surgical revascularization.

**Methods** A systematic search was performed in PubMed, EMBase, and Cochrane Library (up to Mar. 2013). Randomized controlled trials (RCT) about IPC reporting postoperative myocardial biomarkers (CK-MB or troponin) levels in CABG were included. Standardized mean difference (SMD) was used to pool the different types of biomarkers. Random-effect model was used in the pooled analysis in case of significant heterogeneity ( $I^2 > 50\%$ ). 'Trim and fill' method was used in case of significant publication bias (Begg's or Egger's test,  $P < 0.05$ ). Meta regression analyses were used to explore the potential sources of significant heterogeneity ( $I^2 > 50\%$ ) including mean age, mean male proportion, mean bypass time, and baseline left ventricular ejection fraction (LVEF).

**Result** Ten trials included 13 comparisons with 429 study subjects in which 215 ones were preconditioned were selected and identified. Aorta was majorly used for the conditioning protocols which were 1 – 2 cycles of 2 – 5 min occlusion/2 – 5 min reflow. The mean age ranged from 57.0 to 65.0 years and male proportion from 62.5% to 93.0%. The mean bypass time varied from 71.0 to 126.0 min. The baseline LVEF was 40.7% to 71.5%. Troponin levels were reported in 9 trials. Compared with controls, IPC significantly reduced postoperative biomarkers of myocardial injury (SMD =  $-1.25$ ; 95% Confidence Interval,  $-2.25$  to  $-0.24$ ;  $P = 0.0151$ ; heterogeneity test:  $I^2 = 94.5\%$ ; ). Significant publication bias was observed (Begg's test,  $P = 0.028$ ; Egger's test,  $P = 0.191$ ). However, this effect size remained unchanged after 'trim and fill' method was performed. Meta-regression analysis revealed that the major sources of significant heterogeneity was baseline LVEF (regression coefficient  $> 0$ ,  $P < 0.05$ , adjust  $R^2 = 52\%$ ).

**Conclusion** Available data from this meta-analysis suggests that IPC may conferred cardioprotective potential by reducing postoperative biomarkers of injury for patients undergoing coronary bypass surgery. This effect may be more pronounced in patients with low baseline LVEF.

### Usefulness of temporary pacemaker surrounding of non cardiac operation period

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**Objective** To evaluate the safety and importance of temporary artificial cardiac pacemaker during non-cardia perioperative period of lin patients with bradyarrhythmia.

**Methods** Temporary cardiac pacemakers were installed preoperatively in 108 patients with bradyarrhythmia. The patients were



divided into paced and no-paced groups according to the ECG monitoring during perioperative period. Clinical data were compared between the two groups.

**Result** Totally 31 patients needed pacing during perioperative period. They were older than the no-paced 61 patients [(83 ± 11) y vs (72 ± 12) y,  $t = 2.865$ ,  $P = 0.005$ ]. In the paced group, more patients had history of myocardial infarction [58% (18/31) vs 12% (7/61),  $\chi^2 = 19.612$ ,  $P < 0.001$ ], cardiomyopathy [7% (2/31) vs 0% (0/61),  $P = 0.043$ ], and syncope [10% (3/31) vs 0% (0/61),  $P = 0.035$ ], abnormal findings in Holter [97% (30/31) vs 48% (29/61),  $\chi^2 = 26.731$ ,  $P = 0.000$ ] and UCG [97% (30/31) vs 46% (28/61),  $\chi^2 = 26.076$ ,  $P < 0.001$ ].

**Conclusion** Temporary cardiac pacemaker can enhance the perioperative safety and reduce the incidence of cardiovascular complications in patients with bradyarrhythmia. Overall assessments of clinical setting were needed before implantation. The indications for temporary cardiac pacing include bradyarrhythmia with myocardium disorder, which is confirmed by UCG, advanced age, as well as history of syncope. Positive result of atropine test is not one of the significant indications.

### Clinical observation of cardiopulmonary exercise test of patients with idiopathic pulmonary arterial hypertension

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**Objective** To explore the exercise characteristics of patients with idiopathic pulmonary arterial hypertension.

**Methods** From Nov. 2010 to Sep. 2012, 76 consecutive patients with idiopathic pulmonary arterial hypertension (IPAH) and 24 healthy as controls from Fuwai Cardiovascular Hospital were enrolled, who completed cardiopulmonary exercise testing. The exercise parameters were compared between patients with IPAH and controls. Correlations among peak oxygen consumption, anaerobic threshold, peak oxygen pulse, New York Heart Association (NYHA) class, N-terminal pro-brain natriuretic peptide (NT-proBNP), 6 minute walking distance (6MWD) and cardiac index are analyzed in IPAH.

**Result** There were 21 males and 55 females in IPAH and 8 males and 16 females in controls, with mean age (31.5 ± 10.6) years old and (35.5 ± 6.4) years old respectively. There were significant differences ( $P = 0.000$ ) between the patients with and controls in peak oxygen consumption ((12.7 ± 3.3) vs (25.6 ± 5.8) ml/min/kg), anaerobic threshold ((9.8 ± 2.5) vs (16.7 ± 3.9) ml/min/kg), peak oxygen pulse [(5.3 ± 1.6) vs (9.9 ± 2.5) ml/bpm] and ventilator efficiency (the slope of minute ventilation in relation to CO<sub>2</sub> produced) [(42.6 ± 2.0) vs (25.5 ± 3.5)]. In IPAH, peak oxygen consumption was significantly correlated with NYHA class ( $r = -0.509$ ,  $P < 0.001$ ), 6MWD ( $r = 0.443$ ,  $P = 0.002$ ) and NT-proBNP levels ( $r = -0.423$ ,  $P = 0.011$ ). And anaerobic threshold was significantly correlated with NYHA class ( $r = -0.362$ ,  $P = 0.002$ ), 6MWD ( $r = 0.343$ ,  $P = 0.004$ ) and NT-proBNP levels ( $r = -0.275$ ,  $P = 0.017$ ), too. Peak oxygen pulse and ventilator efficiency were both correlated well with total pulmonary vascular resistance. Partial correlation analysis demonstrated that there were still significant correlations after adjusting age, sex and weight.

**Conclusion** Peak oxygen consumption and anaerobic threshold decrease ventilator efficiency increases in patients with IPAH.

Cardiopulmonary exercise testing as an invasive measurement may assess safely the function of patients with IPAH.

### Serum big endothelin-1 predicts non-responder to cardiac resynchronization therapy

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**Aims** To assess the predictive potency of big endothelin-1 (big ET-1) to response to cardiac resynchronization therapy (CRT).

**Methods** We retrospectively analyzed data of patients who underwent CRT-P/Implantation in our single center from Jan 2009 to Dec 2011. Plasma big ET-1 and NT-proBNP were examined by ELISA kit at baseline. NYHA functional class and echocardiography were evaluated both at baseline and follow-up. Simpson method was applied to measure left ventricular ejection fraction (LVEF). Improvement of LVEF by 5% and reduction in NYHA class ≥ 1 grade was defined as responders. Improvement of LVEF by twice or the absolute value ≥ 50% and NYHA class I or II grade was defined as super-responders. Improvement of LVEF < 5% or reduction in NYHA class < 1 grade or the patient died or received heart transplantation for failing heart was defined as non-responders.

**Result** Overall 93 patients average age of 60.8 ± 11 years old included in this observational study. During 27 ± 11 (12 – 50) months follow-up, there were 34 non-responders, 24 responders and 35 super-responders. Concentration of big ET-1 (fmol/ml) in three groups were 1.2 ± 0.9, 0.8 ± 0.4 and 0.8 ± 0.6 ( $P = 0.029$ ) respectively. Correlation between big ET-1 and NT-proBNP and between big ET-1 and response to CRT was  $r = 0.469$  ( $P = 0.001$ ) and  $r = -0.237$  ( $P = 0.022$ ) respectively.

**Conclusion** Plasma big ET-1 correlated with the level of NT-proBNP in a medium degree. It might be a marker of severity of HF and a response predictor after CRT. High level of big ET-1 indicated non-responders.

### Prostacyclin therapy for pulmonary arterial hypertension: a meta-analysis

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**Background** Prostacyclin has played an important role in the treatment of pulmonary arterial hypertension (PAH). However, whether it provides a survival advantage is still not clear. The aim of the present meta-analysis was to evaluate the efficacy and safety of prostacyclin in PAH, focusing on the improvement of short-term survival.

**Methods** Trials were identified from the Cochrane Library, EMBASE, and PUBMED databases. We calculated risk ratios for dichotomous data and weighted mean differences, with 95% confidence intervals for continuous data.

**Result** 14 trials with a total of 2 244 patients (1 189 patients in the prostacyclin treatment group and 1 055 patients in the placebo group) were included in the meta-analysis. All-cause mortality rate in the control

group was 4.17%. In a 13.4-week follow-up, prostacyclin treatment was associated with a reduction in mortality of 44% (RR 0.56; 95% CI 0.35 – 0.88;  $P = 0.01$ ). Compared with placebo, prostacyclin reduced clinical worsening significantly (RR 0.60; 95% CI 0.46 – 0.80;  $P = 0.0003$ ), increased the 6-min walk distance by 27.95 m, reduced mean pulmonary arterial pressure and pulmonary vascular resistance, and increased the cardiac index and mixed venous oxygen saturation. However, prostacyclin treatment showed a much higher incidence (RR 3.25; 95% CI 2.07 – 5.10;  $P < 0.00001$ ) of withdrawn due to its adverse effects.

**Conclusion** The Result of this meta-analysis suggest an improvement of survival in the patients treated with the prostacyclin and its analogues for pulmonary arterial hypertension.

### The effects of adenosine triphosphate on inducing atrial fibrillation after circumferential pulmonary vein isolation in paroxysmal atrial fibrillation: an insight into the mechanism and implication for ablation

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**Introduction** Adenosine triphosphate (ATP) has been widely used to provoke dormant pulmonary vein (PV) conduction after circumferential pulmonary vein isolation (CPVI). However, there has been no systematic study examining the incidence and the mechanism of ATP-induced atrial fibrillation (AF) after CPVI in paroxysmal AF. In this case series study, we explore the mechanism of ATP-induced AF and assess the feasibility of eliminating this response by additional radiofrequency (RF) ablation.

**Methods and Result** A total of 300 consecutive patients with paroxysmal AF underwent CPVI. After all PVs were isolated, intravenous ATP injection was administered during isoproterenol infusion. AF was reproducibly induced by ATP in 39 patients (13%; 32 transient, 7 persistent). Non-PV foci were confirmed and located in 29 of these patients at the onset of AF provoked by ATP, including 27 foci in the superior vena cava (SVC), 1 foci in the middle portion of the crista terminalis, and 1 foci near the antrum of the PV outside the ablation circle. In all these cases, ATP-induced AF was eliminated after the non-PV foci were successfully ablated. For the other 10 patients with ATP-induced AF, the foci triggering AF could not be confirmed and located due to the transient effect of ATP, thus no further ablation were performed. During a follow-up period of  $18.7 \pm 6.4$  (6 – 24) months after the index procedure, 31 of 39 patients (79.5%) in the ATP induced AF group were free from any recurrence of atrial tachyarrhythmias.

**Conclusion** A high proportion of the ATP-induced AF post CPVI were initiated by rapid firing in the SVC. Eliminating this response by additional ablation may have an influence on clinical Result of paroxysmal AF ablation.

### Mapping and ablation of idiopathic ventricular arrhythmias from within coronary vein system

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**Objective** The purpose of this study was to determine the safety and efficacy of radiofrequency catheter ablation (RFCA) of frequent premature ventricular contractions (PVCs) or ventricular tachycardia

(VT) originating from Coronary vein system (CVs).

**Methods** 11 patients (7 men; age,  $47.08 \pm 15.16$  years) were found to have an CVs origin who were diagnosed as PVCs or VT by electrocardiogram or Holter. Radiofrequency application could not abolish PVCs/VT during endocardial mapping and ablation. Then, we considered that PVCs or VT may originated from CVs, so multiple electrode catheter was introduced into great cardiac vein (GCV) or anterior interventricular vein (AIV). After CVs origin for PVCs/VT have been determined by activation mapping and pace mapping, Radiofrequency energy was delivered with the irrigated-tip catheter at a power of 15 to 30 W and a flow rate of 17 to 30 ml/min. Finally, the characteristics of electrocardiogram and result of ablation were analyzed.

**Result** 9 of 11 patients underwent successful ablation within the CVs. In 9 of 11 patients, the site of origin (SOO) of the ventricular arrhythmias was identified from within the GCV ( $n = 7$ ), the AIV ( $n = 2$ ). The mean earliest activation preceding the onset of the QRS complex was  $29.67 \pm 4.35$  ms, and the mean impedance was  $216.8 \pm 47.2 \Omega$ . In the 2 patients with unsuccessful ablation, failure was because the ablation catheter could not be advanced to the SOO within the AIV. No complications occurred. QRS duration of PVCs/VT was  $158.33 \pm 12.09$  ms, pseudo-delta wave was present in 4 patients. Maximum deflection index was  $0.67 \pm 0.27$ . A q wave in lead I (QWL I) were seen in 5 patients with PVCs/VT were successful eliminated in the GCV. SOO within the GCV precordial R-wave transition in lead  $V_1$  exhibited right bundle branch block QRS morphology; SOO within the AIV precordial R-wave transition in  $V_3$ , exhibited left bundle branch block QRS morphology. During a follow-up period of 1 to 10 months, 1 PVCs originating from GCV recurred.

**Conclusion** The presence of a q wave in lead I and  $MDI \geq 0.6$  maybe an important morphology criteria for ventricular arrhythmias originating from the GCV.

### Comparison of the SinoSCORE and the EuroSCORE for predicting in-hospital mortality in patients undergoing coronary artery bypass grafting

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**Objective** The European System for Cardiac Operative Risk Evaluation (EuroSCORE) is a commonly used risk model worldwide for the predicting mortality after cardiac surgery and the Sino System for Coronary Operative Risk Evaluation (SinoSCORE) is a new risk stratification model developed using Chinese multicenter database. We compared the Sinoscore and the Euroscore with regard to their validity to predict in-hospital mortality after coronary bypass grafting (CABG) in a single-centre patient population of China.

**Methods** Detailed data for the EuroSCORE and the SinoSCORE risk factors were collected for 386 patients undergoing CABG or CABG combined other cardiac surgery at this institution between Jan. 2006 and Dec. 2012. All patients were scored according to the additive EuroSCORE and the SinoSCORE model respectively, and the mortality

probability for individual patient was derived using these two models. The patients were divided into low-, intermediate-, and high-risk group according to the risk score Result. Predicted mortality was compared to observed mortality for each risk category. Model discrimination was obtained using the area under the receiver operating characteristics (ROC) curve and calibration of the two risk models was assessed by the Hosmer-Lemeshow goodness-of-fit test.

**Result** According to EuroSCORE, 51.3% (198/386), 30.1% (116/386), and 18.7% (72/386) patients were in the low-risk, intermediate-risk and high-risk group respectively; predicted mortality was 1.2% for the low-risk, 3.6% for the intermediate-risk, 6.7% for high-risk group. Actual mortality was 2.8%, 7.9% and 20.2% among the three groups respectively. Area under the ROC curve was 0.755. Hosmer-Lemeshow of fit test showed  $P = 0.037$ . According to SinoSCORE, 28.7% (111/386), 30.6% (118/386), and 40.7% (157/386) patients were in the low-risk, intermediate-risk, and high-risk group respectively; predicted mortality was 0.9% for low-risk, 2.4% for intermediate-risk, and 16.6% for high-risk group. Actual mortality was 3.3%, 4.7% and 16.5% among the three groups respectively. Area under the ROC curve of SinoSCORE was 0.783. Hosmer-Lemeshow of fit test showed  $P = 0.614$ .

**Conclusion** Both the Euroscore and the Sinoscore have acceptable discriminatory ability in predicting in-hospital mortality in patients undergoing CABG; whereas, the SinoSCORE gives a more accurate prediction for the high-risk patients.

### Radiofrequency catheter ablation of purkinje system involved ventricular tachycardia after myocardial infarction

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**Background** There are rare reports about the mechanism and radiofrequency catheter ablation of ventricular tachycardia (VT) arising from the left posterior Purkinje fibers in patients with a prior myocardial infarction (MI) recently.

**Methods** Three patients were all males, and aged from 55 to 75 years old, with recurrent episodes of VT after anterior MI (LVEF 0.44 – 0.61) despite antiarrhythmic drugs and/or revascularization were studied. The VT or premature ventricular contractions (PVC) presented right bundle branch block with left axis in 3 patients or right axis in 1 patient. CARTO electroanatomic mapping system and saline irrigated radiofrequency catheter were used for mapping and ablating VT/PVC.

**Result** Clinical sustained VT was reproducibly induced by programmed stimulation in 2 patients, and spontaneous clinical non-sustained VT/PVC were observed in 1 patient. Purkinje potentials (PP) or diastolic potentials (DP) were sequentially observed along the left ventricular posterior septum adjacent to the low voltage area during the VT/PVC in all the 3 patients. The typical macro-reentrant VT around the MI scar could not be mapped in anyone of the 3 patients. Radiofrequency energy delivered at the site exhibiting a PP/DP – QRS interval of -20 to -70 ms successfully eliminated the VT/PVC.

**Conclusion** Purkinje system involved monomorphic VT after MI, which is analogous to idiopathic left VT, can develop in the acute or chronic phase of MI. Radiofrequency catheter ablation can effectively eliminate this VT without affecting left ventricular conduction.

### The electrophysiologic characteristics and radiofrequency catheter ablation of ventricular arrhythmias in patients with cardiomyopathy

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**Background** Recently most studies about the electrocardiographic and electrophysiological characteristics of ARVC, but rare big sample of case report about electrocardiographic and electrophysiological characteristics and the Result of radiofrequency catheter ablation of Ventricular Arrhythmias (VA) in patients with cardiomyopathy.

**Methods** 35 patients with cardiomyopathy and Ventricular Arrhythmias underwent cardiac electrophysiological examination and radiofrequency catheter ablation, among whom, 2 patients with hypertrophic cardiomyopathy (HCM) (both male), 6 patients with dilated cardiomyopathy (DCM) (3 male), 24 patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) (17 male and 7 female), 3 patients with left ventricular cardiomyopathy (2 female). Following up the symptom, surface electrocardiogram and/or 24 h Holter electrocardiogram and cardiac ultrasound after ablation.

**Result** 31 patients received radiofrequency catheter ablation of VA. The acute success rate was 68.3%, the effective rate was 22.0% and the unsuccessful rate was 9.7%. There were no serious complications in perioperative periods. During a period of 5 – 114 months of follow-up: (1) both two HCM cases had no recurrence; (2) In 4 of the 6 patients with DCM underwent radiofrequency catheter ablation, 2 patients had no VA recurrence; (3) among the 24 ARVC cases, 12 patients had no VT recurrence after the last catheter ablation procedures, 9 patients had VT recurrence, 1 patient died of cardiac sudden death, and 2 patients lost follow-up; (4) among the 3 left ventricular cardiomyopathy patients, one had no VT recurrence but with few premature ventricular contractions. The other two patients had VT recurrence but felt much improving under anti-arrhythmic drugs.

**Conclusion** Ventricular arrhythmias (VA) in patients with cardiomyopathy are not uncommon. ICD implantation is the preferred treatment in these patients, especially in patients with hemodynamic unstable ventricular tachycardia (VT). Radiofrequency catheter ablation of these VA is more difficult, usually with lower success and higher recurrence. To use the cardiac three dimensional mapping systems, saline irrigated ablation catheter, and to combine the endocardial approach and the epicardial approaches for mapping and ablating VA might improve the successful rate and decrease the recurrence.

### Localization of the origin site of outflow tract ventricular arrhythmias by surface electrocardiogram

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**Background** It has been reported that the origin site of idiopathic ventricular arrhythmias from left or right outflow tract (L/RVOT) can be



judged from the transition of R/S on precordial lead of surface ECG, but its value still need to be confirmed in more studies. This study reports the relationship between surface ECG and the origin of the premature ventricular contractions (PVCs) or ventricular tachycardia (VT) in a large series.

**Methods** The ECG characteristics in 207 consecutive patients who underwent radiofrequency catheter ablation of LVOT or RVOT origin of VT/PVCs were analysis respectively. All the patients had no significant structural heart diseases.

**Result** The number of patients whose transition of R/S on precordial leads was before lead  $V_2$ , in lead  $V_3$  and after lead  $V_4$  were 18 ( $47.6 \pm 8.8$  years old on the average), 75 ( $45.5 \pm 13.1$  years), and 114 ( $42.25 \pm 13.69$ ), respectively. In the 18 cases of R/S wave transition before lead  $V_2$ , LVOT origin was defined in all the patients, with the specificity of 100% and sensitivity of 72.00%. In the 75 cases of R/S wave transition in lead  $V_3$ , the lead  $V_2$  R/S transition during sinus rhythm was earlier than that during PVCs or VT in 66 patients, and RVOT origin was determined in all of them. In the other 9 patients with lead  $V_3$  R/S transition, 7 of them had a LVOT origin with a later R/S transition in lead  $V_2$  during sinus rhythm other than during PVCs or VT. Therefore, in patients with lead  $V_3$  R/S transition, if lead  $V_2$  R/S transition during sinus rhythm was later than that during PVCs or VT, the specificity and the sensitivity of LVOT origin were 97.06% and 100% separately. In the 114 cases of R/S transition after ( $\leq$ ) lead  $V_4$ , RVOT origin was defined in all the patients, with the specificity of 100% and sensitivity of 62.63%.

**Conclusion** There is a high specificity of identifying the origin of ventricular arrhythmias from LVOT by R/S transition before lead  $V_2$ , a high specificity and sensitivity of identifying origin from RVOT by R/S transition after lead  $V_4$ . The specificity and sensitivity are high to define the PVCs or VT origin from LVOT or RVOT by measuring the R/S ratio on lead  $V_2$  between sinus rhythm and PVCs.

### The feasibility and curative effect of cardiac resynchronization therapy by targeted left ventricular lead placement to the latest ventricular electrical activating site mapped in the coronary sinus branches

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**Background** A nonoptimal left ventricular (LV) pacing lead position may be a potential cause for nonresponse to cardiac resynchronization therapy (CRT). The aim of the current study was to investigate the feasibility and curative effect of CRT by targeted LV lead placement to the latest ventricular electrical activating site mapped in the coronary sinus (CS) branches.

**Methods** Ten patients with moderate to severe congestive heart failure, depressed left ventricular ejection fraction (LVEF)  $< 35\%$ , and wide QRS complex  $\geq 120$  ms were included for implantation of a CRT device. Left ventricular (LV) activating sequence was mapped in the CS branches, and the latest ventricular electrical activating site was considered as the target site for LV lead placement. The feasibility and curative effect of this kind of CRT were observed. The clinical variables assessed in this study included QRS duration, NYHA class, 6-min walk test and echocardiography index.

**Result** Seven patients were diagnosed as dilated cardiomyopathy and 3 patients as ischemic cardiomyopathy. Electrophysiological mapping were performed in 28 CS branches which were considered as a possible site for

LV lead placement and LV lead was successfully placed at the latest LV electrical activating site in all 10 patients. There was  $116 \pm 28$  ms activating time delay at the latest LV electrical activating site than the QRS onset of ECG. QRS complex were significantly narrowed immediately after CRT than before CRT ( $121 \pm 17$  ms vs  $153 \pm 30$  ms,  $P < 0.01$ ). The period after CRT procedure exceeded 3 months in 9 of 10 patients. Eight of these 9 patients were classified as responders to CRT (8/9, 89%) and 3 patients as super responders (3/9, 33%), the other 1 ischemic cardiomyopathy patient who died of acute myocardial infarction 2 months after CRT procedure was classified as non-responder to CRT (1/9, 11%). The following clinical variables 3 months after CRT procedure were markedly improved than variables before CRT in these 8 responders (all  $P < 0.01$ ). NYHA class was improved ( $1.6 \pm 0.5$  vs  $3.3 \pm 0.5$ ) and the 6-min walk test was increased ( $405 \pm 92$  m vs  $307 \pm 82$  m). Echocardiography demonstrated LVEF was improved ( $0.42 \pm 0.06$  vs  $0.30 \pm 0.04$ ), left ventricular end-systolic volume (LVESV) was reduced ( $121 \pm 38$  ml vs  $153 \pm 44$  ml) and mitral regurgitation velocity (MRV) was decreased ( $3.9 \pm 1.2$  m/s vs  $4.5 \pm 1.5$  m/s).

**Conclusion** Targeted left ventricular lead placement to the latest ventricular electrical activating site guided by electrophysiological mapping in the CS branches was feasible. This CRT method was effective for improving heart function of heart failure patients during short-term follow-up.

### Clinical characteristics of 4 cases of polymorphic ventricular tachycardia / ventricular fibrillation initiated by idiopathic premature ventricular contraction originating from right ventricular outflow tract

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**Background** Ventricular fibrillation and/or polymorphic ventricular tachycardia are occasionally initiated by ventricular extrasystoles originating from the right ventricular outflow tract (RVOT) in patients without structural heart disease. The aim of this study was to report clinical characteristics of 4 cases of polymorphic ventricular tachycardia / ventricular fibrillation (PVT/VF) initiated by idiopathic premature ventricular contraction (PVC) originating from RVOT.

**Methods** Among 76 patients with ventricular tachycardia (VT) arising from RVOT, the clinical characteristics of 4 patients with PVT/VF triggered by PVC originating from RVOT were investigated and compared with the clinical characteristics of the other 72 patients.

**Result** The same PVC morphology was shown in triggering PVCs which initiated PVT/VF and in isolated PVCs. The coupling intervals of the above two kinds of PVCs were markedly different. The coupling intervals of triggering PVCs were shortened in 2 cases and prolonged in the remain 2 cases compared with those of isolated PVCs, and the variation magnitude of the coupling interval in every case was more than 70 ms. The coupling intervals of isolated PVCs were not fixed in 1 case. The number of PVCs per day, the coupling interval of isolated PVC and the baseline QT interval were  $15427 \pm 1109$ ,  $419 \pm 22$  ms and  $404 \pm 15$  ms respectively in 72 monomorphic VT patients. The numbers of PVCs per day of 3 of the 4 PVT/VF patients were equivalent to those of 72 VT patients, and the same equivalence was found in the coupling intervals of isolated PVC and the baseline QT intervals of the 4 patients. The cycle lengths of PVT/VF were all less than 280 ms which was shorter than

that of monomorphic VT ( $324 \pm 59$  ms) obviously. Among 4 patients, episodes of syncope were documented in 2 patients, and the syncope rate of 72 VT patients was 4.1%. Activating mapping and pacing mapping confirmed that the PVCs of all these 4 patients originated from septal of RVOT, and PVCs were successfully eliminated by radiofrequency catheter ablation.

**Conclusion** PVCs which triggered PVT/VF and originated from tract RVOT had the characteristics of unstable coupling intervals and short circle length of PVT/VF. Radiofrequency catheter ablation was effective as a treatment option for these patients.

### Effect of radiofrequency catheter ablation of left bundle potential on cardiac electrical and mechanical functions in canines

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**Background** Animal model of left bundle branch block (LBBB) is very important for basic study about cardiac resynchronization therapy (CRT). But the preparation of LBBB model was difficult. This study was to explore the effect of radiofrequency catheter ablation of left bundle potential (LBP) on cardiac conduction and mechanical function in canines and evaluate the preparation method of LBBB model by RF catheter ablation.

**Methods** LBP was mapped and ablated by radiofrequency catheter in the left ventricular endocardium in 10 canines. The influence of LBP ablation on cardiac conduction and whether canine LBBB model was successfully created or not were observed. To assess the systolic and diastolic function of left ventricle, echocardiography was performed before and after LBBB model was successfully created.

**Result** After LBP ablation, LBBB was successfully created in 8 (80%) canines. Atrial and ventricular amplitude ratio (A/V) was less than 1: 10 at successful ablation site and the interval of LBP to local ventricular potential (LBP-V) was  $17.1 \pm 3.2$  msec, range from 12 to 22 msec. The QRS duration increased from  $52.8 \pm 4.8$  ms to  $100.5 \pm 11.1$  ms ( $P < 0.001$ ) after LBBB created in these 8 canines, but there were no significant changes in PR intervals, AH and HV intervals after LBP ablation. In the remain 2 canines, a similar LBP potential was identified with LBP-V 30 and 32 msec, but complete AV block was produced during or after RF energy application. In 8 LBBB canines, echocardiography showed that systolic and diastolic functions were all decreased, including left ventricular ejection fraction and aortic blood flow velocity time integral reducing ( $P < 0.05$ ), E/A lowering to  $< 1$ , E wave deceleration time and isovolumetric relaxation time prolonging ( $P < 0.05$ ). Significant prolongation of septal-to-posterior wall motion delay and the increased difference of pre-ejection time ( $P < 0.001$ ) implied intraventricular and interventricular desynchronization after LBBB.

**Conclusion** Radiofrequency catheter ablation of LBP can make a high success rate of LBBB model in canine, but the risk of complete AV block exists. Immediately after isolated LBBB model was created, intraventricular and interventricular desynchronization and left ventricular electrical activation delay occurred, which resulted in decreased cardiac systolic and diastolic functions.

### Safety, efficacy and learning curve of catheter ablation of paroxysmal atrial fibrillation using circumferential pulmonary vein isolation technique in the single center and in a single operator

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**Background** CARTO anatomical mapping system and circumferential pulmonary vein isolation (CPVI) technique has been used to cure paroxysmal atrial fibrillation (PAF) in most hospitals in China, and have achieved a high success rate. But whether the successful rate, the recurrence rate and the safety are related to learning curve is still unclear.

**Methods** From Dec. 2004 to Dec. 2010, 258 consecutive patients who underwent CPVI for PAF in our hospital were collected. The patients were divided into three groups with equal patient numbers according to the time sequences. Group I consisted of the first 86 cases, Group II consisted of the second 86 patients, and Group III consisted of the last 86 cases. Age, gender, course of disease, echocardiography, other atrial arrhythmias, and basic diseases were analyzed statistically. The operation X-ray exposure time, recent recurrence, late recurrence and re-ablation procedures were also analyzed. In addition, the learning curve of CPVI for PAF and its relationship with peri-operative period complications, and the risk factors to predict the recurrence of atrial arrhythmias were analyzed, too.

**Result** There were no significant differences in patients' age, gender, basic diseases and LAD among three groups. The rates of early recurrence in Group I, Group II and Group III were 38/86 (44.2%), 26/86 (30.2%) and 21/86 (24.4%) respectively ( $P < 0.05$ ). The successful rates at 1 year were 44.2%, 51.2%, 64.0% respectively ( $P < 0.05$ ) in three groups. The incidence of general complications was 12.8% in Group I, 4.7% in Group II, and 2.3% in group III. There were statistically significant differences between the total complication rates among the three groups. In many variables, left atrium dimension (LAD) enlargement and early recurrence were the risk factors of recurrent AF ( $P < 0.01$  and  $P < 0.05$ , respectively).

**Conclusion** For an experienced operator, CPVI has a higher success rate, a lower recurrence and a lower complication rate for radiofrequency catheter ablation of PAF. However, for a beginning operator, the success rate was relatively lower, both the recurrence and the complication rate were higher, and the X-ray exposure time was longer. The strengthened training of CPVI technique for PAF may be very important for the new operator to increase the success and to avoid or decrease the incidence of complications.

### CARTO three-dimensional mapping system guided catheter ablation of macro-reentrant atrial tachycardia following cardiac surgery in patients with structural heart disease

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**Background** Because radiofrequency catheter ablation of macro-reentrant atrial tachycardia (AT) following cardiac surgery of structural

heart disease had a low successful rate and a high recurrence, we aimed to explore a successful method to solve this problem. This study was to investigate the electrophysiological mechanisms and radiofrequency catheter ablation of macro-reentrant atrial tachycardia (AT) following cardiac surgery of structural heart disease, and to test the success rate by using CARTO electroanatomic mapping.

**Methods** A total of 20 patients (16 men, aged  $35 \pm 13.5$  years) in Shenyang Northern Hospital were studied. After determining the mechanism of macro-reentrant AT, the electroanatomic structures of the right or/and left atria during AT were constructed by using CARTO electroanatomic mapping system. To combine the Result of entrainment mapping, the possible reentrant circuits of AT were analyzed and the ablation lines were defined. The saline irrigated radiofrequency ablation catheter was used for ablation in all the 20 patients.

**Result** In the 20 patients, 16 patients had 1 form of AT and 4 patients had 2 forms. Twenty-four forms were all macro-reentrant AT confirmed by CARTO system electroanatomic mapping and entrainment. Among the 24 forms of AT, 18 forms were typical atrial flutter of the right atrium, 5 forms were incisional reentrant AT of the right atrium, and 1 form was macro-reentrant AT around the mitral annulus. Eighteen of the 20 patients had a successful ablation, including 17 of 18 forms of typical atrial flutter of the right atrium and 4 of 5 forms of incisional reentrant AT of the right atrium. During the follow-up of 12 months on the average, 17 patients with a successful ablation had no recurrence, and only 1 patient recurred as atrial fibrillation.

**Conclusion** CARTO three-dimensional mapping system guided catheter ablation of macro-reentrant atrial tachycardia following cardiac surgery in patients with structural heart disease had a high success rate and a low recurrence rate.

### Electrophysiological characteristic and ablation of epicardial idiopathic ventricular arrhythmias arising around left fibrous triangle

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**Background** The success rate of radiofrequency catheter ablation of ventricular arrhythmias originating from left fibrous triangle (LFT) is not high. This article was to discuss the characteristics of surface electrocardiogram and the strategy of ablation of ventricular arrhythmias originating from LFT.

**Methods** From Feb. 2002 to Mar. 2012, total 323 patients with outflow ventricular arrhythmias were ablated in our hospital, including 46 patients whose ventricular arrhythmias originated from the LFT. The mean age of the 46 patients was  $44 \pm 13$  years (16 – 87 years), and 24 of them (52.2%) were male. Thirty patients had frequent premature ventricular contractions (PVCs) and 16 patients had both PVCs and nonsustained or sustained ventricular tachycardia (VT). All the patients were examined with ECG, electrophysiology, active mapping and pace mapping. The computer tomography angiogram (CTA) 3D reconstruction of coronary artery, venous was completed in 20 patients.

**Result** Successful ablation was achieved in 41 of the 46 patients (89.1%, 41/46) targeting left coronary cusp (LCC, 30 patients), infra aortic valve (infra AV, 6 patients) and great cardiac vein (GCV, 5 patients). The surface ECG in all the three groups presented with inferior axis and R/S-transition in lead  $V_1$  and  $V_2$ . There were no differences in the total QRS duration in the three

groups. Most of the patients presented with right bundle branch block (RBBB) morphology in infra AV group and GCV group compared with LCC group (67%, 80% vs 15%,  $P = 0.002$ ). Regarding to the classification of the LFT according to CTA, the patterns of distribution were as follows: "closed" in 10 (50%, 10/20) hearts; "completely opened" in 2 (10%, 2/20); "inferiorly opened" in 5 (25%, 5/20) hearts and "superiorly opened" in 1 (5%, 1/20) hearts. In the remaining 2 (10%, 2/20), there were not any distances between cardiac vein and artery. The closest distance between the corner of the GCV and LCC is  $17.6 \pm 4.2$  mm (9.1 – 26.3 mm).

**Conclusion** Ventricular arrhythmias originating from the LFT can be ablated in the nadir of the LCC, infra AV and the GCV. The success rate may be impacted by the distance from the GCV and the LCC.

### Radiofrequency catheter ablation of superior ventricular tachycardia in patients with persistent left superior vena cava

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**Background** Radiofrequency catheter ablation of superior ventricular tachycardia (SVT) is unusual because of the anatomy. The aim of this study is to discuss the strategy of radiofrequency catheter ablation of SVT in patients with persistent left superior vena cava (PLSVC).

**Methods** From Jun. 2008 to Jun. 2011, 17 patients with PLSVC and SVT underwent one of the following RFCA: AV node modification (8 patients), left accessory pathway (6 patients), paroxysmal atrial fibrillation (3 patients).

**Result** Coronary sinus access through left subclavian vein in each patient. AV node modification was carried out in 8 patients. Four patients with left accessory pathway were ablated through aortic retrograde approach, and the other two patients with left side accessory pathway were accomplished through transseptal approach. Three patients with PAF were cured through circumferential pulmonary vein isolation after atrium septum puncture. The success rate was 100%, and complication was not occurred.

**Conclusion** Even though the success rate of RFCA with PLSVC and SVT was high and the complication rate was low, the recognition of PLSVA, the skills of ablation and the precaution of complications should be paid attention.

### Application of a novel pacing guide wire in cardiac resynchronization therapy

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**Background** The implantation of left ventricular (LV) lead was the most complicated process in the cardiac resynchronization therapy (CRT), the aim of this study was to investigate the availability of a novel Vision wire guide wire in the implantation of LV lead in CRT.

**Methods** Five heart failure patients selected for CRT were involved



in the study. The pacing threshold, R-wave sensing, phrenic nerve stimulation at local coronary sinus (CS) branch were measured by the Vision wire guide wire and LV lead separately.

**Result** The pacing parameters were analyzed through the Vision wire guide wire and LV lead separately at the 16 CS branches in 5 patients. There was no significant difference between the pacing parameters measured by the two Methods. Significant correlation was found between LV pacing threshold assessed by the Vision wire guide wire and LV lead ( $r = 0.90$ ,  $P < 0.01$ ). Correlation for R wave sensing was also significant ( $r = 0.67$ ,  $P < 0.01$ ). The pacing sites accompanied with phrenic nerve stimulation while pacing at 10 V/0.42 ms were similar by the two Methods. Vision wire guide wire could be used for local potential electrical mapping. The procedure time for pacing test in a single coronary sinus branch by Vision wire guide wire was much less than that by LV lead. ( $12.4 \pm 7.5$  min vs  $18.3 \pm 12.2$  min,  $P < 0.01$ ).

**Conclusion** Visionwire guide wire facilitated transvenous LV lead implantation by prediction of pacing parameter and locates the target CS branch quickly. The electrophysiological mapping function of Visionwire guide wire as a unipolar lead might have further potential usefulness.

### Long-term performance of active fixation pacing leads in right atrium

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**Background** More and more active-fixation leads were used in the right atrium during the implantation of pacemaker, the aim of this study was to explore the feasibility of active-fixation right atrial leads in the application of pacemaker and observe the changes of long-term pacing parameters.

**Methods** Sixty patients (32 males and 28 females, mean aged  $65.25 \pm 13.95$  years) were involved in this study, 4 cases implanted with single-chamber pacemaker (AAIR) and 56 cases implanted with dual-chamber pacemaker (DDDR), who underwent the active-fixation leads implantation in the right atrium for permanent pacing. The follow-up period was 12 months after implantation.

**Result** The active-fixation atrial leads were successfully implanted in all patients and there were no complication during the operation, 52 leads implanted in the right atrial appendage, 3 in the right atrial septum and 5 in the right atrial lateral wall. The pacing thresholds at the implanted moment were obviously higher and declined rapidly. No thresholds change occurred at the end of the operation, in 48 hours, 3 months, 6 months, 12 months after operation. The impedances were quickly decreased at the end of the operation and 48 hours after the operation, no obvious sense parameters changed. 1 patient (1.7%) with acute atrial electrode dislodgment at 2 hours after operation, we resettled the active-fixation lead successfully. No complications such as lead perforation and cardiac tamponade occurred.

**Conclusion** It was safe and feasible in the implantation of active-fixation leads in right atrium. The pacing parameters of active-fixation leads in right atrium were stable during the periods of 12 months after operation.

### The comparison between the active-fixation leads and passive-fixation leads in right ventricular apical pacing

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**Background** More and more active-fixation leads were used in the implantation of pacemaker, but compared with the traditional passive-fixation leads, the differences of the pacing parameter were not clearly known. The aim of this study was to compare the pacing parameters of active-fixation leads and passive-fixation leads in right ventricular apical pacing.

**Methods** There were 54 patients implanted with single or dual chamber pacemaker involved in this study from Jan. 2010 to May 2010 followed up for 3 months after operation. In these patients 21 with passive-fixation lead (Group I) and 33 with active-fixation lead (Group II). All the leads were implanted in right ventricle apex, the average age was  $66.23 \pm 13.90$  years old, 21 patients with single chamber pacemaker and 33 with dual chamber pacemaker.

**Result** There were no obvious changes in the pacing parameters between the two groups not only during the operation (thresholds:  $0.56 \pm 0.20$  vs  $0.57 \pm 0.21$ ; pacing impedances:  $818.25 \pm 267.71$  vs  $823.59 \pm 284.46$ ; R Wave:  $10.64 \pm 3.08$  vs  $10.47 \pm 3.10$ ) but also at 1 month (thresholds:  $0.55 \pm 0.18$  vs  $0.55 \pm 0.18$ ; pacing impedances:  $542.72 \pm 190.30$  vs  $531.91 \pm 189.48$ ; R Wave:  $10.53 \pm 3.60$  vs  $10.22 \pm 3.63$ ) and 3 months after the operation (thresholds:  $0.57 \pm 0.17$  vs  $0.56 \pm 0.17$ ; pacing impedances:  $499.80 \pm 135.37$  vs  $494.29 \pm 135.74$ ; R Wave:  $10.72 \pm 3.48$  vs  $10.47 \pm 3.53$ ) ( $P > 0.05$ ). But there were 1 of 33 patients in Group II (1/33, 3%) with higher pacing threshold after operation. The threshold reached to 6.0 V at the second day after operation and the patient was dealt with dexamethasone for 1 week, and there was no change of the higher pacing threshold, so we had to implant the new passive-fixation lead in the right ventricular apex and extract the old active-fixation lead simultaneously. The pacing thresholds were stable followed for 3 months. No patients with severely higher pacing thresholds in Group I.

**Conclusion** There were no obvious differences in the pacing parameters between the passive-fixation leads and active-fixation leads in right ventricular apical pacing. But it was possible that the stimulation thresholds were individually higher in patients with active-fixation leads than those with passive-fixation leads (3.3% vs 0). The long-term parameter changes still were observed.

### Initial experience of valve repair for rheumatic mitral valve diseases

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**Background** To investigate the feasibility of valve repair for rheumatic mitral valve disease.

**Methods** From Aug. 2011 to Jan. 2013, fifteen patients (thirteen females and two males), with average age of 42 years, underwent mitral valve repair with clinical diagnosis of rheumatic mitral valve

abnormality. Among them, eight were stenotic predominated cases, six were regurgitated predominated, the remaining one was mixed stenosis and regurgitation. Comorbidities included aortic regurgitation in four cases (three were minimal), tricuspid regurgitation in seven (two minimal, five moderate), cerebral infarction in two, and pulmonary arteriovenous fistula in one. Valvuloplasty was carried out according to Carpentier's classification of mitral valve disease with manipulations for the mitral commissures, leaflets, subvalvular apparatus and mitral annulus. The Result were analyzed by using SPSS13.0. Significance was set at a P value less than 0.05.

**Result** Various repair techniques had been used for different pathological lesions, including commissurotomy in 12 cases, commissurotomy in 2, leaflet thinning in 10, papillotomy in 7, chordal shortening in 1. One patient had his posterior leaflet enlarged with autologous pericardium. Two patients had leaflet deficit at anterior-lateral commissure after radical decalcification, one repaired with autologous posterior tricuspid leaflet, another with glutaraldehyde-tanned autologous pericardium. All patients except one early case received annuloplasty, of them, 13 with Carpentier – Edwards Physio 4450, two with posterior annuloplasty of Paneth type. Concomitant procedures included tricuspid valvuloplasty in 5 cases (Kay's method in two cases, De Vega's in one, bicuspidization in one, and commissurotomy with concomitant anterior leaflet enlargement and MC3 annuloplasty in one), isolation of left atrial appendage from left atrium in 5 cases (four with suture technique, one with ligature method), occlusion of pulmonary arteriovenous fistula in one, radiofrequency atrial fibrillation ablation in four cases, aortic valve replacement in one case. All patients survived the operations with average cardiopulmonary bypass time of 149 minutes and aortic cross clamp time of 108 minutes. The average hospital stay time is 8.8 days and all patients recovered uneventfully. The mitral valve area increased significantly from  $1.07 \pm 0.41$  to  $2.04 \pm 0.29$  cm<sup>2</sup> ( $P < 0.01$ ) in stenotic predominated cases. Five patients had minimal regurgitation and ten with no regurgitation echocardiographically before discharge. The blood flow velocity of the mitral valve orifice decreased significantly from  $1.77 \pm 0.50$  m/s to  $1.48 \pm 0.24$  m/s ( $P < 0.05$ ) with decreases of left ventricular end diastolic and systolic dimension from  $51.53 \pm 10.89$  and  $32.67 \pm 8.78$  cm to  $43.68 \pm 6.38$  cm ( $P < 0.01$ ) and  $27.80 \pm 7.18$  cm ( $P < 0.01$ ) respectively. All patients show an improvement in the grade of NYHA classification with postoperative value of  $1.07 \pm 0.26$  from preoperative value of  $2.33 \pm 0.72$  ( $P < 0.01$ ). Although the left ventricular ejection fraction did not demonstrate an obvious increase ( $63.73 \pm 6.02$  preoperative and  $61.60 \pm 5.78$  postoperative,  $P > 0.05$ ), the postoperative value had revealed a preserved left ventricular function after the rheumatic valve repair.

**Conclusion** Although the repair for rheumatic mitral valve disease is technically demanding, advantage of preservation of ventricular function and avoidance of complications of artificial valves mandate any attempts to restore the normal valve function, whenever repair is technically and anatomically feasible.

### Oral sildenafil therapy for Eisenmenger syndrome: A prospective, open-label, multicentre study

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**Objective** Sildenafil is a phosphodiesterase-5 inhibitor and

pulmonary vasodilator effective for oral therapy of idiopathic pulmonary arterial hypertension (PAH). Eisenmenger syndrome has similar pathology to idiopathic PAH but has less defined treatment evidence. We investigated whether twelve months of sildenafil therapy improves clinical and hemodynamic parameters in patients with Eisenmenger physiology.

**Methods** The effect of long time treatment with sildenafil (20 mg tid) on 6-minutes walking distance (6MWD) and systemic arterial blood oxygen saturation (SaO<sub>2</sub>) was evaluated in a prospective, open-label, multicentre study in 84 patients with Eisenmenger syndrome who were in WHO functional classes II-IV. Other endpoints included hemodynamic parameters assessed by right-heart catheterization, serum biochemical markers, and safety/tolerability.

**Result** The overall treatment effects (expressed as mean and 95% confidence intervals) were 56 m (42 to 69,  $P < 0.0001$ ) in 6MWD and 2.4% (1.8 to 2.9,  $P < 0.0001$ ) in SaO<sub>2</sub>. Statistically significant improvements were also noted in mean pulmonary arterial pressure and pulmonary vascular resistance index [ $-4.7$  mm Hg ( $-7.5$  to  $-1.9$ )],  $P = 0.001$  and  $-474$  dyne·s·cm<sup>-5</sup> [ $-634$  to  $-314$ ],  $P < 0.0001$ , respectively). Sildenafil was well tolerated. Most adverse events were mild and transient and occurred in the first two weeks of treatment.

**Conclusion** Twelve month therapy of sildenafil improved exercise capacity, arterial oxygen saturation and hemodynamics in patients with Eisenmenger syndrome.

### Usefulness of intravenous adenosine in idiopathic pulmonary arterial hypertension as a screening agent for identifying long-term responders to calcium channel blockers

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**Objective** Although intravenous adenosine is recommended for acute vasodilator testing in patients with pulmonary hypertension, the long-term outcomes in acute responders treated with calcium channel blockers (CCBs) who are identified by adenosine remain unknown. In this study, the value of adenosine for identifying long-term responders to CCBs was investigated in patients with idiopathic pulmonary arterial hypertension (IPAH).

**Methods** All acute responders were subsequently treated with high-dose CCB monotherapy, and 6-minute walk distances, hemodynamic data, and WHO functional classifications were followed. Nine of 104 patients presented an acute response with intravenous adenosine (8.7%; 95% CI 3.2% – 14.2%).

**Result** After 12 months of follow-up, all acute responders were still alive; however, only 6 patients showed sustained hemodynamic improvement (5.8%; 95% CI 2% – 13%). Three patients failed on CCB monotherapy and bosentan was added to their treatment. The mean tolerated dose of intravenous adenosine was  $142 \pm 49$  mg/kg/min. No life-threatening adverse events were observed and only 2 patients among the non-responders exhibited a 20% reduction in mean systemic arterial pressure. In non-responders, the 1- and 3-year survival rates were 89% and 75%, respectively.

**Conclusion** Acute vasodilator testing with intravenous adenosine was safe and was able to screen responders to CCB therapy in patients with IPAH, and long-term CCB responders account for about 5.8%.

## A 6-year, single-institution analysis of intra-aortic balloon pump use in cardiac surgery

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**Objective** Intra-aortic balloon pump (IABP) is the most usable tool of temporary mechanical circulatory support for cardiac surgical patients. Its beneficial action is attributed to a concomitant reduction in after load of left ventricle with a substantial increase on coronary perfusion pressure due to an increase of aortic diastolic pressure. The objective of this study was to analyze patient characteristics and the early outcome associated with IABP use.

**Methods** This is a retrospective study including patients who underwent cardiac surgery between January 2006 and December 2012. Within a 6 year period 557 adult cardiac surgical patients required support with an IABP. Based on the cardiac surgery types, patients were divided into 4 groups: CABG, Valve, CABG and Valve, CABG and Other group which included CABG & ischemic Ventricular Septal Defect repair, CABG & left ventricular aneurysectomy or both.

**Result** The mean age was  $61.2 \pm 9.8$  years (range from 25 to 84 years). There were 420 (75.4%) males and 137 (24.6%) female patients. 122 (21.9%) of the patients were diabetics, 305 (54.6%) were hypertensions, 208 (37.3%) have prior myocardial infarction. The CABG, Valve, CABG and Valve population requiring IABP consist of 368 (66.1%), 33 (5.9%) and 63 (11.3%) of the total number of patients treated with an IABP. The CABG and Other group consists of a high risk population, has 67 (12.0%) patients. The overall in hospital mortality was 10.2% (57 patients). The mortality of the CABG group requiring IABP was 8.97% (33 patients). In Valve group, the mortality was 16.7% (6 patients). The mortality of CABG and Valve group was 11.1% (7 patients), 11.9% (8 patients) in CABG and other group. The mortality of Valve group was much higher compared to other groups ( $P < 0.05$ ). There was higher survival on the CABG population. A regression analysis taking into consideration all the variables reveals that advanced age, long cardiopulmonary bypass time and female identified as prognostic risk factors for early mortality.

**Conclusion** The application of IABP especially in Valve population is associated with unfavourable early outcome, CABG patients has a good early prognosis in contrast to other cardiac surgery patients, which possibly due to a better improved of oxygen supply and demand balance in coronary artery disease.

## Clinical study of the left ventricular function for atrial septal defect in adult with pulmonary arterial hypertension

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**Background** To assess the left ventricular function of ASD with PAH patients and to determine whether the left ventricular function and pulmonary pressure could run better after transcatheter closure by

echocardiography.

**Method** There were 75 patients with ASD aged  $\geq 40$  years, 15 males and 60 females, divided them two groups. (1) PAH group: 36 patients with ASD associated with PAH, 6 males and 30 females, aged from 41 to 74 (mean age  $51.7 \pm 9.3$ ) years, ASD diameter aged from 15 to 37 (mean  $22.9 \pm 8.1$ ) mm by using transthoracic echocardiogram (TTE). Systolic pulmonary artery pressure (sPAP)  $40 - 107$  ( $57.8 \pm 16.0$ ) mm Hg, diastolic pulmonary artery pressure (dPAP)  $10 - 40$  ( $22.0 \pm 5.8$ ) mm Hg, mean pulmonary artery pressure (mPAP)  $31 - 62$  ( $37.1 \pm 7.7$ ) mm Hg were measured by using cardiac catheterization. (2) No PAH group (control group): there were 39 patients, 9 males and 30 females, aged from 40 to 63 (mean age  $49.3 \pm 6.0$ ) years, ASD diameter aged from 8 to 33 (mean  $20.6 \pm 6.8$ ) mm by using TTE. The sPAP  $22 - 38$  ( $28.9 \pm 3.9$ ) mm Hg, dPAP  $3 - 20$  ( $10 \pm 3.8$ ) mm Hg, mPAP  $10 - 19$  ( $15.9 \pm 2.8$ ) mm Hg were measured by using cardiac catheterization. Before operation, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), left ventricular stroke volume (LVs V) and left ventricular ejection fraction (LVEF) were measured by using TTE. The sPAP obtained by echocardiography Doppler according to the tricuspid regurgitation gradient pressure of the ASD with PAH patients. Cardiac catheterization was performed before interventional therapy, sPAP, dPAP, mPAP, Qp/Qs were measured. ASD with a diameter ranging from 18 to 42 ( $30.8 \pm 9.1$ ) mm were placed in PAH group, 3 patients of them with severe PAH required a fenestrated device. The immediate sPAP were measured  $28 - 95$  ( $42.7 \pm 15.4$ ) mm Hg after transcatheter closure, mPAP were  $24 - 58$  ( $30.1 \pm 6.7$ ) mm Hg. ASD with a diameter ranging from 9 to 40 ( $27.5 \pm 7.4$ ) mm were placed in control group. Echocardiography were made at 1 day, 1, 3 months after the procedure.

**Result** The LVEDD, LVEDV, LVs V and LVEF of PAH group were all smaller than those of no PAH group. The immediate sPAP, mPAP decreased significant after transcatheter closure. The LVEDD, LVEDV, LVs V and LVEF increased significantly after operation 1 day, whereas LVESD, LVESV were unchanged. The LVEDD, LVEDV, LVs V and LVEF improved 1 - 3 months follow-up. The sPAP decreased significant of the patients with severe PAH, who had the indication could implant a fenestrated ASD, and left ventricular function improved at 1 day, 1 - 3 months after the procedure.

**Conclusion** The left ventricular function lesion of the ASD patients with PAH were more severe than the ASD patients, the left ventricular function improved after transcatheter closure, so interventional therapy could prevent the left ventricular function from deterioration.

## Transcatheter Closure of Patent Ducts arteriosus with severe pulmonary-hypertension using domestic occlude in adults

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**Background** To evaluate the clinical efficacy of transcatheter closure of patent ductus arteriosus (PDA) with severe pulmonary hypertension using domestic occluder in adults.

**Method** From July 2000 to July 2011, 82 adult patients (13 male, 69 females) were treated by transcatheter closure with domestic occluder. Patients mean age was 36.6 years (ranging 18 to 60 years) and the mean PDA diameter at its narrowest segment was ( $9.6 \pm 2.6$ ) (ranging 6.0 to 16.0) mm. 6 patients of them were treated with sildenafil and/or



bosentan before PDA closure. All patients accepted contrast examination of aorta arch-descendens before transcatheter treatment. Patients were classified according to Krichenko grouping method, type A consisted of 35 patients, type B consisted of 4, type C 40 cases, and type E 3 cases. Duct occluder was used in 58, atrial septal defect closure device in 3 and muscular ventricular septal defect closure device in 5. The achievement of permanent transcatheter closure was decided according to the change of the pulmonary arterial pressure, aortic pressure and oxygen saturation

**Result** The devices were successfully placed in all patients except three patients owing to the resistance of pulmonary hypertension. The systolic pulmonary pressure decreased from  $(97.3 \pm 20.4)$  (range 70 to 140) mm Hg to  $(51.2 \pm 19.4)$  (33 to 109) mm Hg, and the mean pulmonary pressure decreased from  $(71.2 \pm 13.5)$  (51 to 105) mm Hg to  $(36.4 \pm 15.1)$  (22 to 71) mm Hg. Complete angiographic closure was seen 10 minutes after the device deployment in 52 out of 82 patients (63.4%), while trivial to small leak was present in 30 (36.6%). During the occlusion, the average X-ray exposure duration was  $16.9 \pm 10.3$  minutes, occlusion time was  $83.5 \pm 39.2$  minutes. 15 of them with systolic pulmonary artery pressure  $> 70$  mm Hg after PDA closure were treated with sildenafil or/and bosentan. Complete echocardiographic closure was demonstrated in 77 out of 79 patients (97.5%) at 1 month, and 100% at 6 month follow-up in all patients. Among successful patients, the dimensions of the left atrium, left ventricle and pulmonary artery attenuated considerably in follow-up except two patients. There were no PDA recanalization and migration of devices after the complete occlusion during following up.

**Conclusion** Transcatheter closure of patent ductus arteriosus with severe pulmonary hypertension using domestic occluder is a safe and effective interventional method in adults.

### The acute hemodynamic responses of pulmonary arterial hypertension associated with congenital heart disease to iloprost

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**Background** Pulmonary arterial hypertension (PAH) is the commonest complication of left-to-right shunt congenital heart disease (CHD). Detection of pulmonary vascular reactivity is important for the evaluation of patient with PAH. This study aimed to investigate the acute hemodynamic responses to iloprost in patients with idiopathic PAH (IPAH) and PAH associated with systemic-to-pulmonary shunt CHD (PAH-CHD).

**Method** This study included a cohort of patients with IPAH and PAH-CHD. The inclusion criteria were: (1) IPAH with pulmonary artery systolic pressure  $> 70$  mm Hg measured by catheter and (2) PAH-CHD with pulmonary artery systolic pressure  $> 70$  mm Hg and pulmonary-to-systemic flow ratio (Qp/Qs)  $< 1.5$ . After determination of baseline haemodynamic parameters by cardiac catheterization,  $10 \mu\text{g}$  of aerosol iloprost was inhaled and right heart catheterization was repeated.

**Result** A total of 165 patients (118 females) aged  $29 \pm 13$  years were recruited, including 24 with IPAH and 141 with PAH-CHD. There were 2 acute positive responders (8.3%) in patients with IPAH who benefited from the treatment of calcium antagonist thereafter. No positive responder was found in patients with PAH-CHD. Inhalation of aerosol iloprost induced significant decrease in pulmonary artery pressure ( $P > 0.01$ ), pulmonary vascular resistance ( $P < 0.01$ ) and pulmonary-to-systemic vascular resistance ratio ( $P < 0.05$ ) in patients with both IPAH

and PAH-CHD. However, significant increase in oxygen saturation of femoral blood was only observed in patient with PAH-CHD. A  $\geq 10\%$  decrease in both pulmonary vascular resistance and pulmonary-to-systemic vascular resistance ratio at the end of drug exposure was observed in 58.9% of patients with PAH-CHD but only in 45.8% of patients with IPAH.

**Conclusion** There are 8.3% of acute positive responders in patients with IPAH but no positive response in patients with PAH-CHD. Although iloprost induces decrease in pulmonary artery pressure and pulmonary vascular resistance in patients with IPAH and PAH-CHD, the acute hemodynamic changes were different.

### Long-term effects of stepwise linear ablation approach in persistent atrial fibrillation

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**Objective** The long-term effects of catheter ablation in patients with persistent atrial fibrillation were controversial. The purpose of this study was to observe the long-term effects of persistent atrial fibrillation ablation using a stepwise linear ablation approach.

**Methods** Eighty-seven patients with drug-refractory persistent atrial fibrillation underwent radiofrequency catheter linear ablation between Jan. 2005 and Dec. 2007 were enrolled. Patients were divided into two groups as Ablation Conversion Group and Ablation plus Cardioversion Group according to the sinus restoration.

**Result** Sinus rhythm was restored directly by linear ablation in 50 patients (57.5%), the others were converted by cardioversion post intensive linear ablation except 1 patient (failed). There was a higher success in Ablation Conversion Group compared with Ablation plus Cardioversion Group (48% vs 27%,  $P = 0.047$ , mean follow-up  $5.3 \pm 1.0$  years). There were no significant difference between the persistent atrial fibrillation subgroup and long-standing atrial fibrillation subgroup (37.9% vs 39.7%,  $P = 0.877$ ). A second procedure was performed in 10 patients. After a median of 1 (1 to 2) procedure, stable sinus rhythm was achieved in 37 (42.5%) patients.

**Conclusion** Linear ablation strategy which aimed at atrial substrate modification, may improve the long-term efficacy of catheter ablation for persistent atrial fibrillation. Sinus rhythm restoration by ablation was a predictive factor for long-term outcome.

### Circulating microRNAs as new biomarkers of perioperative myocardial injury after coronary artery bypass graft surgery

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**Objective** MicroRNAs (miRNAs) are endogenous small RNAs of 21–25 nucleotides that can pair with sites in 3' untranslated regions in mRNAs of protein-coding genes to down regulate their expression, and

play key roles in diverse biological and pathological processes. Recently, miRNAs have been reported to be present in the blood of humans and suggested as promising biomarkers for various pathologic conditions. However, its value in the evaluation of perioperative myocardial injury has not yet been assessed. In the present study, we aim to determine the potential of cardiac-specific miRNAs in circulation to serve as biomarkers for identifying perioperative myocardial injury in cardiac surgery.

**Methods** Thirty two consecutive patients undergoing on pump coronary artery bypass grafting (CABG) were included in a prospective, randomized study using standardized operative procedures and myocardial protection. Serial plasma samples from patients were collected at 7 perioperative time points (Preoperatively, 1, 3, 6, 12, 24, 48 h after declamping), and were tested for miRNAs and cardiac troponin I (cTnI). Total RNA were extracted from plasma with mirVana PARIS Kit. Muscle-enriched miR-499 and cardiac-specific miR-208a were selected as candidates for this study. The levels of circulating miRNAs were measured by TaqMan quantitative reverse transcription-PCR (qRT-PCR), Plasma cardiac troponin I (cTnI) concentrations were measured by electrochemiluminescence based Methods on the Beckman ACCESS2 Analyzer.

**Result** Our study revealed the peak levels of the muscle-enriched miR-499 (150-fold; PP Importantly, miR-499 levels peaked 3 h after declamping, whereas TnI peaked 6 h after declamping

**Conclusion** In this study, we reported the expression of circulating miRs in CABG patients. In comparison to the preoperative, interestingly, plasma levels of miR-499 and miR-208a up-regulated after the declamping. Importantly, an outstanding finding in this study is that both miRNAs and cTnI exhibited the same trend. Thus, our Result clearly hold out that miR-499 and miR-208a can be new biomarkers for identifying perioperative myocardial injury in CABG patients.

### Permanent pacemakers implantation and follow-up in 23 infants and children with perioperative complete atrioventricular block

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**Objective** We analyzed the Result of 23 children with congenital heart diseases (CHD) who underwent pacemaker (PM) implantation at our center with a retrospective analysis and tried to evaluate the clinical outcome of PM implantation for CHD associated complete atrioventricular block (AVB).

**Methods** Between Jan. 2007 and Jul. 2012, 23 children with CHD (13 males, 10 females, aged from 4 months to 8 yrs, average  $2.8 \pm 2.5$  yrs. Weight from 5 to 27 kg, average  $10.7 \pm 6.8$  kg) underwent PM implantation for high degree or complete AVB at our center. Endocardial (ENDO) or epicardial (EPI) pacing systems are implanted in 7 and 16 respectively. Three patients [1 atrial septal defect (ASD)/pulmonary stenosis (PS), 1 partial complete endocardial cushion defect (PECD) and 1 corrected transposition of the great arteries (CTGA)] had complete AVB preoperatively and underwent PM implanted during the surgical operation. Twenty patients (3 PECD and total endocardial cushion defect

(TECD), 3 ventricular septal defect (Vs D), 1 Tetralogy of Fallot (TOF), 6 double outlet right ventricle (DORV), 2 transposition of the great arteries (TGA), 5 CTGA) had complete AVB after CHD repair and underwent ENDO or EPI PM implantation 11 to 48 days later. Follow-up data were obtained on the records made in out-patient (symptoms and signs, ECG, X-ray, echocardiography and the parameters of the permanent cardiac pace makers).

**Result** EPI pacing leads (8 left ventricular leads and 8 right ventricular leads) were implanted via midline thoracotomy and the pulse generator were buried in a subcutaneous pocket on the left abdomen. ENDO pacing systems are implanted via the right (3 cases) or left (4 cases) subclavian vein and the pulse generator were buried in a subcutaneous pocket in the right (3 cases) and left (4 cases) precordial area. No lead fracture and infected wound happened to the patients. Rate-responsive ventricular demand pacing (VVIR) PM were implanted in 1 patient and VVI in 22. All patients with PM implantation had the range of pacing rate 70 – 160 ( $111 \pm 25.5$ ) bpm, pacing threshold 0.5 – 0.75 ( $0.74 \pm 0.30$ ) V, sensitivity threshold 2.5 – 2.8 ( $2.78 \pm 0.11$ ) mV and lead resistance 271 – 726 ( $445.5 \pm 148.9$ )  $\Omega$ . Follow-up from 1 month to 5.5 year was possible in 21 patients (91.3%, 21/23) and the pacing threshold was slightly high early after PM implantation and then maintained steady. One patient with TGA had a sudden death 6 months after switch operation and EPI PM implantation without the known etiology. One patient with TECD had battery changed 4.5 years after EPI PM Implantation. The sinus rhythm recovered in 1 patient with Vs D. Four patients had cardiomegaly and myocardial dysfunction with left ventricular ejection fraction (LVEF)

**Conclusion** The Result of this study show that perioperative permanent pacing therapy for high degree or complete AVB in infants and children with CHD is safe and efficient. ENDO or EPI pacing systems can be implanted according to age and clinical features. Long follow-up will be necessary to determine whether PM implantation may affect the outcome of infants and children with CHD.

### Arterial switch operation in children over 6 months

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**Objective** To investigate effects of arterial switch operation in children.

**Methods** Children scheduled for arterial switch operation (ASO) were grouped as a group (24 cases) and B group (18 cases) by  $\geq 6$  months or not, and arterial switch operation performed. Effects of arterial switch operation and follow up examinations were observed.

**Result** Two infants died in the first day post operation in group A, the others were clinically cured. Sudden death occurred to 1 case in group B in hospital, 7 cases had satisfactory follow-up 3 months later, and 1 case suffered sudden death at home. There was no statistical difference between the two groups as to operating time, cardiopulmonary bypass time. Compared with group A, children in group B had higher PAP, CVP ( $P < 0.05$ ).

**Conclusion** Arterial switch operation in children over 6 months can gain a satisfactory effect, and those children still complicate with pulmonary hypertension, the elder children may be suffered from sudden death.

### Prolonged mechanical ventilation increase long-term cardiac deaths after CABG

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**Objective** To analyze the effects on long-term outcomes of prolonged mechanical ventilation after isolated coronary artery bypass grafting.

**Methods** 4 022 consecutive patients undergoing isolated coronary artery bypass grafting from Jan. 2006 to Dec. 2008 were analyzed retrospectively. The patients were divided into two groups by the time: conventional mechanical ventilation group  $\leq 12$  hours ( $n = 1783$ ) and prolonged mechanical ventilation group  $> 12$  hours ( $n = 2239$ ). All-cause deaths, cardiac deaths, major adverse cardiac and cerebrovascular events (MACCE), angina, rehospitalization for any cardiovascular disease were defined as long-term endpoint events, and multivariate Cox proportional hazard method was used to examine the difference in long-term prognosis.

**Result** The rates of cardiac deaths (HR 2.54, 95% CI, 1.14 – 5.66) and rehospitalization for any cardiovascular disease (HR 1.36, 95% CI, 1.10 – 1.69) were significantly higher in the PMV patients, and there were no significant difference in the rates of all-cause deaths (HR = 1.38, 95% CI, 0.83 – 2.29), MACCE (HR = 1.20, 95% CI, 0.93 – 1.55), angina (HR = 1.29, 95% CI, 0.99 – 1.68).

**Conclusion** PMV increased the events of long-term cardiac deaths and rehospitalization for any cardiovascular disease.

### Effects of B-type natriuretic peptide on plasma NT-proBNP, C - reaction protein in patients with chronic heart failure

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**Objective** To evaluate the efficacy and safety of B-type natriuretic peptide in the treatment of chronic heart failure (CHF) through objective values of NT-proBNP, C - reaction protein on plasma.

**Methods** Randomized, open, control clinical trial was conducted in 61 patients with CHF. Vital signs, dyspnea, ejection fraction (EF), NT-proBNP and C - reaction protein in blood biochemical index before and after drug administration were observed.

**Result** There were significant differences in the increase of the EF, in the decrease of NT-proBNP and C - reaction protein between the trial group and control group.

**Conclusion** Levosimendan is effective in treating CHF and it can relieve dyspnea, improve the general condition, increase EF, decrease NT-proBNP and C - reaction protein.

### Significance of abnormal potentials for guiding successful target of catheter ablation from the aortic sinus cusp ventricular arrhythmia

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**Objective** To investigate the significance of abnormal potentials in predicting target site of ASC-IVAs.

**Methods** Electroanatomical mapping was performed during IVAs/sinus rhythm in 29 patients with ASC-IVAs and 10 control subjects. The characteristics of abnormal potentials were analyzed.

**Result** The incidence and amplitude of pre-potential (PP) and late potential (LP) and QRS-LP interval in IVAs group were greater than those of controls ( $P < 0.05$ ). In IVAs groups, the amplitude of PP at the target site was smaller than that of unsuccessful site ( $P = 0.004$ ). LP was more often recorded than unsuccessful sites before and after RF application ( $P < 0.05$ ). After ablation, the amplitude of LP was decreased ( $P = 0.016$ ) and the QRS-LP interval was longer in 21 patients ( $P = 0.026$ ) at the target site.

**Conclusion** LP has greater significance for guiding ablation in ASC-IVAs, and the increased of QRS-LP interval might be a maker for predicting target site.

### Analysis of short term postoperative prognostic factors in patients with severe pulmonary hypertension related to congenital heart disease

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2. Beijing Anzhen Hospital

**Objective** To analyses the short term postoperative prognostic factors in patients with severe pulmonary hypertension (PAH) related to congenital heart disease (CHD).

**Methods** The clinical data of 34 patients who experienced total repair were retrospectively analyzed. According to their postoperative recovery, patients were separated into two groups. Compared the preoperative clinical data between the two groups and drew the ROC curve to find the data related to the short term postoperative prognostic factors.

**Result** The ROC curve indicated that CTR more than 0.615, BNP more than 391.6 pg/ml and PVRi at vasodilator testing with inhaled iloprost less than 4.915 wood unit·m<sup>2</sup> may predict good short term postoperative prognosis.

**Conclusion** The CTR, BNP and PVRi at acute pulmonary vasodilator testing with inhaled iloprost were competent evaluations to predict the short term postoperative prognosis in patients with severe PAH related to CHD.



### Beneficial effects of catheter ablation on left ventricular function in patients with frequent premature ventricular complexes:

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**Background** Frequent premature ventricular complexes (PVC) are associated with a reversible form of cardiomyopathy.

**Aims** To evaluate the effects of catheter ablation on left ventricular function in patients with frequent PVC.

**Methods** We searched MEDLINE for cohort studies of patients who underwent catheter ablation of PVC. Left ventricular ejection fraction (LVEF) before and post ablation was reported. The primary endpoint was the change in LVEF improvement after ablation. Quantitative analysis of continuous variables was performed according to random-effect Methods by Meta-analyst beta3.13 software. A subgroup analysis of patients with left ventricular dysfunction at baseline was performed.

**Result** 14 studies with 724 patients were ultimately included. The mean burden of PVC before ablation was 24.5% (95% CI: 18.5% – 30.5%). Long-term success rate of PVC ablation was ranged from 81 – 88% among included studies. The mean duration of echocardiogram follow-up was ranged from 4 month to 13 month. The pooled mean change of LVEF improvement was 7.489% (95% CI: 5.777% – 9.201%). Subgroup analysis showed that mean change of LVEF improvement in patients with left ventricular dysfunction at baseline was 10.771% (95% CI: 7.521% – 14.021%).

**Conclusion** Ablation of PVC is associated with an improvement in left ventricular function, especially for patient with left ventricular dysfunction at baseline.

### Effect of right ventricular different pacing site on QRS complex duration

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**Objective** To investigate the effect of right ventricular different pacing site on QRS complex width, and provide a reference for lead location.

**Methods** 216 patients (mean age, 69 ± 13 years) scheduled for a permanent pacemaker, that met the class I or II a pacemaker installed indications, were enrolled for study. Pacing and electrocardiography recording were undergone at right ventricular apex, right ventricular inflow tract (RVIT), mid septum, high septum and right ventricular outflow tract (RVOT), respectively. Then the duration and morphology of QRS complex paced in different right ventricular locations were analysis and compared.

**Result** QRS duration at all different right ventricular pacing sites were significant lengthened compared with baseline electrocardiography ( $P < 0.001$ ). QRS duration with right ventricular apex pacing was most broad (168 ± 16 ms), QRS duration with RVIT pacing was 166 ± 15 ms, and QRS duration with RVOT pacing was 165 ± 15 ms. There were

not significant different in QRS duration with apex, RVIT and RVOT ( $P > 0.05$ ). QRS duration at septum pacing was significant narrower ( $P < 0.001$ ), QRS morphology and electrical axis was normal compared with other right ventricular pacing sites. QRS duration with mid-septum pacing was most narrow (139 ± 19 ms), and shorter than high septum (153 ± 14 ms).

**Conclusion** QRS duration at mid-septum pacing was most narrow, QRS morphology and electrical axis was normal compared with any other right ventricular pacing sites. Mid-septum may be an ideal choice for right ventricular pacing site.

### The efficacy and safety of transradial approach PCI Vs femoral approach PCI for coronary artery disease

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**Objective** To evaluate the efficacy and safety of transradial approach PCI vs femoral approach PCI for coronary artery disease.

**Methods** We searched databases, and include the RCT trials and combine data by Revman software.

**Result** We finally included 27 English RCT. In the index of PCI success rate all-cause mortality, the recurrence of myocardial infarction within one year after PCI, PCI operative time, and stroke, the incidence of thrombosis, the radial PCI group is similar with femoral PCI group. However, the postoperative vascular complications and hospital stay, the radial PCI group is better than the femoral PCI group, with a statistically significant difference

**Conclusion** Radial PCI can be effective and safe method in the treatment of coronary heart disease.

### The training and learning process of transeptal puncture using a modified technique

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**Introduction** As the transeptal (TS) puncture has become an integral part of many types of cardiac interventional procedures, its technique that was initial reported for measurement of left atrial pressure in 1950s, continue to evolve. Our laboratory adopted a modified technique which uses only coronary sinus catheter as the landmark to accomplishing TS punctures under fluoroscopy. The aim of this study is prospectively to evaluate the training and learning process for TS puncture guided by this modified technique.

**Methods** Guided by the training protocol, transeptal puncture was performed in 120 consecutive patients by 3 trainees without previous personal experience in transeptal catheterization and one experienced trainer as a controller. We analyzed the following parameters: one puncture success rate, total procedure time, fluoroscopic time, and radiation dose. The learning curve was analyzed using curve-fitting

methodology.

**Result** The first attempt at transeptal crossing was successful in 74 (82%), a second attempt was successful in 11 (12%), 5 patients failed to puncture the interatrial septal finally. The average starting process time was  $4.1 \pm 0.8$  minutes, and the estimated mean learning plateau was  $1.2 \pm 0.2$  minutes. The estimated mean learning rate for process time was  $25 \pm 3$  cases. Important aspects of learning curve can be estimated by fitting inverse curves for TS puncture.

**Conclusion** The study demonstrated that this technique was a simple, safe, economic and effective approach for learning of transeptal puncture. Base on the statistical analysis, approximately 29 transeptal punctures will be needed for trainee to pass the steepest area of learning curve.

### Ibutilide enhances conversion of permanent atrial fibrillation during valve replacement procedure

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**Background** Patients with rheumatic heart disease scheduled for valve replacement surgery often suffer from permanent atrial fibrillation, which caused hemodynamic deterioration after discontinuation of cardiopulmonary bypass significantly. Ibutilide was used as a first-line agent in chemical cardioversion of recent-onset atrial fibrillation with high success rate. However, the conversion rate of permanent atrial fibrillation was not reported. The aim of this study was to investigate the efficacy and safety of ibutilide for cardioversion of permanent atrial fibrillation during valve replacement procedure.

**Methods** One hundred and twenty patients with permanent atrial fibrillation underwent valve replacement surgery were randomly divided into three groups: controlled group (intravenous infusion of 10 ml 0.9% saline for 10 minutes), ibutilide group (intravenous infusion of 1 mg for 10 minutes), and amiodarone group (intravenous infusion of 150 mg for 10 minutes). There were 40 patients in each group. All preparations were pumped intravenously 10 minutes prior to removing the aortic cross clamping and a second intravenous infusion of 1 mg for another 10 minutes if atrial fibrillation still existed, with a 10-minute interval between the 2 infusions. Termination time of atrial fibrillation was recorded until transferring to ICU. If prior to leaving operating room, sinus rhythm was not achieved, the case was recorded as a failure of ibutilide.

**Result** Of the 40 patients in ibutilide group, 23 cases were converted to sinus rhythm, with a conversion rate of 57.5%. Of the 23 cases, 4 cases received second dose of ibutilide. The average conversion time was ( $14 \pm 3.8$ ) minutes. 15 patients in the amiodarone group were converted to sinus rhythm, with a conversion rate of 37.5%. The average conversion time was ( $13 \pm 3.5$ ) minutes. 9 cases in the controlled group were converted to sinus rhythm, with a conversion rate of 22.5%. The average conversion time was ( $12 \pm 2.7$ ) minutes. Comparing the efficacy of intravenous ibutilide to intravenous amiodarone in the conversion of permanent atrial fibrillation, the conversion rate was significant higher with ibutilide (57.5% vs 37.5%;  $P < 0.05$ ). Ibutilide was well tolerated with no episodes of torsade de pointes.

**Conclusion** Although the use of ibutilide in the conversion of permanent atrial fibrillation is not as effective as the data about use of ibutilide for recent onset fibrillation, administration of ibutilide on patients with permanent atrial fibrillation underwent valve replacement surgery resulted

in greater conversion rate compared to amiodarone or placebo treatment. Ibutilide was more effective than amiodarone in converting permanent atrial fibrillation to sinus rhythm

### Case report: Takotsubo cardiomyopathy

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A 71-year-old woman presented to the emergency department with a 2 day history of chest pain. An electrocardiogram of local hospital showed elevated ST-segment of  $V_2 - V_5$  leads. Cardiac enzymes were negative. She was diagnosed of "acute myocardial infarction of anterior wall" by local hospital and was transferred to ER. The patient had a 20 years history of hypertension and 10 years history of type 2 diabetes mellitus. ECG showed sinus tachycardia with frequent ventricular premature beat and 1 – 3 mm ST elevation in leads  $V_2$  through  $V_5$ . Emergent CAG was normal. Left ventriculography was hypokinesis of apical segments with anterior and inferior wall in a Takotsubo pattern. LVEF was 36.2%. Repeat left ventriculography 4 weeks later showed improvement of previously-noted wall motion abnormalities with a normal ejection fraction of 63.6%. Takotsubo cardiomyopathy, or stress cardiomyopathy, a seemingly rare but in fact underrecognized transient left ventricular dysfunction, is a clinical entity mimicking an acute coronary syndrome. The clinical picture and electrocardiographic findings usually are indistinguishable from those of an acute coronary syndrome. Cardiac imaging studies usually reveal extensive apical and mid-ventricular akinesis or hypokinesis with basal sparing, discordant with minimally increased cardiac enzymes. These wall motion abnormalities typically extend beyond the vascular territory of a single coronary artery. Coronary angiography is necessary to differentiate ACS. The prognosis of TTC is good, with full recovery of cardiac function within 2 – 4 weeks in most of the cases.

### The acute kidney injury in patients undergoing coronary artery bypass graft with cardiopulmonary bypass

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**Objective** To investigate the incidence, implicating factors and outcome of acute kidney injury (AKI) after cardiopulmonary bypass (CPB).

**Methods** We retrospectively reviewed 1 004 patients with no history of chronic kidney disease undergoing CABG with CPB in Fuwai hospital from 2011 – 2012. The patients were assessed and classified according to the definition of acute kidney injury (AKI) by the Acute Kidney Injury Network.

**Result** Among the 1 004 patients, 240 had AKI, with the incidence of 23.9%, with was distributed from stage 1 to 3 at the percentage of 19.9%, 3.78% and 0.2%, respectively. 6 patients required renal replacement therapy. The pump time and ascending aorta blockage time of AKI patients were longer than non-AKI patients. All patients with AKI had a longer stay in ICU and hospital.

**Conclusion** The disadvantages leading to AKI include prolonged duration of CPB and ascending aorta blockage time. AKI is common

and occurred in 23.9% of our patients following CPB.

### Diabetes does not affect acute kidney injury in patients undergoing on-pump coronary artery bypass graft

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**Objective** We investigate the incidence of acute kidney injury (AKI) after cardiopulmonary bypass (CPB) in no-diabetes and diabetes patients undergoing on-pump coronary artery bypass graft (CABG).

**Methods** We retrospectively reviewed patients disease undergoing CABG with CPB in Fuwai hospital from 2011 – 2012. Among 1004 patients, 302 patients had diabetes and 702 was nondiabetic. They were assessed according to the definition of acute kidney injury (AKI) by the Acute Kidney Injury Network.

**Result** Among the 302 diabetes patients 76 had AKI, with the incidence of 26.1%, with was distributed from stage I to III at the percentage of 21.8%, 3.97% and 0.33%, respectively. Among 702 nondiabetic patients, 19.9% developed AKI stage I, 3.7% developed AKI stage II and 0.14% developed AKI stage III. There were no significant difference in diabetes and nondiabetic group.

**Conclusion** Compared with nondiabetic group, diabetes does not affect acute kidney injury in patients undergoing on-pump CABG.

### The effects of sufentanil and fentanyl on blood glucose and lactate in patients undergoing on-pump coronary artery bypass graft

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**Objective** We evaluated effects of sufentanil compared with fentanyl on the blood glucose during CPB in patients undergoing CABG.

**Method** 580 patients were divided into nondiabetic sufentanil (NS) group, nondiabetic fentanyl (NF) group, diabetes sufentanil (DS) group and diabetes fentanyl (DF) group. Data on glucose and lactate were collected at the following points: before CPB (T<sub>1</sub>), 10 min after CPB (T<sub>2</sub>), 10 min after rewarming (T<sub>3</sub>), 10 min after CPB (T<sub>4</sub>), reaching at ICU (T<sub>5</sub>), 6 h after operation (T<sub>6</sub>), 12 h after operation (T<sub>7</sub>), and 24 h after operation (T<sub>8</sub>).

**Result** The blood glucose levels on T<sub>2</sub> – T<sub>8</sub> were significantly increased in each group as compared with T<sub>1</sub>. Blood glucose in NS group were significantly lower than NF group on T<sub>2</sub> – T<sub>5</sub> points. In DS group, blood glucose levels were significantly lower than DF group on T<sub>3</sub> and T<sub>4</sub> points.

**Conclusion** Compared with fentanyl, sufentanil can significantly decreased the level of blood glucose during the CPB for diabetes and nondiabetic patients underwent CABG.

### Diabetes does not affect acute kidney injury in patients undergoing on-pump coronary artery bypass graft

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**Objective** We investigate the incidence of acute kidney injury (AKI) after cardiopulmonary bypass (CPB) in no-diabetes and diabetes patients undergoing on-pump coronary artery bypass graft (CABG).

**Methods** We retrospectively reviewed patients with no history of chronic kidney disease undergoing first-time CABG with CPB in Fuwai hospital from 2010 – 2011. Among 1 004 patients, 302 patients had diabetes and 702 were nondiabetic. They were assessed and classified according to the definition of acute kidney injury (AKI) by the Acute Kidney Injury Network. Changes in serum creatinine levels and urine output were used to define and stage three levels of renal dysfunction.

**Result** The blood glucose levels of diabetes group before surgery and cardiopulmonary bypass were  $7.36 \pm 2.30$  and  $7.04 \pm 1.95$  mmol/L, nondiabetic group were  $5.52 \pm 1.32$  and  $5.17 \pm 1.28$  mmol/L. Among the 302 diabetes patients 76 had AKI, with the incidence of 26.1%, with was distributed from stage I to III at the percentage of 21.8%, 3.97% and 0.33%, respectively. Among 702 nondiabetic patients, 140 (19.9%) developed AKI stage I, 26 (3.7%) developed AKI stage II and 1 developed AKI stage III (0.14%) ( $P < 0.001$ ). There were no significant difference in diabetes and nondiabetic group.

**Conclusion** Compared with nondiabetic group, diabetes group has higher blood glucose levels before surgery and cardiopulmonary bypass and does not affect acute kidney injury in patients undergoing on-pump coronary artery bypass graft.

### The acute kidney injury in patients undergoing coronary artery bypass graft with cardiopulmonary bypass

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**Objective** To investigate the incidence, implicating factors and outcome of acute kidney injury (AKI) after cardiopulmonary bypass (CPB) in patients admitted to intensive care unit (ICU).

**Methods** We retrospectively reviewed 1004 patients with no history of chronic kidney disease undergoing first-time CABG with CPB in Fuwai hospital from Jul. 2010 to Jun. 2011. The patients were assessed and classified according to the definition of acute kidney injury (AKI) by the Acute Kidney Injury Network in Sep. 2005. Changes in serum creatinine levels and urine output were used to define and stage three levels of renal dysfunction.

**Result** Among the 1004 patients, 240 had AKI, with the incidence of 23.9%, with was distributed from stage I to III at the percentage of 19.9% (200), 3.78 (38)% and 0.2 (2)%, respectively. Only 6 patients required renal replacement therapy. Compared with non-AKI patients, there were longer pump time and ascending aorta blockage time in AKI patients. All patients with AKI had a longer stay in ICU and hospital.

**Conclusion** The disadvantages leading to AKI include prolonged duration of CPB and ascending aorta blockage time. AKI is common and occurred in 23.9% of our patients following CPB; however, AKI requiring renal replacement therapy is uncommon. We should evaluate outcome of AKI and development of strategies to improve outcomes.



### Impact of onset and duration of diabetes on short- and long-term outcomes after primary elective percutaneous coronary intervention (PCI): a 5-year follow-up study

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**Objective** To evaluate the impact of diabetes onset and duration on short- (1-year) and long-term (5-year) clinical outcomes after primary elective percutaneous coronary intervention (PCI) in patients with stable coronary artery disease (CAD).

**Methods** A total of 1743 patients undergoing primary elective PCI for stable CAD in Fuwai hospital were consecutively included in this study. They were divided into two groups: 1292 patients (74.13%) with diabetes (DM group) and 451 patients (25.87%) without diabetes (non-DM group). Subsequently the diabetes group was further stratified into two subgroups by duration of diabetes: < 5 years (subgroup A, with 223 patients) and  $\geq 5$  years (subgroup B, with 228 patients). The rates of major adverse cardiovascular events (MACEs), defined as the need for revascularization, non-fatal myocardial infarction, or cardiovascular death, were measured at 1- and 5-year time points, respectively. Multivariate Cox regression analysis was employed to evaluate the independent effect of diabetes onset and duration on MACE rates.

**Result** Baseline analysis showed that patients in DM group were older, more likely to be female, nonsmokers, with higher prevalence of hypertension, hypercholesterolemia, and multivessel disease (all  $P < 0.001$ ), but without any difference in rates of previous chronic heart failure or myocardial infarction. However, the baseline characteristics between the two diabetic subgroups were much similar ( $P > 0.05$ ), except that they were significantly different in hypercholesterolemia, smoking, and gender statuses (all  $P < 0.05$ ). At 1-year follow-up (356  $\pm$  16 days), diabetes was associated with significantly higher rates of MACEs (8.31% vs 4.46%;  $P < 0.001$ ) in comparison to control patients. Similar Result were also observed at 5-year follow-up (2123  $\pm$  93 days). In subgroup analysis, subgroup B had a higher rate of MACEs at 1-year time point, but it did not approach statistical significance (9.61% vs 6.10%;  $P = 0.20$ ). However, at 5-year follow-up, the rate of MACEs in subgroup B became significantly higher than that of subgroup A (29.94% vs 18.24%;  $P = 0.015$ ). Multivariate Cox regression analysis revealed that the onset and duration of diabetes ( $\geq 5$  years) were independent predictors for the incidence of MACEs at 5-year follow-up (HR = 1.61, 95% CI 1.03–2.50,  $P = 0.04$ , and HR = 1.85, 95% CI 1.02–3.34,  $P = 0.04$ , respectively).

**Conclusion** Diabetes is associated with worse clinical outcomes following primary elective PCI. A longer duration of diabetes ( $\geq 5$  years) was associated with higher rates of MACEs during a long-term (5-year) follow-up.

### Surgical treatment of right atrial myxoma and pulmonary embolism

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Myxomas are rare benign tumor, with an estimated incidence of 0.5 per million populations per year. It is most commonly of left atrial origin (75% to 90%), less commonly right atrial (10% to 25%), and rarely ventricular (1%

to 4%). Right atrial myxoma generally present as right sided cardiac failure, with signs of tricuspid valve disease. The association of pulmonary embolism with right atrial myxoma has been recognized at necropsy for many years. Chiari et al. reported the first case in 1931.

We report a case of a 33-year-old man admitted to the hospital with sudden episode of moderate dyspnea and fever 2 days previously. An echocardiogram and pulmonary computed tomography angiography showed right atrial myxoma complicated with bilateral pulmonary embolism. Complete surgical resection of the right atrial myxoma and pulmonary tumor embolism was successfully performed with moderate hypothermia and low circulatory flow. Histologic investigations of the primary tumor as well as the emboli revealed benign myxoma. The patient has had complete recovery with no evidence of recurrence over a 1-year period.

In conclusion, we suggest that right atrial myxoma associated with pulmonary embolism treatment should aim at total removal of masses both from the atrium and pulmonary arteries. Pulmonary embolism should be conducted under moderate or deep hypothermia, low circulatory flow or total circulatory arrest on the basis of the sites and the extent of the thrombi. Postoperative V/Q scan, echocardiogram and computed tomography pulmonary angiography for long-term surveillance should be followed up to detect eventual recurrence of new myxoma and pulmonary embolism.

### Ascending aortic cannulation in acute stanford type a aortic dissection

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**Objective** To summarize the clinical experience of ascending aortic cannulation in acute Stanford type A aortic dissection.

**Methods** 45 patients with acute Stanford type A aortic dissection underwent operation with ascending aortic cannulation. Cardiopulmonary bypass was installed through ascending aortic cannula and the right atrium with a two-stage cannula.

**Result** No malperfusion and aortic rupture occurred. The in-hospital mortality was 6.7% (3/45). The complications included transient neurologic deficit in 6 (13.3%), Cerebrovascular accident in 2 (4.4%), hemorrhage of anastomose which was treated by reoperation in 3, hoarseness in 1, Renal failure in 1. One case died of the cerebral hemorrhage after 4 months due to inappropriate anticoagulation.

**Conclusion** Cardiopulmonary bypass is established quickly via ascending aortic cannulation in acute Stanford type a aortic dissection, which can provide antegrade perfusion and attain satisfactory organism protection.

### Application of central venous oxygen saturation monitoring during off-pump coronary artery bypass graft surgery

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**Objective** To analyze the alterations of ScvO<sub>2</sub> and SvO<sub>2</sub> and the hemodynamic changes during off-pump coronary artery bypass graft (OPCABG) surgery, detect the correlation and consistency between

ScvO<sub>2</sub> and SvO<sub>2</sub>, and the correlation between ScvO<sub>2</sub>/SvO<sub>2</sub> and CI, respectively. To investigate the possibility of replace SvO<sub>2</sub> with ScvO<sub>2</sub>, and to guide the management of the mismatch of oxygen demand and consumption during OPCABG.

**Methods** 37 patients' underling selective OPCABG were included in this study. The central venous catheter and pulmonary artery catheter were inserted into the right internal jugular vein after anesthesia induction. The variables were measured after the anesthesia induction (basic value, T<sub>1</sub>), 5 min after the tissue stabilization was positioned for the LAD, LCX and RCA anastomosis (T<sub>2</sub>, T<sub>3</sub> and T<sub>4</sub>, respectively) and after the sternum was closed (T<sub>5</sub>). Following datas were collected: central venous oxygen saturation (ScvO<sub>2</sub>), mixed venous oxygen saturation (SvO<sub>2</sub>), oxygen delivery (DO<sub>2</sub>), oxygen consumption (VO<sub>2</sub>), oxygen extraction rate (O<sub>2</sub>ER), heart rate (HR), cardiac output (CO), cardiac index (CI), mean arterial pressure (MAP), mean pulmonary arterial pressure (MPAP), central venous pressure (CVP), pulmonary arterial wedge pressure (PAWP). The ECG changes and the using of positive inotropic drug were recorded at each time point.

**Result** The tendencies of ScvO<sub>2</sub> and SvO<sub>2</sub> during OPCABG were same, the values of ScvO<sub>2</sub> were lower than the SvO<sub>2</sub> at each time point. When LAD was anastomosed, oxygen metabolism was changed with significant increase of CI, VO<sub>2</sub>, O<sub>2</sub>ER, significant decrease of ScvO<sub>2</sub> (P < 0.05), DO<sub>2</sub> and SvO<sub>2</sub> changed insignificantly (P > 0.05). When LCX and PDA were anastomosed, oxygen metabolism was changed with significant decrease of ScvO<sub>2</sub>, SvO<sub>2</sub>, DO<sub>2</sub>, PvO<sub>2</sub>, CI, Hb, significant increase of O<sub>2</sub>ER, and significant increase of VO<sub>2</sub> during LCX (P < 0.05). After the sternum was closed, oxygen metabolism was changed significantly: ScvO<sub>2</sub> and Hb were increasing, but still lower than the basic value; SvO<sub>2</sub>, DO<sub>2</sub> and VO<sub>2</sub> were increasing and higher than both basic value and PDA; O<sub>2</sub>ER was decreasing, but still higher than basic value (P < 0.05). Correlation index of ScvO<sub>2</sub> and SvO<sub>2</sub> were 0.35, 0.169, 0.568, 0.311 and 0.446, respectively. The correlation of SvO<sub>2</sub> and CI was better compared to ScvO<sub>2</sub>, the correlation of ScvO<sub>2</sub> and Hb was better compared to SvO<sub>2</sub>. The bias range between ScvO<sub>2</sub> and SvO<sub>2</sub> were (-5.46 ± 4.97)%, (-7.84 ± 6.50)%, (-8.52 ± 5.62)%, (-9.73 ± 7.96)% and (-10.5 ± 5.96)% respectively.

**Conclusion** When LAD, LCX and PDA were anastomosed, DO<sub>2</sub>, ScvO<sub>2</sub> and SvO<sub>2</sub> decreased significantly, and CI and Hb decreased simultaneously, O<sub>2</sub>ER increased significantly, VO<sub>2</sub> was nearly unchangeable. The tendencies of ScvO<sub>2</sub> and SvO<sub>2</sub> during OPCABG were unanimous, their correlation and consistency were moderate. There is some feasibility to replace SvO<sub>2</sub> with ScvO<sub>2</sub> for patients undergoing OPCABG.

### Application of central venous oxygen saturation monitoring during off-pump coronary artery bypass graft surgery

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**Objective** To investigate the possibility of replace SvO<sub>2</sub> with ScvO<sub>2</sub>, and to guide the management of the mismatch of oxygen demand and consumption during OPCABG.

**Methods** 37 patient's underling selective OPCABG were included. The variables (ScvO<sub>2</sub>, SvO<sub>2</sub>, CI, et al) were measured after the anesthesia induction (T<sub>1</sub>), 5 min after LAD, LCX and RCA anastomosis (T<sub>2</sub>, T<sub>3</sub> and T<sub>4</sub>, respectively) and after the sternum was closed (T<sub>5</sub>).

**Result** The tendencies of ScvO<sub>2</sub> and SvO<sub>2</sub> during OPCABG were

same, the values of ScvO<sub>2</sub> were lower than the SvO<sub>2</sub> at each time point. At T<sub>2</sub>, ScvO<sub>2</sub> decreased significantly (P < 0.05). At T<sub>3</sub> and T<sub>4</sub>, ScvO<sub>2</sub>, SvO<sub>2</sub>, DO<sub>2</sub>, CI and Hb decreased, O<sub>2</sub>ER increased (P < 0.05). At T<sub>5</sub>, ScvO<sub>2</sub> and Hb increased; SvO<sub>2</sub>, DO<sub>2</sub> and VO<sub>2</sub> increased (P < 0.05). There were good correlation index between ScvO<sub>2</sub> and SvO<sub>2</sub>.

**Conclusion** The tendencies of ScvO<sub>2</sub> and SvO<sub>2</sub> during OPCABG were unanimous, their correlation and consistency were moderate. There is some feasibility to replace SvO<sub>2</sub> with ScvO<sub>2</sub> for patients undergoing OPCABG.

### Long-term Result of tetralogy of fallot and treatment for the complications

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**Purpose** The long-term postoperative result of treatment for the Tetralogy of Fallot (TOF) are disappointing. Based on the retrospective study of TOF after radical surgery, the long-term Result and complications of the disease are discussed.

**Methods** We have retrieved articles reported within 10 years on long-term Result of TOF. The patients of TOF who have received radical surgery at Fu Wai Hospital over 10 years have been followed up.

**Result** The survival rates of TOF after radical surgery at 10, 20, and 25 years are 94.8%, 92.8% and 92.8%, 5-, 10- and 20-year freedom from reoperation rates are 81.5%, 68.9% and 46.6%. The main issues include: pulmonary valve regurgitation, right ventricular dilatation, tricuspid regurgitation, right ventricular outflow tract/pulmonary residual stenosis, heart failure, decreased activity, arrhythmias and sudden death.

**Conclusion** The long-term Result of TOF are not good. These patients may need lifelong follow-up and repeated therapy intervention.

### The experience of left ventricle retraining for transposition of the great arteries

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**Objective** To explore the clinical Result of left ventricle retraining procedure.

**Methods** From Jan. 2001 to Dec. 2011 atotal of 38 cases of TGA underwent left ventricle retraining procedure, which was composed of aorto-pulmonary shunt and pulmonary artery banding. At the operation, the ratio of systolic pulmonary/systemic pressure increased from 0.34 to 0.76. Contemporary atrial septum excision was performed in 3 cases.

**Result** The oxygen saturation increased from preoperative 72.6% ± 9.1% to 83.9% ± 8.1, left and right ventricular pressure ratio increased from preoperatively to 0.36 ± 0.04 to 0.75 ± 0.09, There was 3 died in the serises. 23 cases underwent second stage arteries switch operation (ASO) successfully after primary retraining procedure.

**Conclusion** Left ventricle retraining is safe and necessary preparation for ASO in case of simple TGA beyond the neonatal period. The surgical Result of rapid two-stage ASO are satisfactory.

## Effects of statins on preventing paroxysmal atrial fibrillation after pacemaker implantation

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**Objective** To observe the effects of statins on preventing paroxysmal atrial fibrillation (PAF) after pacemaker implantation in patients with sick sinus syndrome.

**Material and Method** 68 patients were selected in which the pacemakers had been implanted due to sick sinus syndrome, and were randomly divided into a statins treatment group and a control group. After the pacemaker implantation, only the patients in treatment group were given 20 mg atorvastatin once per night, with other conditions basically similar to those in the control group. At the 3<sup>rd</sup>, 9<sup>th</sup>, 15<sup>th</sup>, and 21<sup>st</sup> months after the implantation, the pacemakers were programmed, and the PAF-related information stored in the pacemaker were recalled and analyzed statistically.

**Result** After administration of statins for 9 months since the implantation, the occurrence rates of PAF in the treatment group were relatively lower than those in the control group; after further administration of statins for 15 months, both the occurrence rate of PAF and the burden of atrial fibrillation in the treatment group had significantly declined; after continuous administration of statins for 21 months, both the occurrence rates of PAF and the burden of atrial fibrillation in the treatment group were significantly lower than those in the control group.

**Conclusion** Long-term administration of statins can reduce the risk of PAF after implantation of a pacemaker in patients with sick sinus syndrome.

## Assessing the rationality of treatment strategy for CAD patients in single center

Chenfei Rao

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**Objective** To assess the rationality of treatment strategy for 3-vessel and/or left main coronary artery disease in single center.

**Method** Consecutively registered patients diagnosed by elective coronary angiography as 3-vessel and/or left main ( $\geq 50\%$  luminal diameter narrowing) CAD from Jul. 2011 to Sep. 2012 in Fuwai hospital. The rationality of treatment strategy was adjudicated using Appropriate Use Criteria 2012 for Coronary Revascularization Focused Update.

**Result** The study registered 2240 3VD/LM CAD patients. According to AUC, 81.0% (n = 1814) were classified as appropriate for revascularization, 426 (19.0%) as uncertain or inappropriate. Among patients appropriate for revascularization, 100% were appropriate for coronary artery bypass graft (CABG); 33.1% were appropriate for percutaneous coronary intervention (PCI), 41.3% were uncertain, 25.6% were inappropriate. For these patients, 61.7% undertook RATIONAL treatment strategy (appropriate for CABG or PCI, actually received revascularization respectively). 14.9% chose IRRATIONAL medical therapy but they were appropriate for revascularization; 23.5% undertook IRRATIONAL PCI but they were only appropriate for CABG. For patients who were uncertain or inappropriate for revascularization (n

= 426), 85.2% (n = 363) actually undertook revascularization strategy, mostly PCI (n = 285).

**Conclusion** For patients with stable 3VD and/or LM CAD and appropriate for revascularization, 61.7% received rational CABG or PCI, 14.9% chose irrational medical therapy, 23.5% undertook irrational PCI treatment. For patients who were uncertain or inappropriate for revascularization, 85.2% undertook revascularization strategy.

## Surgical treatment for aortic dissection manifesting simple aortic insufficiency

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**Objective** To discuss clinical features and treatment of aortic dissection manifesting aortic insufficiency.

**Methods** Retrospectively analyses 5 cases and summarize the clinical manifestation, assistant examination, intro-operative findings, surgical options and follow-up Result.

**Result** All cases were diagnosed as aortic dissection during operation. 1 patient underwent aortic valvuloplasty, 1 underwent Wheat procedure, 3 underwent Bentall procedure. The 5 patients all survive when following up after 2 – 5 years. The echocardiography of the patient undergoing aortic valvuloplasty demonstrating mild aortic regurgitation, and the other 4 patients all have normal function of mechanical prosthesis.

**Conclusion** Aortic dissection manifesting aortic insufficiency is rare and easily misdiagnosed. Analysing history and examination contribute to avoiding misdiagnosis. It is appropriate to choose surgical method according to the degree of intimal tear and damage of aortic sinus.

## Clinical analysis of Ensite–NavX system and conventional mapping of catheter ablation for PSVT

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**Objective** To assess the clinical efficacy and safety of catheter ablation for PSVT guided by Ensite–NavX system.

**Methods** 80 patients with PSVT were enrolled into this study. The procedure time, fluoroscopic time, the number of energy application, the effective rate of energy application, the success rate and 1-year recurred rate were compared between these two groups.

**Result** All cases were ablated successfully, no complication occurred in two groups. There were no significant difference in the success rate and 1-year recurred rate between two groups. The Ensite–NavX system group had shorter mapping fluoroscopic time than the control group.

**Conclusion** Comparing with the control group, the procedure time, the number of energy application, the effective rate of energy application were better in right pathways/AVNRT ablation; while comparing with left pathway ablation, these were better in the control group



### Nonfluoroscopic radiofrequency catheter ablation for paroxymal supraventricular tachycardia guided by tri-dimensional electronic navigation system.

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**Objective** To discuss the feasibility and safety of nonfluoroscopic radiofrequency catheter ablation (RFCA) for paroxymal supraventricular tachycardia (PSVT) by tri-dimensional navigation system (NavX).

**Methods** 78 PSVT patients were enrolled in the research and received RFCA guided by NavX system.

**Result** 45 patients were found atrioventricular node reentrant tachycardia (AVNRT) and 33 were atrioventricle reentrant tachycardia (AVRT) (10 cases of right pathway, 22 cases of left pathway, 1 case of bi-pathways). All procedures were successful without serious complications. 6 cases of left pathway need transient fluoroscopy during the procedure, 2 cases need fluoroscopic guidance for atrial septal puncture. 1 case of left pathway repulsed during 6-month follow-ups.

**Conclusion** Nonfluoroscopic RFCA for PSVT with NavX is feasible and safe.

### The changes of heart function, TIMP-1, ADM, IL-6, hs-CRP and NT-proBNP after advanced echo-guided cardiac resynchronization therapy in patients with heart failure

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**Objective** To observe the improvement degree of cardiac function on advanced echo-guided cardiac resynchronization therapy (CRT) in patients with chronic heart failure (CHF), to measure of concentration of NT-proBNP, TIMP-1, ADM, IL-6, hs-CRP in the serum and try to explore whether we can predict the effect of CRT in patients with CHF and investigated the correlation of left ventricular ejection fraction (LVEF) and the serum level of NT-proBNP and analysis the difference of survival index in patients with a widened QRS complex group or not.

**Methods** ① We evaluated mechanical dyssynchrony with the DTI, the STI and the RT-3DE. The patients chosen by adoption standards are divided into 3 groups: control group (20 cases), chronic heart failure with a widened QRS complex (12 cases) and chronic heart failure with a shortening QRS duration (10 cases). ② The concentration of NT-proBNP, TIMP-1, ADM, IL-6, hs-CRP in serum have been test in Preoperation and postoperative 3 months. ③ To observe the correlation of the improvement degree of cardiac function and NT-proBNP in serum level.

**Result** ① In CHF groups (including narrow QRS group and broad QRS group), the mean levels of serum NT-proBNP, TIMP-1, ADM, IL-6, hs-CRP were higher than control group ( $P < 0.05$ ). ② However, in preoperation the serum concentration of NT-proBNP, TIMP-1, ADM, IL-6, hs-CRP showed no statistically significant difference between the broad QRS group and the narrow QRS group ( $P > 0.05$ ). ③ In CHF groups (including narrow QRS group and broad QRS

group), the serum levels of NT-proBNP, TIMP-1, ADM, IL-6, hs-CRP in Preoperation were greater more than them in postoperation ( $P < 0.05$ ). ④ In postoperation, the concentration of NT-proBNP, TIMP-1, ADM, IL-6, hs-CRP in the serum showed no statistically significant difference between the broad QRS group and the narrow QRS group ( $P > 0.05$ ). ⑤ There are significant negative correlations between the LVEF and the level of Serum NT-proBNP ( $P < 0.001$ ).

**Conclusion** ① Serum NT-proBNP, TIMP-1, ADM, IL-6, hs-CRP related with Left ventricular remodeling and initiation, process and outcome of cardiac dysfunction. ② Echocardiography can be used to screen patients, improve the effect of CRT, and left ventricular synchronous (including narrow QRS) can be also benefited from CRT.

### Efficacy and safety of clopidogrel added proton pump inhibitors vs clopidogrel in the treatment of cardiovascular patients after PCI

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**Objective** To evaluate the efficacy and safety of clopidogrel added proton pump inhibitors vs clopidogrel in the treatment of cardiovascular patients after PCI.

**Methods** We search databanks; the retrieval time is ended until Oct. 2012. We selected the clinical trails, evaluate the quality of clinical trails following the Cochrane Handbook 5.0, And the datas are solved by the RevMan 5.0 software.

**Result** Our review included 13 RCT covering 55 592 patients. Meta-analysis Result show there is no statistical difference among incidence of MACE, the rate of All-cause mortality, and the rate of gastrointestinal bleeding in clopidogrel added Proton Pump Inhibitor (PPI) group or clopidogrel group. While there is low incidence rates of myocardial infarction, stent thrombosis, Target Vessel Revascularization (TVR).

**Conclusion** the incidence rate of MACE, stent thrombosis, and gastrointestinal bleeding is similar in added or not added PPI patients.

### Video-assisted thoracoscopic left atrial segregation for non-valvular atrial fibrillation

Fang Fang, Zhe Zheng, Hansong Sun, Xianqiang Wang, Fujian Duan

Video-assisted thoracoscopic left atrial segregation for non-valvular atrial fibrillation

**Objective** To explore the feasibility and security of video-assisted thoracoscopic left atrial segregation for non-valvular atrial fibrillation.

**Methods** Patients who undergoing video-assisted thoracoscopic left atrial segregation for non-valvular atrial fibrillation in Fuwai Hospital from Sep. 2010 to May 2013 were enrolled in our study. The video-assisted thoracoscopic left atrial segregation is routinely performed under general anesthesia with double lumen endotracheal intubation and 3-port incisions both sides of chest. In the surgery, the epicardial radiofrequency ablation for atrial fibrillation was done under the monitoring of thoracoscope. And bipolar radiofrequency ablation clamps and ablation pen was used to isolate left pulmonary vein openings, right pulmonary vein openings and left room wall. We melted the ceiling and bottom of atrium to form big circle in order to completely isolate the back of the left atrium. The dragon and warfarin were used in these patients until to

3 month after surgery. We follow up these participants for the data of 24 hours dynamic electrocardiogram (DCG) at 1 month, 3 month, 6 month, 12 month and every year after surgery.

**Result** In total 44 participants who undergoing video—assisted thoracoscopic left atrial segregation for non-valvular atrial fibrillation from Sep. 2010 to May 2013 were enrolled in this study, average age  $59.9 \pm 6.0$  years, 28 male patients, 12 patients with hypertension, average fibrillation persistent time is  $6.8 \pm 4.1$  years, All patients no death. These patients included 26 patients with paroxysmal atrial fibrillation, 14 patients with persistent atrial fibrillation. The average left atrial diameter was  $42.1 \pm 5.3$  mm and in all patients 24 had done the intervention radiofrequency catheter ablation before surgery. The average postoperative respiratory machine use time was  $10.5 \pm 2.1$  hours, the average ICU stay time was  $29.4 \pm 21.9$  hours and the average postoperative hospitalization time was  $6.9 \pm 1.5$  days. 40 patients discharged alive from hospital with sinus rhythm and no complications. 44 patients have been followed up ranged from 1 to 24 months. Just 1 patient got stroke, another one got acute pericarditis, 40 patients were sinus rhythm by the examination of 24 hours dynamic electrocardiogram.

**Conclusion** Video-assisted thoracoscopic left atrial segregation is feasible and safe minimally invasive treatment operation method for patients with non-valvular atrial fibrillation.

### Surgical strategies for aortic insufficiency for patients less than 12 years of age

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**Objective** To discuss the surgical strategies of aortic insufficiency (AI) by summarizing the surgical experience of Fuwai hospital for patients with congenital or acquired AI less than 12 years of age.

**Methods** From Jan. 2008 to Dec. 2012, aortic valve surgery were performed in 40 patients of AI. AVR were performed in 11 cases, Ross procedures were performed in 3 cases, and Aortic valve plasty (AVP) were performed in 26 cases.

**Result** There was no operative death. All patients under the age of 3 underwent AVP. For patients of 3 – 6 years, AVP were performed in 18 and AVR were in 4 cases. For the patients of 7 – 12 years, AVR were performed in 7 cases, Ross were adopted in 3 cases and AVP were performed in 4 cases.

**Conclusion** For patients of Vs D + AI less than 6 years, AVP should be the first choice whereas for patients older than 7 years of Vs D + AI, AVR is preferred. For patients of AS + AI, more surgeons tend to adopt AVR. For patients of Iatrogenic AI, AVP is preferred

### The clinical characteristics and treatment for pacemaker devices related infection in 23 patients

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**Objective** Retrospectively analyze the clinical characteristics of cardiac pacemaker devices related infections.

**Methods** 23 patients have cardiac pacemaker devices related

infections were enrollment in this retrospective study.

**Result** Pocket infection in 21 cases, systemic infection in 2 cases. The incidence of pacemaker devices related infection was 0.77%. The incidence of infection was 0.69% for the implant patients vs 1.36% for replacement patients, there were no statistical difference in two groups ( $P = 0.17$ ). For the treatment, 2 patients only intravenous antibiotics and local treatment; 3 patients underwent local debridement; 18 patients remove and reimplanted pacemaker. There are 2 cases of recurrence infection in local debridement group and 1 case of recurrence in device removal group (5.6%).

**Conclusion** Pacemaker related infection is a serious complications after implantation, the best treatment for this situation is remove the pacemaker device.

### Catheter ablation of epicardial accessory pathway associated with coronary sinus musculature: single-center clinical experience

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**Objective** To report the single-center clinical experience of catheter ablation of epicardial accessory pathway (AP) associated with coronary sinus (CS) musculature.

**Methods** The data of 721 cases of left sided AP were analyzed. Ablation in the CS was performed in 17 (2.4%) cases [11 males, mean age ( $37 \pm 11$ ) years].

**Result** Among the 17 cases, the AP was ablated in middle cardiac vein and posterior lateral CS in 11 and 6 cases, respectively. Deventiculum of middle cardiac vein was seen in 2 cases. Mean time required to block the AP was  $4.7 \pm 2.7$  s. An AP potential could be recorded at the target site in 10 (59%). During a mean  $21 \pm 16$  months follow up, only one patient experienced recurrence who was successfully cured by a second ablation session. No procedure related complication was reported.

**Conclusion** About 2.4% of left AP may have epicardial connection locating at CS. The epicardial ablation is safe and effective, warrants an excellent long-term Result.

### Long-term effect of right ventricular outflow tract vs apical pacing on cardiac function and synchrony

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**Background** Right ventricular outflow tract (RVOT) has been encouraged as an alternative pacing site to avoid long-time detrimental effect induced by right ventricular apical (RVA) pacing, but there hasn't been definitely evidence on the benefit of RVOT pacing. This study aimed to evaluate the long-term impact of RVOT vs RVA pacing on cardiac function and synchrony.

**Methods** 42 patients with inclusion criterion were randomly assigned to receive a screw-in lead either in RVA ( $n = 14$ ) or in RVOT ( $n = 28$ ). 3D-Echocardiography, electrocardiogram, and X-ray were used to

determine the pacing sites. Cardiac function, inter- and intra-ventricular dyssynchrony were evaluated. Patients with VP% > 10% were enrolled into the final analysis.

**Result** After mean follow-up of  $7.1 \pm 0.4$  years, paced QRS interval for RVA pacing was longer than RVOT pacing ( $155.8 \pm 7.1$  ms vs  $143.8 \pm 14.4$  ms,  $p < 0.05$ ). LV end-diastolic diameter ( $44.5 \pm 5.5$  mm vs  $47.6 \pm 1.8$  mm,  $p > 0.05$ ), LV ejection fraction ( $66.1 \pm 5.0\%$  vs  $67.0 \pm 4.1\%$ ,  $P > 0.05$ ), and intraventricular dyssynchrony ( $29.9 \pm 15.6$  ms vs  $27.3 \pm 14.1$  ms,  $P > 0.05$ ) showed no significant difference between the two groups. Tei index and interventricular dyssynchrony were worse in RVAP than in RVOT ( $0.7 \pm 0.2$  vs  $0.5 \pm 0.2$ ;  $-15.9 \pm 20.5$  ms vs  $-9.1 \pm 19.0$  ms, respectively). Compared with baseline, Tei index in RVA pacing was impaired significantly ( $0.7 \pm 0.2$  vs  $0.5 \pm 0.08$ ,  $P < 0.01$ ) but not RVOT pacing ( $0.5 \pm 0.2$  vs  $0.4 \pm 0.03$ ,  $P > 0.05$ ); both RVA and RVOT pacing were associated with impaired interventricular ( $-15.9 \pm 20.5$  ms vs  $11.3 \pm 4.9$  ms,  $-9.1 \pm 19.0$  ms vs  $9.3 \pm 6.3$  ms, respectively,  $P < 0.05$ ) and intraventricular synchrony ( $29.9 \pm 15.6$  ms vs  $9.7 \pm 1.1$  ms,  $27.3 \pm 14.1$  ms vs  $8.5 \pm 2.5$  ms, respectively,  $P < 0.05$ ).

**Conclusion** RVOT pacing didn't show much superiority over RVA pacing in cardiac function and synchrony. Both pacing groups showed worse dyssynchrony than baseline.

### The treatment and prognosis of acute pulmonary embolism after off-pump coronary artery bypass graft surgery

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**Objective** To assess the incidence, treatment and prognosis of acute pulmonary embolism (PE) after off-pump coronary artery bypass graft (CABG).

**Methods** From Dec. 2009 to Sep. 2012, 582 consecutive patients underwent off-pump CABG by a same surgeon. The 64-slice coronary MDCT was performed to assess the graft patency on postoperative day 5-7.

**Result** There were no in-hospital death. PE was detected on the CT images of 10 patients (1.7%). All patients received anticoagulation with warfarin for 3 to 6 months except one. Three to six months after discharge, 8 patients received repeated MDCT, which showed diminish of PE.

**Conclusion** Acute PE after off-pump CABG was an uncommon complication. MDCT played an important role in examining the patency of graft vessels and helped detect asymptomatic PE in CABG patients. The prognosis of acute PE after off-pump CABG was acceptable. PE diminished after 3 months of anticoagulation with warfarin.

### Comparison of characteristics and outcome from infective endocarditis in blood-culture endocarditis negative vs blood-culture positive endocarditis

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**Objective** Diagnosis and management of blood culture-negative

endocarditis (BCNE) constitute a formidable clinical challenge.

**Methods** This study was designed to explore the characteristics and outcomes of patients with IE in Fuwai hospital and compare these data between BCNE and BCPE.

**Result** BCNE accounted for 43.3% (220 cases) of all IE cases. Patients with BCNE, compared with BCPE, were more likely to affect mitral valve, more common in moderately severe regurgitation and perivalve complications ( $P < 0.01$ ). Streptococcus viridans remained the predominant causative pathogen (27.6% of all IE). Patients with BCNE, were more likely to have heart failure, severe sepsis, and operation ( $P < 0.05$ ). In-hospital mortality rate was 10.2%, and the 12-month cumulative mortality rate was 27%. Recurrence of IE was more common in BCNE during the 3-month follow-up.

**Conclusion** BCNE is associated with high moderately severe regurgitation, heart failure, peri-valve complications and recurrence rates.

### The application of intra-aortic balloon pump in cardiac surgery: Result of a survey

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**Objective** Intra-aortic balloon pump (IABP) is an established tool in the management of cardiac dysfunction in cardiac surgery. In 2010, the number of cardiac surgery procedures reached 170 000 in China, meanwhile IABP application increased. In order to generate baseline data describing clinical practice of intra-aortic balloon pump (IABP) in cardiac surgery of China, Cardiac Critical-care Medicine of Chinese Medical Doctor Association performed this survey.

**Methods** A questionnaire consisted of IABP indications, anticoagulation therapy, and weaning, was mailed in Nov. 2012 to 60 surgical intensive care units in China.

**Result** The top three indications in these centers for IABP were postoperative low cardiac output syndrome, weaning from cardiopulmonary bypass and cardiogenic shock. As the increasing early use and effectiveness of the IABP in the world, the proportion using IABP of prophylactic preoperatively in high-risk coronary bypass was low (13%) in this survey. In 98% SICU, heparin or low molecular heparin was routinely given as standard anticoagulation therapy during IABP. In 78% centers, IABP was removed on the third to fifth postoperative day. The practice of weaning IABP support was homogeneous: 95% centers weaned by reducing the ratio of beat assistance whereas the other centers weaned by reducing ratio and balloon volume. In 72% centers, it was routinely removed after extubation of the patients whereas in 25% centers it was removed while the patients were mechanically ventilated.

**Conclusion** We conclude that the management of IABP is homogeneous in this survey. The indications of IABP, not only in therapeutic but also prophylactic in high risk coronary bypass need more attention.



## Design and animal experiment for remote-controlled pulmonary artery banding device

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**Purpose** We invented the remote-controlled pulmonary artery banding device, to make the PA banding operation safer and more facile.

**Methods** We designed the device, which had got the national invention patent certificate issued by the national Patent Office. Patent number; ZL 2011 1 0074076.5. Using two experimental beagles, we freed pulmonary artery and placed the device. Then we adjust PA banding bilaterally in vitro.

**Result** Before and after operation, we tested the PA diameter and pressure change around the PA artificial narrow. 10 days after operation, the physiological index levels of right ventricle and pulmonary artery, such as PA diameter, pressure around the PA artificial narrow, RV diameter, right ventricular anterior wall and interventricular septum thickness, all heightened obviously ( $P < 0.01$ ). The RV myocardial thicken could be observed under optical microscope.

**Conclusion** The reasonable design with many advantages is stable and reliable.

## The strategies in the rehabilitation of gastrointestinal motility of the non-postpone extubation patients after cardiac surgery

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**Objective** Due to the latest study on the importance of enteral nutrition in critically ill adult, the early usage and recovery of the gastrointestinal function could result in the decrease of total time of hospitalization, ICU hospitalization, ICU infections, the time of mechanical ventilation, the time of duration of renal replacement therapy, and the cost in the health care. But for the patients after cardiac surgery the situation is completely different. Before surgery, the patient with rheumatic heart disease may have the congestion of the gastrointestinal system, for the patients with coronary heart disease; the usage of the anti-platelet drug could result in the bleeding of the gastrointestinal mucosa. During the surgery, the applications of cardiopulmonary bypass may result in the low perfusion, the embolisms, and a great amount of inflammation mediators of the gastrointestinal organs. And the usage of sedative drugs and muscle relaxants could also lead the paralysis of the gastrointestinal muscles. After the surgery, any mechanical assistant machine could lead to the damage of the gastrointestinal systems. These reasons make the patients special in the gastrointestinal function recovery process and hamper the early enteral nutrition. So we compared 3 different ways of enhancing the motility of the gastrointestinal systems and observe the efficacy.

**Methods** 60 patients' extubated within 1 – 2 days after cardiac surgery from Jan. to May 2013 in our hospital were included. They all got the conventional oral or enteral gastric therapy of enhancing gastrointestinal functions the day after surgery. These patients who didn't have bowel sound, no fart, no defecation on the 3 day post-operative were divided into 3 groups randomly, each group 20 patients. The basic data of the patients, the amount of vasoactive drugs during the operation and post-operative don't have any difference among the 3 groups. We

treated 3 groups of patients in 3 different ways until they defecated: group A, only the conventional gastrointestinal active drug; group B, besides administrating the conventional gastrointestinal active drug, we used anal entry of glycerin enema 110 ml twice a day; group C, the special treatment of this group of patients is muscle injecting 0.5 mg neostigmine in the acupuncture point of zusanli at both sides of the legs besides the conventional drugs, twice a day.

**Result** In the group A patients, the hours till the first appearance of bowel sound, bowel fart and defecation are  $1.47 \pm 0.17$  h,  $2.00 \pm 0.96$  h, and  $30.80 \pm 8.28$  h respectively. B group are  $1.41 \pm 0.16$  h,  $1.57 \pm 0.18$  h, and  $33.9 \pm 7.75$  h respectively. C group are  $0.56 \pm 0.24$  h,  $0.68 \pm 0.27$  h, and  $9.95 \pm 9.74$  h respectively. The recovering time of the bowel sounds and farts in group A is longer than group B, but no significant variation ( $P_1 = 0.216$ ,  $P_2 = 0.057$ ). The recovering time of defecating in group A is shorter than group B, but no significant variation ( $P = 0.229$ ). The recovering time of the bowel sounds, fart and defecating in the group C are shorter than group A and B patients, the variation is significant ( $P < 0.05$ ).

**Conclusion** Among the 3 recipes enhancing the mobility of gastrointestinal systems in non-postpone extubation patients after cardiac surgery, the conventional drug recipes and anal entry of glycerin enema don't have the definite efficacy in enhancing the motility of the gut. Comparing with the other 2 therapy, the injecting of neostigmine in the acupoint of zusanli at both sides of the legs has the definite efficacy in enhancing the recovery of the gastrointestinal functions.

## Modified ultrafiltration combined with conventional ultrafiltration used for the evaluation of the effect of severe valvular heart disease valve replacement surgery

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**Objective** To investigate the effect of modified ultrafiltration combined with conventional ultrafiltration for severe valvular heart disease valve replacement surgery.

**Methods** 100 cases of patients with severe heart valve patients were randomly divided into a control group and the observation group during 2006.07 – 2012.07, the control group using conventional ultrafiltration method, the observation group combined with routine use of modified ultrafiltration ultrafiltration method to compare the early postoperative.

**Result** The two groups of patients in the control group and the observation group, the preoperative and ultrafiltration hematocrit (Hct) difference was not statistically significant ( $P > 0.05$ ), the observation group was significantly higher Hct level after ultrafiltration, and two significant by the difference was significant ( $P < 0.01$ ); postoperative bleeding, and the use of banked blood volume of the observation group than in the control group, and the difference was statistically significant ( $P < 0.05$ ); observation group postoperative blood flow dynamics relatively stable, shorter ventilator support and 24 h after urine output was significantly reduced. The postoperative ICU residence time, patient ambulation time after discharge time was no significant difference ( $P > 0.05$ ), and 3 months after surgery, the patient's overall quality of life score was no significant difference ( $P > 0.05$ ).

**Conclusion** Modified ultrafiltration technology postoperative shorter blood play better concentrate role, Hct levels, improve lung function, and has considerably reduced the amount of bleeding with the use of banked blood, but can not be significantly improved the patient's

long-term prognosis.

### Surgical treatment for ventricular septal defect with pulmonary hypertension

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**Objective** To evaluate the effectiveness of urgent surgical correction for ventricular septal defect with pulmonary hypertension in infants and children.

**Methods** 525 (284 males, 241 females) with Vs D and PH received surgical correction in our department. The age ranged from 1 month To 39 months, the mean body weight was  $6.3 \pm 3.4$  kg (1.2 – 10 kg). 73 patients were associated with ASD, 59 with PFO, 48 with PDA, 34 with PS, the pressure of pulmonary artery was 4.73 – 12.23 kpa. All patients were discharged withcardiopulmonary bypass.

**Result** Urgent operations were performed and 7 early deaths occurred surgery. Complications included low cardiac output syndrome (21 cases), 5 cases was dead. Inhalation of nitric oxide was given to 8 cases for the management of significant Postoperative pulmonary hypertension, 2 cases was dead. Pneumothorax (8 cases), atelectasis (5 cases). RBBB (43 cases), SVT (13 cases), transient AVB of grade 3 occurred in 7.

**Conclusion** Operation for Vs D with PH on urgent basis may provide Favorite outcomes.

### Female and off-pump patients may have better cardiac function preservation effect of Sevoflurane compared with Propofol: the result of a meta-analysis

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**Objective** We sought to perform a systematic review and meta-analysis to compare propofol and sevoflurane on cardioprotective effects and explore potential relevant factors for patients undergoing coronary artery bypass grafting (CABG).

**Methods** The MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched for relevant randomized controlled trials (RCTs) published in English from their inception up to Nov. 1, 2012. Data on cardiac index (CI), mean arterial pressure (MAP), central venous pressure (CVP), pulmonary capillary wedge pressures (PCWP), systemic vascular resistance index (SVRI), troponin I level (cTnI), mechanical ventilation time, postoperative inotropic requirement, length of stay (LOS) in intensive care unit (ICU) and hospital stay, postoperative complications, major adverse cardiovascular and cerebrovascular events (MACCE) were analyzed.

**Result** Seventeen studies of 1253 patients were included out of

1 010 retrieved citations. Sevoflurane group had higher post-bypass CI (WMD, -0.55, 95% CI: -0.63 to -0.47), less postoperative inotropic requirement (RR, 2.08, 95% CI: 1.72 to 2.51), higher CVP (WMD, 0.45; 95% CI, 0.1 to 0.79; P = 0.011) and PCWP (WMD, 0.85; 95% CI, 0.32 to 1.37; P = 0.002). Univariate meta-regression analysis suggested the major sources of significant heterogeneity for CI were male proportion (coefficient = -0.018; P = 0.091; adjusted R<sup>2</sup> = 30.47%) and CPB application (coefficient = -0.413; P = 0.06; adjusted R<sup>2</sup> = 42.51%).

**Conclusion** Sevoflurane was associated with higher post-bypass CI and less postoperative inotropic drug requirement. The cardiac function preservation effects of sevoflurane were more pronounced among female and off-pump patients in CABG.

### Surgical treatment of functional tricuspid valve regurgitation after left ventricular valve replacement

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**Objective** To explore the best operation time and the etiological features of the functional tricuspid regurgitation (FTR) after left ventricular valve replacement.

**Methods** From 2005 to 2013, 73 patients (mean age  $52.1 \pm 8.4$  years) underwent tricuspid valve annuloplasty or tricuspid valve replacement for FTR. There were New York Heart Association (NYHA) functional class II in 15 patients, NYHA III in 50 patients, NYHA IV in 8 patients. And there were 71 cases of rheumatic heart disease, 1 case of congenital heart disease, 1 case of infective endocarditis. Before operation, there 40 cases complicated with atrial fibrillation. Pulmonary hypertension was mild in 4 cases, 9 cases of moderate and severe in 1 case.

**Result** There were re-TVP in 51 cases, and 22 cases with re-TVR. At the same time, 5 patients were done with re-BVR, 16 patients with re-MVR, and 11 patients with re-AVR. 6 patients were dead after operation, including 2 severe TR cases with preoperative BVR and 4 severe TR cases with preoperative MVR. All patients died of right ventricular dysfunction. There were 23 cases with right ventricular dysfunction after operation, and 12 cases combined with acute renal insufficiency. 15 cases need to use venous - venous blood filter.

**Conclusion** Aggressive surgical treatment can reduce the mortality of the patients with functional tricuspid regurgitation after left ventricular valve replacement. Right heart failure is the common complication and the main risk of death after operation. Positive blood filtration treatment after operation can improve clinical outcomes. Rheumatic heart disease, atrial fibrillation and pulmonary hypertension may be the relevant risk factors with the occurrence of functional tricuspid regurgitation.

### Surgical correction of atrioventricular septal defect in the first year of life

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**Objective** We try to analyze surgical result of Atrioventricular septal defect (AVs D) in our institute in young infants, and discuss the

timing of this procedure.

**Methods** From Jun. 2007 to Jan. 2013, 65 consecutive AVs D infants younger than 12 months of age were operated in our institute. Infants were divided into two groups, group A includes patients whose age was no more than 6 months, and group B consists of patients whose age was over 6 months.

**Result** There were 65 cases, 27 boys and 38 girls, aged  $7.5 \pm 1.9$  months, weighted  $6.2 \pm 1.0$  Kg, cross-clamp time was  $89.3 \pm 18.5$  minutes, CPB time was  $126.5 \pm 24.7$  minutes, ventilation time was  $41.8 \pm 38.3$  hours, the in-hospital stay was  $19.9 \pm 7.3$  days, there were 5 in-hospital death, and the mortality was 7.7%. No significance was found in the parameters between the two groups except body weight ( $P < 0.01$ ).

**Conclusion** The early mortality was comparable with other institutions. There was no significant difference between the two age groups.

### Circulating microRNAs associated with perils of QRS duration on the relationship between electrical delay and clinical response after cardiac resynchronization therapy

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**Purpose** The impact of QRS duration on the relationship between left ventricle lead electrical delay (LVLED) and clinical response of cardiac resynchronization therapy (CRT) has not been defined.

**Methods** We studied 81 consecutive patients undergoing CRT implantation according to standard techniques and clinical indications during a  $15 \pm 3$  months follow-up. Patients were separated by the QRS duration  $\geq 150$  ms or  $< 150$  ms, as wide ( $n = 61$ ) or narrow ( $n = 20$ ) QRS groups.

**Result** After adjustment for bundle-branch block, ischemia cardiomyopathy, sex, and age by multivariate logistic regression analysis, wide QRS patients in the highest quartile of LVLED had a 4.12 fold increase (OR: 4.12, 95% CI: 2.17 to 8.68,  $P = 0.012$ ) in odds ratio of clinical response. But LVLED was irrespective to LV ejection fraction in narrow QRS patients.

**Conclusion** LVLED is strongly associated with improvement in LV ejection fraction after CRT only in patients with QRS  $\geq 150$  ms, but not in patients with QRS  $< 150$  ms.

### Administration of fibrinogen on perioperative blood protection and clinical recovery for severe cyanotic patients undergoing complex cardiac surgery

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**Objective** To assess the effects of a new transfusion therapy using fibrinogen administration on blood protection and clinical recovery

during cardiac surgery.

**Methods** Forty severe cyanotic children (hematocrit HCT  $\geq 54\%$ ), undergoing arterial switch operation (ASO) or double roots transplantation (DRT) were divided into two groups: in group I ( $n = 20$ ), after cardiopulmonary bypass (CPB) fibrinogen administration guided by TEG combined with traditional transfusion was performed; in group II ( $n = 20$ ) only traditional transfusion was performed.

**Result** Compared with group II, the patients in the group I had significant reductions in the amount of first 24 hrs FFP usage in the ICU, total perioperative FFP usage and the time of using mechanical ventilator supporting, ICU stay, hospitalization were significantly reduced in the group I ( $P = 0.06$ ,  $P = 0.06$ ,  $P = 0.09$ ,  $P = 0.09$ ,  $P = 0.06$  respectively).

**Conclusion** Fibrinogen could be a useful substitute for FFP to restore perioperative hemostasis and improve the prognosis for the severe cyanotic pediatric patients after complex cardiac surgery.

### Peri-operative monitoring on haemostasis and therapy for cyanotic infants undergoing complex cardiac surgery

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**Objective** This study investigated features and treatments of peri-operative coagulopathies in cyanotic infants with complex congenital heart disease (CCHD).

**Methods** Thirty six infants with cyanotic CCHD were involved and divided into two groups: In group H ( $n = 20$ ), hematocrit (HCT)  $> 54\%$ , and in group L ( $n = 16$ ), HCT  $< 54\%$ . Blood was sampled at anesthesia induction ( $T_1$ ), rewarming to  $36^\circ\text{C}$  ( $T_2$ ), after heparin neutralization ( $T_3$ ), and 4 hours after operation ( $T_4$ ). The haemostatic changes were evaluated by thromboelastograph (TEG). After surgery, the group H was treated with fibrinogen combined platelet (PLT), while group L was only with PLT.

**Result** We observed the effect at  $T_4$ . At  $T_1$ , the haemostatic function in group H, deteriorating with the increase of HCT ( $P < 0.01$ ), was obviously lower than that in group L ( $P < 0.01$ ), but the PLT function was still complete. In group H, the haemostatic function at  $T_2$  decreased with a significant drop of PLT function ( $P < 0.01$ ) and had little change of functional fibrinogen (Ffg) ( $P > 0.05$ ). At  $T_3$ , compared with  $T_2$ , there were improvements in haemostatic function and Ffg ( $P < 0.01$  respectively) without increase of PLT ( $P > 0.05$ ) in group H. After therapy, PLT function in both groups restored to  $T_1$  level ( $P > 0.05$ ), Ffg at  $T_4$  was significantly better than it at  $T_1$  ( $P < 0.01$ ) in group H, but Ffg at  $T_4$  with still normal function was lower than it at  $T_1$  in group L ( $P < 0.01$ ). Whole haemostatic function at  $T_4$  was back to normal and had no differences between two groups.

**Conclusion** So we proposed fibrinogen combined PLT should be better for high HCT CCHD infants, but PLT alone might be enough for low HCT ones.



## Extracorporeal membrane oxygenation for primary graft failure after heart transplantation

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**Objective** To analyze the clinical effectiveness of the application of ECMO to the patients who suffered primary graft failure. To summarize the ECMO administration experience during heart transplantation.

**Methods** From Jan. 2008 to Dec. 2011, 181 heart transplantation cases were studied retrospectively. 16 cases of them had received ECMO treatment after the transplantation. Data of the relevant parameters during ECMO, mechanism assistant duration and complications of the patients were collected. The lactic acid (LA) level at the onset and 24 hours of ECMO were measured. The dosages of dopamine and adrenergic pre and after 24 hours of ECMO were recorded.

**Result** Fourteen patients (87.5%) were successfully weaned from ECMO and 13 (81.3%) survived to hospital discharge. Among the 16 cases of ECMO, 2 cases abandoned therapy for no cardiac function promotion was obtained. 1 of them died of multiple organ failure (MOF) and chronic rejection were the main cause of death. All patients had received artery-vein (A-V) ECMO. The average level of LA at before, 24 hours and the end of ECMO were  $8.36 \pm 3.41$ ,  $2.42 \pm 1.53$ ,  $2.25 \pm 2.17$  mmol/L, respectively. The LA level was significantly decreased at the 24 hours and the end of ECMO, compared with pre ECMO period ( $P < 0.05$ ). The dosage of dopamine pre and after 24 hours of ECMO were  $7.38 \pm 3.42$ ,  $5.29 \pm 1.93$   $\mu\text{g}/\text{min}/\text{kg}$ , no significant differences were observed. However, after 24 hours of ECMO, the dosage of adrenergic significantly decreased  $0.17 \pm 0.11$ ,  $0.02 \pm 0.03$   $\mu\text{g}/\text{min}/\text{kg}$ , ( $P < 0.05$ ).

**Conclusion** ECMO is an effective mechanism support treatment for circulation and respiration failure. It could significantly decrease the early postoperative mortality rate of the patients who were at the terminal stage of cardiac diseases and received heart transplantation.

## The effect of delayed recovery of normal rhythm and hyponatremia induced by HTK solution on short-term outcomes in children undergoing congenital heart surgery

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**Objective** The effect of HTK-induced delayed cardiac rhythm restoration and hyponatremia on postoperative outcome of children undergoing congenital heart surgery remains unclear. This retrospective investigation was designed to determine whether or not delayed rhythm restoration and hyponatremia induced by HTK solution influence the short-term outcome of pediatric patients after cardiac surgery.

**Methods** Group I: From Jun. to Dec. in 2012, there were 169 pediatric patients who underwent selective complex congenital heart surgery with CPB. HTK solution was used as cardioplegia during operations in all children. The cardiac resuscitation after declamping was observed. The correlation between recovery time of normal heart rate/rhythm and perioperative factors were analyzed. The risk factors of using

pacemaker after surgery were also determined by Logistic regression. Group II: From Feb. to Dec. in 2012, HTK solution was applied to 322 children with congenital heart disease during cardiac surgery. Perioperative factors, including age, gender, weight, surgical type, prime volume, HTK volume, ventricular fibrillation after declamping, antegrade cerebral perfusion duration, lowest nasopharynx temperature, ACC and CPB duration, change of blood sodium concentrations above 15 mmol/L, highest sodium concentration, lowest sodium concentration, highest glucose, lowest glucose, using pacemaker after surgery, accumulated thoracic drainage on postoperative 1 day, mechanical ventilation time, intensive care unit lengths of stay, were used to analyze the risk factors of postoperative cerebral morbidity such as dysphoria and seizure.

**Result** Group I: The incidence of ventricular fibrillation after declamping was significantly higher in children above 3-year-old than that in infants. The recovery time of normal rhythm is positively correlated to cardiothoracic ratio, ACC and CPB time, postoperative 24 h milrinone dose, and ICU length of stay in infants undergoing congenital heart surgery, respectively. Moreover, the recovery time is negatively correlated to nasopharynx temperature at aortic declamping. Surgical type (TGA), milrinone dose, and adrenaline dose were independent factors of using pacemaker after surgery in infants. Group II: the incidence of hyponatremia was 71.9% (220/306),  $\leq 125$  mmol/L was 4.2%,  $\leq 130$  mmol/L was 18%,  $\leq 135$  mmol/L was 49.7%. Compared with the baseline levels, sodium concentrations decreased at early after aortic clamping ( $P = 0.000$ ). Sodium concentrations at PICU and postoperative 12 h significantly higher than that before operation ( $P = 0.000$ ). The incidence of postoperative sodium concentrations  $> 146$  mmol/L was 38.9% (119/306),  $\geq 150$  mmol/L was 10.1% (31/306). Change of plasma osmolarity is consistent with the changes in sodium concentrations. However, osmolarity was lower than normal values during and immediately after CPB, and returned to normal levels after entering PICU. The incidence of seizure and dysphoria were 0.9% (3/306) and 18% (55/306), respectively. The highest sodium concentration was the independent factor of postoperative brain morbidity.

**Conclusion** Larger cardiothoracic ratio, longer ACC and CPB duration, and lower nasopharynx temperature make the restoration of normal cardiac rhythm prolonged in infants undergoing congenital heart surgery. There are correlations between the recovery time of normal rhythm and postoperative milrinone dose or ICU length of stay, suggesting that elevated temperature at declamping may be helpful to improve the early outcome of the pediatric patients. Atrioventricular block and delayed rhythm restoration induced by HTK are not the independent factors predicting the use of pacemaker in children after cardiac surgery. However, for some surgical types such as TAPVC and TECD, ICU length of stay in children with atrioventricular block is longer than that in children without cardiac block. Postoperative hypernatremia is associated with the incidence of seizure and dysphoria in pediatric patients. Moreover, plasma sodium concentrations at postoperative 12 h have predictive values in the incidence of brain morbidity.

## Myocardial protection of HTK added by Ebselen on immature heart during cardiopulmonary bypass

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**Objective** Modified HTK solution giving better myocardial protection to mature heart has been documented. However, the role of HTK added by antioxidant Ebselen on immature heart is unknown. The purpose of this study was to compare myocardial protection using Histidine-tryptophan-ketoglutarate (HTK) added by Ebselen and HTK in a neonatal piglet model.

**Materials and Methods** Fifteen piglets were randomized to three groups: the control group (C group,  $n = 5$ ), a single dose of HTK group (HTK group,  $n = 5$ ), a single dose of HTK added by Ebselen (10 nM) group (HTK+E group,  $n = 5$ ). Animals in the two experimental groups were placed on hypothermic cardiopulmonary bypass, after which the ascending aorta was clamped for 2 h. The control animals underwent normothermic CPB without cardiac arrest. Oxidative stress biomarkers, antioxidant activity, and mitochondrial structures were assessed. Myocardial ATP content was measured. TUNEL positive myocytes were also counted. The release of cytochrome c and the expression of Bax, Bcl-2 and HSP72 in myocardium were examined by using western blotting. The expression of HSP72 mRNA was also detected by RT-PCR.

**Result** Transfusion requirement was no significant differences between the HTK group and the HTK + E group ( $P < 0.01$ ). HTK+E group showed increased superoxide dismutase (SOD) content and higher Mn-SOD activity ( $P = 0.021$  and  $P = 0.020$ ) compared with the HTK group. Increased MDA in myocardium in the HTK group was observed compared to the control group ( $P = 0.038$ ). Meanwhile, myocardial TUNEL positive cells and the release of cytochrome c were reduced in the HTK+E group as compared to the HTK group ( $P = 0.045$  and  $P = 0.010$ , respectively). The Bax/Bcl-2 ratio in the HTK group were significant higher than those in the control group ( $P = 0.024$  and  $P = 0.028$ , respectively). The expression of HSP72 protein and mRNA increased in the HTK+E group when compared to the HTK group ( $P = 0.039$  and  $P = 0.035$ , respectively). There was positive correlation between the HSP72 and Mn-SOD content ( $r = 0.581$ ,  $P = 0.023$ ). Mitochondrial score under electronic microscopy in the HTK+E group was lower than that in the HTK group ( $P = 0.047$ ). Myocardial ATP content in the HTK group was lower than that in the control group ( $P = 0.011$ ).

**Conclusion** Reduced myocardial oxidative stress and apoptosis, as well as better preserved myocardial mitochondrial structure were observed in the HTK+E group, and the release of cytochrome c decreased in the HTK+E group compared with the HTK group. Moreover, increased expression of HSP72 in the HTK+E group suggests improved antioxidant defense. HTK solution added by Ebselen provides better myocardial protection to HTK solution for the neonatal heart with equivalent transfusion requirement. Therefore, HTK+E solution would be a better alternative cardioplegia to blood cardioplegic solution for the immature heart.

## Apseudo-decremental accessory pathway: where did it block?

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A 47-year-old woman was admitted for paroxysmal palpitations, with the wide QRS complex tachycardia (WCT) characterized by a cycle length (CL) of 390 ms, RBBB morphology and an RP relationship of 1:1. Atrial pacing could readily entrain and terminate the tachycardia, and a premature ventricular contraction (PVC) with a coupling interval (CI) of 370 ms, which fell into the effective refractory period (ERP) of the His bundle, could reset the tachycardia. Thus, the diagnosis of ventricular tachycardia, atrial tachycardia or atrioventricular node reentrant tachycardia was precluded.

During ventricular programmed stimulation, the VA interval in the coronary sinus (CS) gradually prolonged, which seemingly indicated the diagnosis of the permanent junctional reciprocating tachycardia (PJRT), with the atrioventricular node (AVN) as the anterograde limb of the circuit and the decremental accessory pathway (AP) as the retrograde one. However, the target, which was localized to the 7 o'clock of the tricuspid valve annulus (TVA), showed a VA-fusion pattern, which was paradoxical to the "decremental conduction". A single application of radiofrequency energy interrupted AP conduction permanently.

After ablation, the retrograde ERP of the His-Purkinje system was determined as 600 ms, which meant that the retrograde pathway during previous ventricular pacing did always be the AP sole, without the participation of the AVN. Surprisingly, such phenomenon was found to be no decrement conduction at all, with the critical reason being the delay and block at the region of cavo-tricuspid isthmus (CTI) when the baseline data was reanalyzed. The right atrium was activated along the TVA from both clockwise and counter-clockwise directions simultaneously during a relatively long CI, with the A wave in coronary sinus orifice (CSO) ahead of that in His Bundle electrogram (HBE). During a shorter CI, however, the activation appeared to gradually delay and eventually block at the region of CTI, leading to a significantly delayed A wave in CSO and an unchanged timing of A wave in HBE.

We describe a pseudo-decremental AP due to the delay and block at the region of CTI, which could be misleading only according to the sequence of A wave and VA relationship in the CS. Therefore, to determine where the delay or block appears, a simultaneous redording of HBE is essential in such cases.

## Comparative expression of proteins in serum from patients with sinus rhythm and atrial fibrillation

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**Purpose** Proteomics is an emerging field that has the potential to uncover new therapeutic targets for the treatment and prevention of cardiovascular disease, as well as new diagnostic biomarkers for early disease detection. We believe that the two-dimensional electrophoresis

(2-D) based serum proteome analysis can be useful in discovering new biomarkers that may aid in mechanism research and therapy of atrial fibrillation (AF) patients. The aim of this study was to compare the 2-D profiles of AF patients with the controls with sinus rhythm by serum proteomics technology.

**Materials and Methods** Sera from 5 patients with atrial fibrillation and 5 controls with sinus rhythm was investigated using two-dimensional polyacrylamide gel electrophoresis (2-DE) and nanoliquid chromatography coupled to tandem mass spectrometry (nano LC-MS/MS).

**Result** 13 differentially expressed proteins were successfully identified, of which, transthyretin (TTR) Val30met Variant was expressed significantly and constantly only in atrial fibrillation patients. Haptoglobin Hp2 was down-regulated in atrial fibrillation group compared with the sinus rhythm group, and serum dermcidin preproprotein and transferrin (TRF) were up-regulated in rheumatic heart disease (RHD) patients compared the patients with non-valvular diseases. Furthermore, increased expression levels of glutathione peroxidase 3, plasma glutathione peroxidase, plasma GSHPx, peroxiredoxin-2 isoform a, complement component C4a and complement C4B precursor were observed in RHD patients compared with non-valvular diseases.

**Conclusion** During atrial fibrillation, TTR or TTR variant may be involved in the maintenance of development of atrial fibrillation. The course of rheumatic heart disease is accompanied by the oxidative stress and activation of the complement system.

### The association between atrial amyloidosis and atrial fibrillation

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**Background** Structural changes, like atrial fibrosis, may increase the likelihood of atrial fibrillation (AF) occur in response to triggering events. The influence of atrial amyloidosis is largely unknown.

**Methods and Result** Right atrial appendages (1 or 2 entire cross sections) were obtained from 27 patients undergoing open-heart surgery. Atrial amyloid was identified by Congo red staining and classified by immunohistochemistry. Amyloid was found every patient, significant amyloidosis (the Amyloidosis area accounted for more than 50% of the total area) was found in 20 (74.1%) of 27 patients, and all deposits were immunoreactive for transthyretin (TTR) and atrial natriuretic peptide (ANP), of which TTR is more significant. Fourteen (51.9%) patients suffered from persistent AF. The presence of amyloid correlated with age and P-wave duration and was related to sex, valve diseases, and the presence of AF ( $P = 0.043$ ). The association between atrial amyloid, AF, and P-wave duration was independent of age and sex. According to multiple logistic regression analysis, amyloid was the only age- and sex-independent predictor for the presence of AF. Atrial fibrosis was not a predictor for AF, but the amount of atrial fibrosis was related with atrial fibrillation.

**Conclusion** Our study provides evidence that atrial amyloidosis affects atrial conduction and increases the risk of AF. The occurrence of atrial amyloidosis depends on age leading to the formation of an amyloid nidus. The progression and consequences of atrial amyloidosis are then influenced by pathological conditions, such as valve diseases. The correlation between atrial amyloidosis and atrial fibrillation suggests that these patients may not benefit from treatment with ACE inhibitors to reduce the amount of atrial fibrosis.

### The fixed frequency spectral components may reflect the drivers of the paroxysmal atrial fibrillation

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**Aims** This study aims to investigate if the frequency spectral components reflect the drivers of the paroxysmal atrial fibrillation

**Methods** Two simple signals were constructed and integrated to one. The spectral analysis was performed on these three signals in the pilot study. 60 patients with paroxysmal AF were included in the clinic study. Spectral analysis was performed before and after Pulmonary vein (PV) isolation. During ablation, drivers of the AF were identified. The dominant frequency (DF) of the coronary sinus (CS) ostium and PVs, and the fixed frequency spectral components of the CS ostium were identified. Changes of the DF and fixed frequency spectral components before and after PV isolation were studied. The distance from the recording site to the PV was measured in each patient.

**Result** The spectra of the integrated signal has two components, each reflect previous simple signal. In clinic study, fixed frequency spectral components were identified in 30 patients. The distance from the recording site to the PV in these patients were significantly different than other patients (to the right PV:  $48 \pm 9$  mm vs  $64 \pm 8$  mm,  $P < 0.05$ ; to the left PV:  $51 \pm 9$  mm vs  $65 \pm 8$  mm,  $P < 0.05$ ). The frequency of the fixed frequency spectral components was equal to (or within 0.1 Hz) the DF of the driving PV. The fixed frequency spectral component whose frequency equal to the DF of the driving PV decreased or disappeared accordingly after the driving PV isolation.

**Conclusion** The fixed frequency spectral components may reflect the drivers of the paroxysmal AF

### Mitral valvuloplasty in infective endocarditis with mitral insufficiency

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**Objective** To discuss clinical outcomes of mitral valvuloplasty in infective endocarditis with mitral insufficiency.

**Method** During 2002 – 2012, 34 patients of infective endocarditis with mitral insufficiency underwent mitral valvuloplasty. There were 25 male and 9 female patients, with an average age of  $36 \pm 16$  years old. 7 patients had previous heart disease. 23 patients had severe mitral regurgitation, 9 patients had moderate and 2 patients had mild regurgitation assessed by echocardiography. There were 5 patients in NYHA functional class, I, 24 patients in class II, 3 patients in class III and 1 patient in class IV. 2 operations were performed in acute phase and other 32 operations were in subacute and chronic phase. There were 7 patients underwent aortic valve replacement, 5 patients received tricuspid valvuloplasty, 1 patient received CABG and 1 patient had resection of myxoma at the same time. The surgery consisted of complex Methods, including pericardial patch closure of leaflet perforation in 5 patients, wedge shape excision and suturing in 15 patients, double-orifice method in 5 patients, chordae transference and artificial chordae in 4 patients



and quadrangular resection in 5 patients. 15 annuloplastic rings were used.

**Result** 1 patient died in perioperative period and other 33 patients survived when following up after  $75 \pm 38$  months. The echocardiography of postoperation and follow-up showed an decrease of LVEDD (from  $62 \pm 8$  mm to  $50 \pm 7$  mm and  $49 \pm 5$  mm,  $P < 0.05$ ) and LAD (from  $44 \pm 12$  mm to  $33 \pm 8$  mm and  $36 \pm 9$  mm,  $P < 0.05$ ). 30 patients had no and 2 patients had mild mitral regurgitation. 1 patient received mitral valve replacement 3 years later due to mitral stenosis and other patients survived free of reoperation. There were 28 patients in NYHA functional class, I, 4 patients in class II, 1 patients in class III.

**Conclusion** The outcomes of mitral valvuloplasty in infective endocarditis with mitral insufficiency are reliable. The diameter of LV and LA decreased and cardiac function improved obviously.

### Coronary CT analysis of 150 heart transplants

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**Objective** Retrospective analysis of cardiac allograft vasculopathy (CAV) in patients after heart transplantation by coronary CT in our hospital.

**Method** As a single center, in Jun. 2004 to Oct. 2011, we completed a total of 272 heart transplants, in which postoperative coronary CT Result of 150 orthotopic heart transplants were retrospectively analyzed. According to the presence or absence of CAV, these patients were divided into CAV group and normal group. Preoperative and intraoperative status was compared, and to explore the possible risk factors related to the incidence of CAV.

**Result** 150 donors were brain dead. Recipients with panel reaction antibody (PRA)  $> 10\%$  accounted for 5.3% (8/150). The cold ischemic time, total cardiopulmonary bypass time and aortic clamping time were ( $4.66 \pm 1.94$ ), ( $3.06 \pm 0.86$ ) and ( $1.34 \pm 0.31$ ) hours, respectively. According to the international CAV definition on CT images, CAV was defined as the presence of any coronary plaque. 18 cardiac allografts were suffered from CAV in the 150 orthotopic heart transplants through carefully analysis of their postoperative coronary CT Result, including 11 cases of calcification, 3 cases of coronary intimal thickening, 2 cases of stenosis, 1 case of artifact, 1 case of coronary wall irregularity. Thus, the morbidity was 12.0%. In normal group, there were a higher percentage of patients whose mean pulmonary artery pressure (mPAP)  $> 30$  mm Hg than CAV group, 68 (59.1%) and 3 (23.1%), respectively ( $P = 0.01$ ). So were patients of mPAP  $> 50$  mm Hg, 52 (44.8%) and 2 (15.4%), respectively ( $P = 0.04$ ). The donor age of patients in CAV group was  $33.1 \pm 7.4$  years, the normal group  $28.1 \pm 7.5$  years, with a

significant difference ( $P = 0.043$ ). There were no significant differences between the two groups about other intraoperative status. Compared with normal group, there were a higher fraction of patients of left ventricular noncompaction in CAV group, 1.5% and 11.1%, respectively. We did not detect any significant differences among other heart diseases between two groups.

**Conclusion** This study found a lower postoperative pulmonary artery pressure and an older donor are the risk factors of CAV. However, other international reports found high pulmonary artery pressure was the risk factor of CAV after heart transplantation, which is somewhat inconsistent with our study. Taking the incomplete clinical follow-up data, the dis-matched sample size and only part of patients underwent coronary CT examination into account; it is still difficult to identify all the risk factors of CAV in Chinese heart transplants. A further detailed study is needed.

### Analysis on outcome of 3537 patients with coronary artery disease: integrative medicine for cardiovascular events

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**Objective** To investigate the treatment of hospitalized patients with coronary artery disease (CAD) and the prognostic factors in Beijing, China.

**Methods** This is a multicenter prospective study. By means of a unified clinical and research information platform, we collected clinical information of hospitalized patients with CAD in cardiovascular department of 12 hospitals in Beijing from Sep. 2009 to May 2011. Then, we evaluate the effect of secondary prevention in patients with CAD through the clinical information and cardiovascular events during one-year follow-up. Meanwhile, a logistic regression analysis with standard technique was used to identify independent prognostic factors.

**Result** The average age of these 3537 patients is ( $64.88 \pm 11.97$ ), and 65.42% of these patients is male. The usage of drugs is as follows: Anti-platelet drugs accounting for 91.97%, statin accounting for 83.66%,  $\beta$ -blockers accounting for 72.55%, ACEI/ARB accounting for 58.92% and revascularization (including PCI and CABG) accounting for 40.29%. The overall incidence of cardiovascular events was 13.26% (469/3537). The logistic stepwise regress analysis showed that heart failure (OR, 3.707, 95% CI: 2.756 – 4.986), age  $\geq 65$  years old (OR, 2.007, 95% CI: 1.587 – 2.53), and myocardial infarction (OR, 1.649, 95% CI: 1.322 – 2.057) were independent risk factors for one-year follow-up cardiovascular events. Integrative medicine (IM) therapy showed the trend of decreasing incidence of cardiovascular events, but no statistical significance (OR, 0.797, 95% CI: 0.613 – 1.036).

**Conclusion** Heart failure, age  $\geq 65$  years old, myocardial infarction increased the incidence of cardiovascular events. IM therapy showed a trend of decreasing incidence of cardiovascular events, but it need to further study.

### ITIH4: A new biomarker of “toxin syndrome” in coronary heart disease patient identified with proteomic method

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**Objective** “toxin syndrome” is a special pattern in traditional Chinese medicine (TCM) diagnosis, which has been extensively investigated in multiple diseases. According to a recent hypothesis, “toxin syndrome” might be related to the relapse of cardiovascular events in stable coronary heart disease (CHD) patients. However, the biologic basis underlying TCM “toxin syndrome” in CHD patients remains unclear. This trial aims to look for the protein biomarker of “toxin syndrome” of CHD patients, which is anticipated to help early identification of high-risk CHD patients in stable period.

**Methods** We have performed two trials in this paper. The first trial was a randomized controlled trial (RCT) of the plasma proteome in unstable angina (UA) patients by Moldi-ToF Mass. We compared plasma differential protein between 31 patients in activating-blood-circulation group (Xiongshao capsule, group A) and 30 patients in activating-blood-circulation & detoxicating group (Xiongshao capsule and Huanglian capsule, group B) to identify the potential biomarker of “toxin syndrome”. The second trial was a nested case-control study in 1503 stable CHD patients with one-year follow-up for acute cardiovascular events (ACEs). We selected 10 patients with follow-up ACEs and another 10 patients with no ACEs matched in a 1: 1 ratio by sex, age ( $\pm$  5 years), hypertension history, diabetes history and myocardial infarction history. All the sera at the admission of these 20 patients were adopted for verifying the differential protein of “toxin syndrome” obtained from RCT by Western blot method.

**Result** In the RCT study, 12 protein spots were found that displayed significant differences in difference before-after treatment in group A and group B, 2 of them (3207.37Da and 4279.95Da) was considered to be unique to “toxin syndrome” for being differential proteins of group B but not group A. These 2 spots were identified as Isoform 1 of Fibrinogen alpha chain precursor (FGA, 3207.37Da) and Isoform 2 of inter-alpha-trypsin inhibitor heavy chain H4 (ITIH4, 4279.95Da) respectively. In the nested case-control study, the result of Western blot demonstrated that protein expression of ITIH4 in the group with follow-up ACEs was significantly lower than the matched group without follow-up ACEs ( $P = 0.027$ ).

**Conclusion** ITIH4 might be a new biomarker of CHD “toxin syndrome” in TCM, indicating the potential role in early identifying high-risk CHD patients in stable period.

### A systematic review of randomized controlled trials

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**Objective** This systematic review aims to evaluate current evidence for the benefit and side effect of oral Panax Notoginseng Preparation for coronary heart disease (CHD).

**Methods** Six electronic databases were searched. All randomized clinical trials (RCTs) with oral Panax Notoginseng in treatment group for CHD were included (co-intervention treatment was excluded) comparing with positive therapeutic medicine or placebo or no treatment on the basis of conventional therapy. Two reviewers extracted data and assessed the quality of trials independently. RevMan 5.1 software was used for data analysis. For continuous data, mean difference (MD) and its 95% confidence interval (CI) were calculated and for categorical data, relative risk (RR) and 95% CI was supplied. Fixed model was used to do meta-analysis while random model was adopted when substantial heterogeneity existed.

**Result** We included 17 randomized trials (17 papers and 1747 participants). Comparing with conventional therapy done, additional oral panax notoginseng did not show significant effect on decreasing cardiovascular events, but it could decrease the recurrence of angina pectoris [including improve the syndromes of angina pectoris. RR 1.20; 95% CI 1.12 to 1.28; 7 trial, n = 7910), improve Electrocardiogram (RR 1.35; 95% CI 1.19 to 1.53; 8 trial, n = 727), decrease the recurrence of angina pectoris (RR 0.38; 95% CI 0.16 to 0.94; 1 trial, n = 60), period of angina pectoris (RR -1.88; 95% CI -2.08 to -1.69; 2 trial, n = 292) and dosage of nitroglycerol (MD -1.13; 95% CI -1.70 to -0.56; 2 trial, n = 212)]; Oral panax notoginseng had no significant difference comparing with isosorbide dinitrate on immediate effect for angina pectoris (RR 0.96; 95% CI 0.81 to 1.15; 1 trial, n = 80).

**Conclusion** Oral panax notoginseng preparation relieved angina pectoris related symptoms. However, the small sample size and potential bias of most trials influenced the convincingness of this conclusion. More rigorous trials with high quality are needed to give high level of evidence, especially for the potential benefit of cardiovascular events. Quality of life should also be considered in the future.

### An overview of systematic reviews/meta-analyses

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**Background** Oral Chinese proprietary medicine (CPM) has been

commonly used to treat angina pectoris, and many relevant systematic reviews/meta-analyses were available so far. However, these reviews haven't been systematically summarized and evaluated. Therefore we conducted an overview of these reviews, and explored their methodological and reporting quality.

**Methods** We included systematic reviews/meta-analyses on oral CPM in treating angina until March 2013 by searching PubMed, Embase, the Cochrane Library and four Chinese databases. We extracted data according to a pre-designed form, and assessed the methodological and reporting characteristics of the reviews in terms of AMSTAR and PRISMA respectively. Most of the data analyses were descriptive.

**Result** 36 systematic reviews/meta-analyses involving 82, 105 participants with angina reviewing 13 kinds of oral CPM were included. The main outcomes assessed in the reviews were surrogate outcomes (34/36, 94.4%), adverse events (31/36, 86.1%), and symptoms (30/36, 83.3%). Six reviews (6/36, 16.7%) drew definitely positive Conclusion, while the others suggested potential benefits in the symptoms, electrocardiogram and adverse events. The overall methodological and reporting quality of the reviews was limited, with many serious flaws such as the lack of a protocol and incomprehensive literature search.

**Conclusion** Though many systematic reviews/meta-analyses on oral CPM for angina suggested potential benefits or definitely positive effects, authors should interpret the findings of these reviews cautiously, considering the overall limited methodological and reporting quality. The further researchers should appropriately conduct and report relevant systematic reviews according to international standards or recommendations such as AMSTAR and PRISMA.

### Optimizing prescription of Chinese herbal medicine for unstable angina based on partially observable markov decision process

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**Objective** Initial optimized prescription of Chinese herb medicine for unstable angina (UA).

**Methods** Based on partially observable Markov decision process model (POMDP), we choose hospitalized patients of 3 syndrome elements, such as qi deficiency, blood stasis and turbid phlegm for the data mining, analysis, and objective evaluation of the diagnosis and treatment of UA at a deep level in order to optimize the prescription of Chinese herb medicine for UA.

**Result** The recommended treatment options of UA for qi deficiency, blood stasis, and phlegm syndrome patients were as follows: Milkvetch Root + Tang shen+ Milkvetch Root + Largehead Atractylodes Rhizome (ADR = 0.96630); Danshen Root + Chinese Angelica + Safflower + Red Peony Root + Szechwan Lovage Rhizome Orange Fruit (ADR = 0.76); Snakegourd Fruit + Long stamen Onion Bulb + Pinellia Tuber + Dried Tangerine peel + Large head Atractylodes Rhizome + Platycodon Root (ADR = 0.658568).

**Conclusion** This study initially optimized prescriptions for UA based on POMDP, which can be used as a reference for further

development of UA prescription in Chinese herb medicine.

### The progress of kidney–nourishing herbal medicine for treating hypertension with insulin resistance

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Hypertension with insulin resistance is becoming focus of study both in cardiovascular and endocrine field. A variety of drug combination therapy can be used for lower blood pressure while improving insulin resistance. However, there are still a considerable number of patients with hypertension and insulin resistance that cannot be treated well. Traditional Chinese medicine is needed to enhance the therapeutic efficacy. Recently, it has been proved that kidney-nourishing herbal medicine has good effects on treating hypertension with insulin resistance. This paper reviewed the clinical and experimental studies of kidney-nourishing herbal medicine for treating hypertension with insulin resistance, and explored its mechanism in order to provide a new strategy for future rational antihypertensive treatment.

### Chinese herbal medicine Qi Ju Di Huang Wan for the treatment of essential hypertension: a systematic review of randomized controlled trials

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**Background** To assess the effectiveness and safety of QJDHW for essential hypertension (EH).

**Methods** Pubmed, CBM, CNKI, VIP, and online clinical trial registry websites were searched for published and unpublished randomized controlled trials (RCTs) of QJDHW for EH up to January 2013 with no language restrictions.

**Result** A total of 10 randomized trials involving 1 024 patients were included. Meta-analysis showed that QJDHW combined with antihypertensive drugs was more effective in lowering blood pressure and improving TCM syndrome for the treatment of essential hypertension than that antihypertensive drugs used alone. No trials reported severe adverse events related to QJDHW.

**Conclusion** Our review suggests that QJDHW combined with antihypertensive drugs might be an effective treatment for lowering blood pressure and improving symptoms in patients with EH. However, the finding should be interpreted with caution because of the poor methodological quality of included trials.

### Changes of plasma ADMA levels and intervention of irbesartan in patients with essential hypertension and stroke

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**Objective** To study the levels of plasma asymmetric dimethylarginine in patients with essential hypertension and stroke.



Moreover, the effects of irbesartan were investigated.

**Methods** 289 cases with essential hypertension and ischemic stroke were randomly divided into two groups: amlodipine group (146 cases) and irbesartan group (143 cases). In 1 year's follow-up, the plasma ADMA levels, blood pressures and cerebrovascular events were observed.

**Result** The blood pressure of the patients significantly decreased, with a statistically significant difference ( $P < 0.05$ ). But the blood pressure levels between the two groups has no statistically significant difference ( $P > 0.05$ ). In irbesartan group, the plasma ADMA levels were significantly lower ( $P < 0.05$ ). While the amlodipine group showed no significant difference ( $P > 0.05$ ). There was statistically significant difference in the incidence of cerebrovascular events between the two groups ( $P < 0.05$ ).

**Conclusion** It's may be one of the beneficial mechanisms of irbesartan to patients with hypertension and stroke that it can reduce recurrence of cerebrovascular events and decreased plasma ADMA levels.

### Relationship between the polymorphism of the ACE2 gene and the response to ACE inhibitor in hypertensive patients

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**Objective** The polymorphic angiotensin converting enzyme 2 (ACE2) genes is one of the most promising candidates for essential hypertension. The aim of this study was to examine the association between the G8790A variant of the ACE2 gene and the blood pressure, pulse pressure, and mean arterial pressure response to angiotensin-converting enzyme (ACE) inhibitor in hypertensive subjects.

**Methods** Benazepril (10–20 mg/day) was administered for 6 weeks to 215 essential hypertensive. ACE2 genotyping was performed by direct polymerase chain reaction amplification and DNA nucleotide sequencing from peripheral blood. Genotype data were analyzed in relation to interindividual differences in the response to ACE inhibitor therapy.

**Result** The relationship between the polymorphism and the drug response was found in male patients. After 6 weeks of treatment the reductions in mean arterial pressure response were significantly greater in male subjects carrying G allelic variant compared to male subjects carrying A allelic variant ( $14.7 \pm 7.5$  mm Hg vs  $10.1 \pm 7.4$  mm Hg, respectively;  $P < 0.05$ , ANOVA).

**Conclusion** These findings suggest that the G8790A variant of the ACE2 gene was related to blood pressure lowering response in hypertensive patients treated with ACE inhibitor.

### Left radial artery approach for coronary angiography and percutaneous coronary interventions in 2135 case

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**Objective** To evaluate the clinical efficacy and methodology of

coronary angiography and percutaneous coronary intervention via left radial artery approach.

**Methods** From Jan. 2007 to Dec. 2011, A total of 2 135 patients underwent coronary angiography and/or percutaneous coronary interventions via left radial artery approach were retrospectively reviewed. The success rate and related complications were recorded and analyzed.

**Result** The success rate of coronary angiography was 97.7% and the success rate of percutaneous coronary interventions was 96.68%. The failed 30 cases were satisfied via right radial artery approach. The failed 19 cases were satisfied via alternative femoral artery approach. No serious complications occurred except 22 local hematomas, 9 arterial occlusion but without hand ischemia.

**Conclusion** Coronary angiography and coronary intervention therapy through left radial artery are safe and feasible. It is worth using in clinic.

### Meta-analysis of randomized controlled trials of intracoronary vs intravenous administration of tirofiban during percutaneous coronary intervention for acute coronary syndrome

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**Background** It remains unclear whether intracoronary (IC) or intravenous (IV) administration of Tirofiban is superior for patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI).

**Methods** A meta-analysis of randomized controlled clinical trials (RCTs) was conducted based on the identification of relevant trials ( $n = 8$ ). Primary end-points were short-term (1–3 months) major adverse cardiovascular events (MACEs) [e.g., mortality, reinfarction, target vessel revascularization (TVR)]. Secondary end-points included thrombolysis in myocardial infarction (TIMI) grade flow and TIMI myocardial perfusion grade (TMPG) flow. Bleeding complications were evaluated as safety end-points.

**Result** IC administration of Tirofiban was found to decrease short-term MACEs, including mortality, reinfarction, and target vessel revascularization (OR: 0.24, 95% CI: 0.13–0.44,  $P < 0.0001$ ). Short-term mortality (OR: 0.40, 95% CI: 0.12–1.33,  $P = 0.13$ ), reinfarction rate (OR: 0.48, 95% CI: 0.18–1.27,  $P = 0.14$ ), and TVR rate (OR: 0.46, 95% CI: 0.10–2.03,  $P = 0.30$ ) also showed an apparent decrease with IC vs IV administration of Tirofiban, although the differences were not statistically significant. However, a significant increase in TIMI grade 3 flow (OR: 3.67, 95% CI: 2.26–5.95,  $P < 0.00001$ ) and TMPG grade 2–3 flow (OR: 3.88, 95% CI: 2.44–6.15,  $P < 0.00001$ ) were observed for IC vs IV administration. In contrast, no significant difference was observed in bleeding complications reported for the two groups.

**Conclusion** IC administration of Tirofiban in patients with ACS undergoing PCI can significantly increase target coronary flow and myocardial reperfusion without increasing the risk of bleeding complications. It can also decrease total short-term MACEs, yet does not improve clinical outcome compared with IV administration.

### Study on the efficacy and safety of transradial approach for primary coronary angioplasty in acute myocardial infarction with power antithrombotic therapy

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**Objective** To evaluate the efficacy and complications of transradial approach and transfemoral approach in the treatment of acute myocardial infarction with primary percutaneous coronary intervention (PCI) with power antithrombotic therapy and to explore whether transradial approach could be the first approach.

**Methods** A prospective study was conducted with the data of 89 patients (group A) with acute myocardial infarction (AMI) who underwent transradial primary PCI, 83 patients (group B) underwent transfemoral primary PCI compressing to stop bleeding by hand and 80 patients (group C) underwent transfemoral primary PCI compressing to stop bleeding by stapler. The incidence of major adverse cardiovascular events (MACE), including death, myocardial infarction, target lesion revascularization found in 90 days, were compared among the three groups, the rates of stent thrombosis and restenosis were also compared. The complications were compared among the three groups.

**Result** No significant differences in baseline characteristics were observed among the three groups. PCI was successfully accomplished in all patients. After 3 month follow-up, no significant difference was found in the MACE rate among the three groups ( $P > 0.05$ ). The complications in group A were moreless compared with that of group B and C ( $P < 0.01$ ) and there was no difference between B and C ( $P > 0.05$ ).

**Conclusion** The transradial approach primary PCI in the treatment of acute myocardial infarction has a similar efficiency in group A with that of group B and C. The complications were much less in group A than that of group B and C. The transradial approach primary PCI in the treatment of acute myocardial infarction should be the first selection of approach.

### Study on the efficacy and safety of transbrachial approach for complex coronary lesions

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**Objective** To explore the possibility of percutaneous coronary interventions (PCI) for Complex coronary lesions transbrachial approach.

**Methods** 100 patients with Complex coronary lesions were divided into two groups randomly. Fifty patients of group A will take PCI with transbrachial approach; fifty patients of group B will take PCI with transfemoral approach. Success rate of operation, operation and X-ray time, average hospitalizing time, the complications and fee were compared between the two groups.

**Result** No significant differences in baseline characteristics were observed between the two groups. PCI was successfully accomplished in all patients. No significant difference was found in the success rate of operation, operation and X-ray time ( $P > 0.05$ ). The complications, average hospitalizing time and fee in group A were less than that of group B ( $P < 0.05-0.01$ ).

**Conclusion** The transbrachial approach PCI for Complex coronary lesions which not suit for transradial approach could be the first selection

of approach.

### Affection for selective percutaneous coronary intervention with high dose clopidogrel

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**Objective** To study therapeutic efficacy and safety of high dose clopidogrel in patients with coronary heart diseases (CHD) who underwent selective percutaneous coronary intervention (PCI).

**Methods** A total of 173 CHD patients underwent PCI were divided into strong clopidogrel group (received 600 mg of plavix,  $n = 87$ ) and standard clopidogrel group (received 300 mg of plavix,  $n = 86$ ). Before PCI, the two groups were respectively given 600 mg and 300 mg of plavix, They were respectively given 150 and 75 mg every day for 7 days after PCI. Then they were all given 75 mg every day over one year. Therapeutic efficacy and occurrence of adverse reactions were observed in the two groups.

**Result** There were significant difference in complete revascularization rate (93.8% vs 87.2%,  $P < 0.05$ )major adverse cardiovascular-cerebral events (MACCE) (2.0% vs 6.8%,  $P < 0.01$ ), There were no differences in bleeding and vascular complications (1.6% vs 1.7%,  $P > 0.05$ ) between strong clopidogrel group and standard clopidogrel group.

**Conclusion** Strong clopidogrel is more effective and safe than standard clopidogrel in selective PCI of CHD.

### Effects of regularly clinic follow-up on prognosis and cost-benefit of outpatients with chronic heart failure

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**Objective** To study the efficacy of regularly clinic follow-up for outpatients with chronic heart failure (CHF) on prognosis and cost-benefit

**Methods** All patients diagnosed as CHF in our cardiovascular department between Jan. 2011 to Jun. 2012 were included in this study. They were divided into regularly follow-up (RF) and usual care (UC) groups. Investigating the Endpoints including death or rehospitalization, medication, cost-benefit with the data collected through hospital records or by telephone and post survey.

**Result** A total of 264 patients were enrolled (102 patients in RF group and 162 in UC group). The mean follow-up duration was 392 days for RF group and 428 days for UC group. Mortality and rehospitalization rate (37.41% vs 68.1%,  $P < 0.01$ ) and mortality rate (1.92% vs 12.75%,  $P < 0.01$ ) were significantly higher in UC group than in RF group. The percentage of patients receiving ACEI/ARB (64.70% vs 34.72%,  $P < 0.01$ ; 15.49% vs 9.28%,  $P < 0.05$ ) and beta-adrenergic receptor blocker (90.13% vs 29.83%,  $P < 0.01$ ) were higher in RF group than in the UC group. Hospital cost (4218.16 RMB less per patient in this period) was significantly lower in RF group than in UC group.

**Conclusion** Regularly clinic follow-up can decrease the mortality rate and the readmission rate of patients with heart failure. And improve the application of drugs which can improve the prognosis of patients with CHF, furthermore, can reduce health care costs.

## Impact on QTc interval and safety evaluation after amiodarone injection in hospitalized patients

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**Objective** To evaluate the impact on QTc interval and relevant adverse drug reaction after amiodarone injection in hospitalized patients.

**Methods** 1111 hospitalized patients from 4 upper first class hospitals in Beijing were enrolled from May 2011 to Jul. 2012, the QTc intervals were measured to evaluate whether there would be change before and after amiodarone injection within 24 hours, and suspected proarrhythmia adverse effects due to study drug were monitored during the entire period of administration.

**Result** The average heart rate was slowed ( $87.4 \pm 21.2$  bpm vs  $99.6 \pm 27.9$  bpm,  $P < 0.001$ ) and QT interval was prolonged ( $388.5 \pm 55.9$  ms vs  $366.0 \pm 55.9$  ms,  $P < 0.001$ ) significantly after amiodarone administration as compared with the baseline, but QTc interval was not changed with statistical significance ( $456.8 \pm 51.0$  ms vs  $457.8 \pm 50.2$  ms,  $P = 0.554$ ). One patient with atrial tachycardia experienced TdP after 54 hours amiodarone injection concomitant with oral amiodarone showed a prolonged QTc interval up to 756 ms previously, TdP was not occurred again after amiodarone discontinuation and appropriate treatment.

**Conclusion** Amiodarone injection within 24 hours does not impact on QTc interval with statistical significance in hospitalized patients. Electrocardiograph should be monitored in a continuous amiodarone injection to avoid the relevant adverse drug reaction, especially when using concomitant amiodarone orally.

## The impact of hypertension history and baseline blood pressure levels on the cardiovascular outcomes in patients with atrial fibrillation

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**Objective** To explore the hypertension history and baseline blood pressure levels on the treatment of atrial fibrillation patients and the impact on one year follow-up cardiovascular outcomes.

**Methods** This prospective study consecutively enrolled patients presenting to an emergency department with atrial fibrillation at 20 hospitals in China from 2009 to 2011. Baseline data and treatment were recorded, all patients were followed up for one year, and major cardiovascular outcomes were recorded. A total of 2015 atrial fibrillation patients were enrolled, and all the patients were divided into 4 groups according to the previous history of hypertension and baseline blood

pressure levels: group 1: patients have previous hypertension history and baseline blood pressure greater than 140/90 mm Hg; group 2: patients have previous hypertension history and normal baseline blood pressure; group 3: patients have no hypertension history but baseline blood pressure greater than 140/90 mm Hg; group 4: patients have no hypertension history and normal baseline blood pressure.

**Result** The average age of all patients was  $68.5 \pm 13.3$  years, average systolic blood pressure and diastolic blood pressure were  $131.9 \pm 23.3$ ,  $79.9 \pm 14.7$  respectively. 1118 patients (55.5%) had a history of hypertension, and about 91.1% hypertension patient received antihypertensive treatment. The difference of mortality, non central nervous system embolism incidence and major bleeding incidence in the 4 groups was not statistically significant (P values were 0.685, 0.893, 0.204 respectively). The stroke incidences of group 1, 2, 3, 4 were 8.3%, 9.4%, 6.2% and 5.2% ( $\chi^2 = 8.721$ ,  $P = 0.033$ ). Univariate Cox regression analysis of risk factors for stroke, group 1 and 2 were the risk factors for stroke (HR 1.613, 95% CI 1.054 – 2.469,  $P = 0.028$ ) HR 1.83, 95% CI 1.179 – 2.864,  $P = 0.007$ ) compared to group 4. The variables included in the multivariate Cox regression model was based on the baseline data and univariate analysis of meaningful factors as well as some common clinical risk factors, including hypertension groups, age, sex, history of coronary artery disease, history of heart failure, myocardial infarction history, history of rheumatic heart disease, a history of left ventricular hypertrophy, COPD history, history of stroke, history of diabetes, history of dementia, major bleeding history, diuretics, digoxin, beta-blockers, ACE inhibitors, ARB, clopidogrel, aspirin, warfarin, anti-arrhythmic drugs, statins. After adjusting the other risk factors, showed that hypertension and baseline blood pressure levels did not have independent predictive value ( $P = 0.737$ ). And multivariate Cox regression analysis showed that age, sex, history of stroke, dementia/cognitive defects history were independent risk factor for one year follow-up of stroke in atrial fibrillation patients.

**Conclusion** History of hypertension and baseline blood pressure levels was not the risk factors for one year cardiovascular outcomes of atrial fibrillation patients. Elderly female atrial fibrillation patients with previous stroke and dementia history had a higher risk of stroke incidence.

## The analysis of Chinese atrial fibrillation patients presenting to the emergency department during 1 year follow-up

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**Objective** Atrial fibrillation (AF) is the most common serious cardiac arrhythmia, and its prevalence is expected to increase. There is lack of data about patient characteristics, practice patterns, and outcomes of AF in Chinese patients.

**Methods** The Chinese AF registry is a prospective, observational registry of AF patients which present to emergency department (ED) either as primary or secondary diagnosis. Data collected included patient demographics, medical history, treatment and outcomes of emergency visit. For admitted patients, a follow-up was completed to obtain the major adverse events during 1 year.

**Result** From Nov. 2008 to Oct. 2011, 2016 consecutive patients were enrolled from twenty representative centers of China. The mean age was 68.5 years and 54.8% was female. AF was the primary reason



for this ED visit in 40.9% and 80.9% had a known prior diagnosis of atrial fibrillation before. The most common concomitant condition was hypertension, present in 1118 (55.5%) patients. At enrollment, the rates of permanent, persistent and paroxysmal AF was 47%, 22.3%, and 30.7%, respectively. 1992 AF patients (98.8%) had completed 1 year follow-up. Of these, all cause mortality was 288 (14.5%) cases, stroke/non-CNS systemic embolism was 159 (8.0%) cases, and major bleeding was 26 (1.3%) cases. Heart failure was the major cause of mortality, which accounted for 42.4% death. Of 375 (18.6%) patients used warfarin at baseline, only 217 patients was stick to anticoagulation therapy during 1 year follow-up. Compared with anticoagulation patients, the mortality rate of non-anticoagulation patients was much higher (15.7% vs 5.5%,  $P < 0.001$ ), and the risk of stroke was also higher in those without anticoagulation although it was not statistically significant (8.4% vs 6.0%,  $P = 0.29$ ).

**Conclusion** The annual rates of mortality and stroke were high in AF patients who presenting to the emergency department, and heart failure was the major cause of death. Patients may benefit more from anticoagulant treatment and the anticoagulation rate was low in China.

### Risk factors and incidence of stroke and MACE in Chinese atrial fibrillation patients – A nationwide database analysis

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**Objective** Atrial fibrillation is the most common cardiac rhythm disorder, which is associated with a substantial risk of stroke and mortality. Contemporary clinical risk stratification schemata for predicting stroke and thromboembolism in patients with atrial fibrillation are largely derived from western cohorts. The purpose of the present study is to assess the risk factors of stroke and MACE in a group of large-scale Chinese AF patients.

**Methods** We enrolled patients who present to an emergency department (ED) with atrial fibrillation or atrial flutter from Nov. 2008 to Oct. 2011, either as the primary or secondary diagnosis. A follow-up was performed to assess stroke and incidence of major adverse cardiac events (MACE) during 1 year. The major adverse cardiac events included all cause mortality, stroke, non-central nervous systemic embolism and major bleeds.

**Result** A total of 2 016 AF patients (1 104 women) were included in the final analysis. 33.7% of the subjects aged  $< 65$  years, 28.3% aged 65 – 74 years and 38.0% aged over 75 years. The mean age was 68.5 years. AF was the primary reason for this ED visit in 40.9% and 80.9% had a known prior diagnosis of atrial fibrillation before. Hypertension was the most prevalent comorbidity (55.5%), followed by coronary artery disease (41.8%). Of the 1 108 patients with hypertension, 101 (9.1%) was untreated. During 1 year follow-up, stroke was 148 (7.4%) cases, and MACE was 436 (21.9%) cases. Cox regression analysis showed that the risk factors for ischemic stroke were female gender (HR 1.470, 95% CI 1.048 – 2.063,  $P = 0.026$ ), age over 75 years (HR, 2.717, 95% CI 1.690 – 4.367,  $P < 0.001$ ), prior stroke/TIA (HR, 2.021, 95% CI 1.408 – 2.900,  $P < 0.001$ ), left ventricular systolic dysfunction (LVSD) (HR, 1.701, 95% CI 1.024 – 2.827,  $P = 0.040$ ), prior major bleeding (HR, 2.506, 95% CI 1.162 – 5.406,  $P = 0.019$ ), hypertension without medically treated (HR, 1.948, 95% CI 1.101 – 3.446,  $P = 0.022$ ). For MACE, age over 75 years (HR, 3.451, 95% CI 2.623 – 4.540,  $P < 0.001$ ), heart failure (HR, 1.356, 95% CI 1.078 – 1.706,  $P = 0.009$ ), prior stroke/TIA (HR, 1.531, 95% CI 1.221 – 1.918,  $P < 0.001$ ), LVSD (HR, 1.444, 95% CI 1.101 – 1.893,  $P =$

0.008), hypertension without medically treated (HR 1.752, 95% CI 1.228 – 2.500,  $P = 0.002$ ) were the independent predictors. The c-statistics for predicting stroke was 0.671 (95% CI: 0.625 – 0.716) and for MACE was 0.703 (0.675 – 0.730), respectively.

**Conclusion** In Chinese AF patients presenting to the emergency department, the stroke and MACE rates were high, 7.4% and 21.9% respectively. The Cox regression prediction models show that the risk factors for stroke and MACE were similar to CHADS<sub>2</sub> scheme. In addition, clinicians should pay more attention to patients with prior major bleeding.

### Meta analysis of acute myocardial infarction following drug-eluting and bare stents implantation

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**Objective** To explore the difference in incidence of acute myocardial infarction between coronary drug stents and bare-stent after implantation.

**Methods** Computer-based online search of Cochrane Library CNKI, PubMed, Embas, CBM and VIP were performed to collected related articles. Retrieval time up to Apr. 2012. Article screening, data collected and quality evaluation were performed by two authors. The included studies were reviewed and analyzed.

**Result** A total of 10 articles were in accordance with the inclusion criteria, involving 2 477 cases, including 1 652 cases undergoing drug-eluting stents and 825 cases undergoing bare stents. Meta analysis of 10 studies showed that incidence of acute myocardial infarction endovascular restenosis in patients with coronary atherosclerotic heart disease 0.5 to 4 years after drug-eluting stent was lower than bare stent group [edge ratio = 0.27, 95% CI (0.21 – 0.34),  $P < 0.05$ ]; significant difference was found between two groups in intervention related complications [edge ratio = 0.50, 95% CI (0.38 – 0.67),  $P > 0.05$ ].

**Conclusion** After 0.5 – 4 years of implantation, drug-eluting stent for the acute myocardial infarction of coronary atherosclerotic heart disease has reduced incidence of in-stent restenosis, but there is significant difference was found in intervention related complications compared with bare stents.

### First-in-human use of the V<sup>2</sup> renal denervation System™ in China

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Catheter-based renal artery denervation (RDN) is a novel treatment for patients with resistant hypertension (HTN) who have been proved

effective and safe in clinical research. Besides the reduction of blood pressure, RDN can also improve glycemic control, renal function, sleep apnea, heart failure and reverse left ventricular hypertrophy. This report describes the first patient treated by the V<sup>2</sup> Renal Denervation System™ (Boston Scientific Corporation) in China. 6-month follow-up showed that the procedure was safe and effective, blood pressure and symptoms were remarkable improved, office blood pressure had fallen by 38/43 mm Hg to 118/79 mm Hg, ABMP decreased by 33/28 mm Hg to 113/73 mm Hg, medication had also been reduced compared with baseline, and no complications are observed.

### Bifurcation stenting for unprotected left main coronary artery distal lesions in the drug eluting stent era: One-year clinical follow-up Result from a single center

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**Background** The unprotected left main coronary artery (ULMCA) bifurcation stenosis remains challenging for percutaneous coronary intervention (PCI). The aim of the study was to evaluate the effectiveness and safety of bifurcation technique on the treatment of ULMCA bifurcation stenosis in drug eluting stent era.

**Methods** Between Mar. 2004 and Nov. 2011, a total of 224 patients (168 male) underwent bifurcation technique with drug eluting stent for true bifurcation lesions of ULMCA. Patients with cardiogenic shock were excluded from the analysis. We defined true bifurcations as Medina1, 1, 1 or 1, 0, 1 or 0, 1, 1. The indexes of in-hospital, angiographic restenosis at 12-months and major adverse cardiac events (MACE) including cardiac death, myocardial infarction or any target lesion revascularization were evaluated.

**Result** The procedural was successful in all patients. Bifurcation techniques included T stenting in 78 (34.8%), Culotte stenting in 69 (30.8%) and Crush stenting in 77 (34.3%) patients. Final “kissing balloon” inflation was preferred in 196 cases (87.5%). Intravascular ultrasound (IVUS) was performed in 79 cases during procedural. The mean stent diameter was (3.4 ± 0.40) mm in ULMCA. The overall rate of MACE was 1.3% (3/224) during hospital stay, including one acute stent thrombosis during procedure and 2 patients underwent repeat angioplasty for subacute stent thrombosis after PCI procedure. One patient died for subacute stent thrombosis during hospital stay. All patients were followed-up for at least 12 months. Two patients died for congestive heart failure during follow-up. Angiographic follow-up was obtained in 96 (42.9%) patients. Binary in-stent restenosis occurred in 15 (6.7%) patients and all of them were treated with CABG (7/15) or repeat PCI (8/15). The rate of target vessel revascularization was significantly lower in patients with final kissing inflation during the index procedure compared with those without final kissing [4.1% (8/196) vs 25.0% (7/28);  $P < 0.01$ ].

**Conclusion** Our experience indicated that bifurcation stenting for LMCA bifurcation lesions in elective patients could achieve a high technical success rate. Final kissing balloon might reduce the need for target vessel revascularization.

### Primary percutaneous coronary intervention for acute myocardial infarction caused by unprotected left main coronary artery lesions – a single centre study

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**Background** Acute myocardial infarction (AMI) due to unprotected left main coronary artery (ULMCA) occlusion has a poor prognosis. There is limited Result in patients undergoing primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI) caused by ULMCA stenosis. Previous studies have reported in-hospital mortality rates of 50% – 60%. The purpose of this study was to determine the clinical features and in-hospital outcomes of patients who underwent primary PCI for AMI due to ULMCA lesions.

**Methods** Between Jul. 2002 and Aug. 2012, a total of 86 AMI patients (65 male, 75.6%) underwent primary PCI on ULMCA lesions. Among them, 72 (83.7%) patients presented with acute ST elevation myocardial infarction and 14 (16.3%) patients with acute non-ST elevation myocardial infarction. The culprit lesions in all patients located in ULMCA diagnosed by angiography. The target lesion included de novo lesion located in ostial, shaft and distal bifurcation. The indexes of clinical, in-stent thrombosis and major adverse cardiac events (MACE) including death, myocardial infarction or target lesion revascularization were evaluated.

**Result** The mean age of patients was 67.6 ± 13.9 years. Cardiogenic shock was observed in 66 (76.7%) patients and cardiac arrest in 16 (18.6%). Prior to commencing PCI, 61 (70.9%) patients received the intra-aortic balloon pump. Angiographic success was achieved in all patients. Lesion location was ostial in 13 (15.2%), body in 25 (29.1%) and distal in 48 (55.8%). After PCI procedure, TIMI III flow were achieved in 79 (91.9%) patients. All patients had the ULMCA successfully dilated. Stent were deployed in 82 (95.3%) patients with drug eluting stent used in 72 (83.7%) patients. In-hospital death occurred in 7 (8.1%) patients [the mortality rate was 10.6% (7/66) in patients with cardiogenic shock]. On univariate analysis, age > 75 years ( $P < 0.01$ ), cardiogenic shock ( $P < 0.0001$ ), and stenting failure ( $P < 0.01$ ) were associated with in-hospital mortality.

**Conclusion** Despite the high mortality rate in patients with cardiogenic shock, our data have shown that primary PCI is a valuable therapeutic strategy for ULMCA in the setting of AMI. But the long-term outcomes should be observed by follow-up.

### Thrombus aspiration followed by direct stenting during primary percutaneous coronary intervention in ST-segment elevation myocardial infarction

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**Background** Previous studies have reported that low final

thrombolysis in myocardial infarction (TIMI) flow and/or myocardial blush grade (MBG) are independent predictors of mortality in patients with ST-elevation myocardial infarction (STEMI). Several studies with thrombus aspiration (TA) showed different Result, mainly due to use of TA as an additional device not instead of balloon predilatation (BP). The aim of the present study was to assess impact of TA followed by direct stenting during primary percutaneous coronary intervention (PPCI).

**Methods** Between Dec. 2008 and Jun. 2011, a total of 429 patients (107 patients in TA group and 322 patients in BP group) who were eligible for the observation criteria, admitted with STEMI (within 9 h from symptoms onset) and candidates for PPCI were enrolled. Exclusion criteria were a previous PCI on infarct-related artery, infarct-related artery balloon predilatation and TA simultaneously, and calcium or tortuous infarct-related lesion. The main indexes of this study were the TIMI flow grade, MBG, and the rate of 60-min ST-segment resolution > 50% after PCI and in-hospital major adverse cardiac events (MACE). Secondary indexes included distal embolizations of infarct-related artery, peak CK-MB release, and MACE after one year.

**Result** Baseline clinical and angiographic characteristics, initial TIMI flow and initial MBG did not differ between the two groups. Procedural success was obtained in all patients. Stent length, number of stents per patient, and stent/vessel ratio were similar between both groups. The rate of 60-min ST-segment resolution > 50% was significantly more frequent in TA group than in BP group (69.2% vs 48.5%,  $P$  flow grade after PCI was significantly higher among patients in TA group compared with BP group ( $2.65 \pm 0.49$  vs  $2.44 \pm 0.61$ ,  $P \pm 0.34$  vs  $2.41 \pm 0.56$ ,  $PP \pm 144$  U/L vs  $711 \pm 165$  U/L,  $P$  There was no difference in between the groups in in-hospital MACE (0.9% vs 2.8%,  $P > 0.05$ ), in 12-month cardiac mortality (1.2% vs 2.2%,  $P > 0.05$ ), reinfarction rate (0.9% vs 3.1%,  $P > 0.05$ ) and target vessel revascularization (2.8 vs 6.5%,  $P > 0.05$ ). But total MACE was significantly higher in BP group compared with the TA group (6.5% vs 14.5%,  $P < 0.05$ ).

**Conclusion** Compared with conventional PCI, TA and direct stenting before primary PCI improved final myocardial reperfusion and the long-term outcome for STEMI patients.

### Clinical investigation of effects of intravenous vs intra-coronary injection of tirofiban during primary PCI

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**Background** To investigate effects of intravenous vs intra-coronary injection of tirofiban on myocardial reperfusion during primary PCI in patients with STEMI.

**Methods** A total of 314 patients admitted to our hospital with myocardial infarction within 12 hours were enrolled in this study. Three hundred milligrams aspirin and 600 mg clopidogrel were given before PCI. Patients were randomized into intra-coronary injection or intravenous injection of tirofiban (10  $\mu$ g/kg). Primary endpoints included disappear of ST segments elevation, myocardial reperfusion grade, infarction size by cardiac biomarker and major adverse cardiac events within 30 days. Second endpoints include clinical events of bleeding.

**Result** There was no difference in rate of disappear of ST segments elevation (57% vs 58%). TIMI flow was better in intra-coronary group (84% vs 67%) and there was more myocardial reperfusion grade 2 (81%

vs 63%). There was no difference in cardiac bio-marker level. There was no difference in rate of thrombocytopenia or major organ bleeding.

**Conclusion** Intra-coronary injection of tirofiban during primary PCI in patients with STEMI can Result in better myocardial reperfusion grade, smaller infarction size, and better reperfusion, but has no effects on short-term prognosis. There was no increase of major clinical bleeding, so it is safe.

### Retrospective study on the relation between the level of thyroid hormone and coronary atherosclerotic heart disease

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**Background** To observe the changes of the level of thyroid hormone in the patients with coronary atherosclerotic heart disease (CHD).

**Methods** According to the Result of coronary artery angiography, 299 patients were divided into experimental group ( $n = 208$ ) and control group ( $n = 91$ ). And the experimental group were divided into three groups: the single vessel disease group ( $n = 72$ ), the double vessel disease group ( $n = 87$ ) and the triple vessel disease group ( $n = 49$ ). The levels of thyroid hormone were measured by radio-immunity method before coronary artery angiography, and then the levels of FT3, FT4, TT3, TT4 and TSH were compared between the two groups.

**Result** Comparison with the control group, the plasma level of FT3 of experimental group was significantly lower ( $P < 0.05$ ), but no significant difference of the plasma levels of TT4, TT3, FT4 and TSH was found between the two groups. And the plasma level of FT3 in the triple vessel disease group was significantly lower than double vessel group and single vessel group ( $P < 0.05$ ).

**Conclusion** The plasma level of FT3 was in low levels in patients with coronary atherosclerotic heart disease, which may have clinical significance for the treatment and prevention of CHD.

### Strengthening the reversal effect of lipid-lowering on patients with stable angina plaque

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**Background** To explore atorvastatin, a lipid-lowering therapy, and its reversal effect and safety on patients with stable angina plaques.

**Methods** In 50 cases of patients with stable angina whose coronary artery CT display plaque narrow area were below 70%, in contrast with coronary artery angiography and intravascular ultrasound, some patients chose only and coronary artery imaging contrast, patients whose coronary artery imaging hemal stricture and intravascular ultrasound display plaque narrow area were under 70% were chosen as study objects. They were divided into two groups, atorvastatin with 20 mg and 40 mg respectively. They received followed-up survey. Half a year's later, their coronary artery CT were checked again, a few patients with frequent angina pectoris mobility rate received the examination of



coronary angiography and intravascular ultrasound.

**Result** The chosen patients aged 40 to 77 years old, including 38 men and 12 women. Their cardiac functions were normal. Besides, there were 37 cases of line intravascular ultrasound, 26 cases of coronary artery lesions of the left anterior descending branch (LAD), 7 cases of left cyclotron branch (LCX), and 17 cases of right coronary artery (RCA), nearly 47 patients with middle lesions, 3 cases for far segment lesions in 3 patients. In the postoperative period, they received liver function examination every one, three and 6 month, and the blood fat examination 6 month later. There were 1 (atorvastatin 20 mg group) patients, due to frequent mobility of angina, whose plaque area increased from 62% to 75%, his minimum pipe cavity area decreased from 6.6 mm<sup>2</sup> to 4.03 mm<sup>2</sup>. This patient no longer suffered from angina symptoms angina symptoms after taking the operation of implanting coronary artery stent. The blood fat total cholesterol (TC) of who received follow-up examination decreased to 1.76 mmol/L on average, while their low density lipoprotein (LDL-C) to 1.83 mmol/L on average, their liver functions are in the normal range, gao min c-reactive protein (Hs - CRP) are also in the normal range. At present, they are receiving the continuing follow-up examinations, which is about to end in 2 months.

**Conclusion** The coronary artery CT examination for plague volume showed that, after half a year's intensive lipid-lowering therapy, the intensive lipid-lowering therapy can reverse plaque volume, improve symptoms, and prevent cardiovascular adverse events.

### Comparison of the clinical characters of the early and median stage after the systemic-pulmonary shunts and the right ventricular to pulmonary artery connection for pulmonary atresia with ventricular septal defect

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**Objective** Comparing the clinical characters of the early and median stage after the systemic-pulmonary shunts and the right ventricular to pulmonary artery connection (RV-PA connection) for pulmonary atresia with ventricular septal defect (PA/Vs D), we try to assess the effects of the two different palliative procedures.

**Methods** We retrospectively analyzed the clinical data of the 89 patients with PA/Vs D who had undergone the systemic-pulmonary shunts or the RV-PA connection in Fu Wai Hospital from Jan. 2009 to Dec. 2011. Compare the clinical characters including the time with ventilator, the time in ICU, the complication, the improvement on oxygen saturation (SpO<sub>2</sub>), the improvement on Nakata index, the rate of complete repair and the mortality in two groups, with the desire to obtain the effects respectively.

**Result** 59 patients performed systemic-pulmonary shunts, 30 patients performed RV-PA connection. There was no statistically difference at age and weight of the two groups when they got operations. The time with ventilator after operation was 34.8 ± 33.5 h and 44.3 ± 39.6 h (P > 0.05), respectively; The time in ICU was 3.6 ± 2.5 d and 4.2 ± 5.1 d (P > 0.05); The incidence of the complication was 37.2% and 30% (P > 0.05); The rate of reoperation was 15.3% and 13.3% (P > 0.05); The incidence of the severe complication was 25.4% and 6.67% (P < 0.05); The improvement on percentage of the oxygen saturation was 22.2 ± 21.4 and 31.7 ± 28.3 (P < 0.05); The Nakata index increased was 74.1 ± 23.4 mm<sup>2</sup>/m<sup>2</sup> and 84.2 ± 48.7 mm<sup>2</sup>/m<sup>2</sup> (P > 0.05); The rate of complete repair was 37.2% and 36.7% (P > 0.05). The interphase between initial palliative procedure and complete repair was 15.2 ± 4.7 m

and 14.3 ± 4.7 m (P > 0.05); the mortality was 8.5% and 0 (P = 0.248).

**Conclusion** Patients who underwent RV-PA connection can have a relative stable period after operation. The improvement on oxygen saturation is significant, which may better promote the diminutive pulmonary rehabilitation. The mortality under this procedure is subsequently low. As a result, the RV-PA connection can be taken as the first palliative management for PA/Vs D. Numerous cases and longer follow-up are still needed.

### A meta-analysis of percutaneous coronary intervention for chronic total coronary occlusions recanalization

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**Objective** To perform an evaluation (meta-analysis) on short-term and long-term prognosis of percutaneous coronary intervention (PCI) for patients with chronic total occlusions (CTO) recanalization.

**Background** Despite advances in procedural techniques and expertise, PCI for CTO recanalization in select patients remains a challenge.

**Methods** Data sources include published studies from a search of PUBMED, ELSEVIER, and CLINICAL.COM from Jan. 2000 to Jul. 2012. Selected studies were either observational studies or randomized clinical trials that compared PCI treatment of CTO recanalization to medical management. The endpoints were analyzed using pooled estimates for death, myocardial infarction (MI), coronary artery bypass surgery (CABG), angina symptoms, repeat revascularization, and major adverse cardiac events (MACE).

**Result** Sixteen observational studies comparing outcomes after failed or successful CTO recanalization with PCI were included in the current analysis. Collectively, these studies enrolled 10 256 patients who were observed at an average follow-up period of 5 years. Patients with successful CTO recanalization demonstrated significantly reduced rates of all-cause death (P < 0.00001), cardiac death (P < 0.00001), MACE (P < 0.0001), MI (P = 0.003), subsequent CABG (P < 0.00001), and long-term repeat revascularization (P = 0.03). In addition, successful CTO improved quality of life (P = 0.0001), reduced both MACE (P < 0.00001) and mortality (P = 0.004) in patients with multivessel disease; although there was no difference in the rates of death and MACE in patients with SAD.

**Conclusion** PCI should be considered an effective option for the patients with CTO lesions.

### Efficacy and safety of bivalirudin vs heparin plus glycoprotein IIb/IIIa inhibitors in patients undergoing percutaneous coronary intervention: a meta-analysis of randomized trials

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**Background** Recently, several randomized trials which compared bivalirudin with heparin plus glycoprotein IIb/IIIa inhibitors (GPIs) in patients undergoing percutaneous coronary intervention (PCI) had been published. The purpose of this study was to perform an up-to-date meta-analysis of randomized trials on the effectiveness and safety of bivalirudin vs heparin plus GPIs in patients undergoing PCI.

**Methods** All published clinical randomized trials which compared heparin plus GPIs with bivalirudin in patients undergoing PCI were

included. The literature was searched by electronic databases which contained MEDLINE, Pubmed, Elsevier, Cochrane clinical trials and Clinical Trials.gov database from January 2000 to December 2011.

**Result** Ten randomized trials enrolling 21 932 patients were included. Compared with heparin plus GPIs, bivalirudin associated with lower rates of major bleeding ( $P < 0.00001$ ), minor bleeding ( $P < 0.00001$ ), long-term mortality ( $P = 0.02$ ), and short-term net clinical adverse events ( $P = 0.004$ ). There was no significantly different rates of the major adverse cardiovascular events ( $\leq 30$  days:  $P = 0.26$ ;  $> 30$  days:  $P = 0.10$ ) and myocardial infarction events ( $\leq 30$  days:  $P = 0.19$ ;  $> 30$  days:  $P = 0.84$ ) between two groups. However, bivalirudin administration resulted in an increased long-term incidence of target vessel revascularization ( $P = 0.02$ ) and a high trend in individual definition of revascularization ( $P = 0.07$ ).

**Conclusion** Among the patients who undergoing PCI, anticoagulation with bivalirudin Result in significantly lower rates of bleeding, long-term mortality and short-term net clinical adverse events when compared with heparin plus GPIs. Even that bivalirudin had high long-term risk of target vessel revascularization, there are no different in MACE and MI events between two groups.

### Interventional treatment in maintenance hemodialysis patients with acute coronary syndrome

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**Background** To observe the efficacy of percutaneous coronary intervention (PCI) in maintenance hemodialysis (MHD) patients with acute coronary syndrome (ACS).

**Methods** From Jan. 2008 to Oct. 2011, we completed PCI in the 38 MHD patients with ACS in our hospital hemodialysis Division, including 23 males and 15 females, aged 48 – 74 (mean  $64.2 \pm 8.2$ ) years old. Protopathies were diabetic nephropathy in 25 cases, hypertensive renal disease in 11 cases, chronic glomerulonephritis in 2 cases; 33 patients were unstable angina, 4 patients were acute non-ST-segment elevation myocardial infarction, and 1 patient was acute ST-segment elevation myocardial infarction. 1 day before PCI, all patients took aspirin 300 mg and clopidogrel 300 mg then took clopidogrel 75 mg for 1 year and aspirin 100 mg for lifetime. The Result of coronary angiography were observed. All cases received 1-year follow-up about the adverse cardiovascular and cerebrovascular events (MACCE).

**Result** coronary angiography showed all patients with multi-vessel disease, double-vessel disease in 28 patients (73.7%) and three-vessel disease in 10 patients (26.3%). All patients were deployed with drug-eluting stents (DES). Implanted stents diameter was an average of  $3.0 \pm 0.3$  mm, and length were an average of  $37.7 \pm 23.9$  mm. The angina symptoms disappeared in all patients, while no intraoperative deaths happened. Postoperative angina occurred in 4 cases (10.5%), which relieved after medication adjustment and no one accepted coronary angiography again. NO acute myocardial infarction happened. 1 patient died of acute left ventricular failure, and 1 patient died of cerebral hemorrhage. MACCE occurred in 5.3%.

**Conclusion** Interventional therapy can improve quality of life and survival in MHD patients with ACS.

### Long-term follow-up study of patients with covered stent implantation after coronary perforation

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**Background** To evaluate the long-term efficacy of covered stent implantation to the patients with coronary perforation occurred in percutaneous coronary intervention (PCI).

**Methods** From Jun. 2004 to Mar. 2011, a total of 8 cases received 8 covered stents implantation because of coronary perforation in our center. Ellis grade III coronary perforation occurred in 7 patients and Ellis grade I in 1 patient. The patients took clopidogrel 75 mg/d for 2 years, and 100 mg/d for lifetime. The major adverse cardiac events (MACE) were observed in the 8 patients through long-term follow-up.

**Result** There were 5 males and 3 females in the 8 patients who aged 63 – 76 (mean  $69.3 \pm 4.7$ ) years. Six patients had multi-vessel disease. The target vessels were left anterior descending artery (LAD) in 7 patients. Calcified lesions emerged in 3 patients and total occlusion lesions in 3 patients. In addition to 2 patients with balloon dilating after guidewire into the false lumen, the coronary artery perforation of the remaining six patients were associated with too high pressure of stent expansion or balloon dilating. Pericardial tamponade happened in 7 patients, and pericardial effusion of 100 – 470 ml was drained by pericardiocentesis. Implanted covered stents average diameter was  $3.3 \pm 0.3$  mm, and average length was  $21.3 \pm 4.1$  mm. All perforation of the patients were successfully closed, while no patients died in PCI. During follow-up of 0.6 – 67 months (mean  $35.3 \pm 25.1$  months), 2 patients died. Nineteen days after PCI, one patient died of multiple organ failure due to lung infection. Thirteen months after PCI, another patient died of cardiac sudden death. One patient was hospitalized with angina pectoris after 53 months, and the symptoms were relieved. The imaging was not reviewed. After 6 months one patient received multi-slice CT examination, and no restenosis was found. He was currently asymptomatic. The remaining four patients were reviewed coronary angiography after 15 – 67 months. Only one patient showed LAD stent restenosis and received target vessel revascularization. The remaining 3 patients had no restenosis within the stent. During the entire follow-up, restenosis rate was 20% (1/5), mortality rate was 25% (2/8) and MACE rate was 50% (4/8). If follow-up after PCI was 12 months, MACE rate decreased to 25% (2/8).

**Conclusion** Treatment of covered stent to coronary perforation can achieve good long-term efficacy. Two-year dual antiplatelet drugs can be effective in preventing covered stent thrombosis.

## Effects of intracoronary sodium nitroprusside compared with adenosine on fractional flow reserve measurement

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**Background** At present, adenosine (AD) is the most widely used agents in fractional flow reserve (FFR) measurement but has the disadvantages of higher rate of complications including atrioventricular block. So it's necessary to explore other stimulus equivalent to or better than AD in effects on FFR measurement with less complications and lower costs.

**Methods** In 40 patients with 53 moderate coronary stenosis, intracoronary (IC) AD in 2 serial doses (A1: 40 µg; A2: 60 µg) was administered in the standard bolus to calculate FFR, followed by a repeat FFR measurement with IC Sodium Nitroprusside (SNP) in 3 serial doses (S1: 0.3 µg/kg; S2: 0.6 µg/kg; S3: 0.9 µg/kg).

**Result** ① Target lesions were located in the left anterior descending (n = 24), left circumflex (n = 13) and right coronary artery (n = 16). The mean stenosis rate was  $62.8 \pm 8.6\%$ . ② FFR value decreased significantly from  $0.90 \pm 0.05$  at baseline to  $0.83 \pm 0.06$ ,  $0.82 \pm 0.07$ ,  $0.83 \pm 0.07$ ,  $0.81 \pm 0.07$  and  $0.81 \pm 0.07$  in A1, A2, S1, S2 and S3 (F = 16.877, P < 0.001). ③ Systolic blood pressure decreased by 3.99%, 6.64%, 6.87%, 10.56% and 15.55% in A1, A2, S1, S2 and S3. ④ Heart rate was increased by 2.01%, 0.84%, 1.23%, 1.34% and 3.11% in A1, A2, S1, S2 and S3. ⑤ The mean time to peak value of FFR delayed in S1, S2 and S3 compared with A2 (F = 15.593, P < 0.001). ⑥ The meanduration of the plateau phase was longer in S1, S2 and S3 compared with A2 (F = 34.445, P < 0.001), and longer in S3 than S1 (F = 7.392, P = 0.008). ⑦ Immediate complications occurred in 15.1% of patients, including transient atrioventricular block (6 patients), chest pain (1 patient) and stomachache (1 patient) after the 60 µg dose of IC AD bolus was administered. No adverse events were found after 3 serial of doses IC SNP were used. ( $\chi^2 = 8.171$ , P = 0.004).

**Conclusion** Compared with IC AD, IC SNP has equivalent effects on FFR measurement as well as the advantage of lower rate of complications and cost. But duration of the plateau phase by IC SNP is twice as much by IC AD, and time to peak FFR value was delayed 50%.

## Safety and long-term efficacy of left subclavian artery coverage during thoracic endovascular aortic repair

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**Background** To observe the safety and long-term efficacy of left subclavian artery (LSA) coverage during thoracic endovascular aortic repair (TEVAR).

**Methods** Retrospectively analyzed the clinical data and outcomes

perioperatively and during follow-up in 278 patients who were suffered from Stanford B aortic dissection and accepted TEVAR between Apr. 2002 and Jul. 2011. Among those patients, 77 had lesions that required LSA coverage and 201 had their LSA uncovered.

**Result** The patients with coronary artery disease and hypertension were more often seen in LSA-uncovered group, while those with penetrating atherosclerotic ulcer were less seen in this group (P < 0.05). The other clinical baseline data had no statistics differences between two groups. The success ratios of TEVAR were both 100% in two groups. The proximal landing zones were shorter ( $8.0 \pm 6.5$  mm vs  $28.3 \pm 10.1$  mm, P = 0.000) while the aortas covered by stent grafts were longer ( $132.6 \pm 24.7$  mm vs  $122.0 \pm 38.9$  mm, P = 0.011) in LSA-covered group compared with those in LSA-uncovered group. The postoperative systolic pressures of left and right upper limbs were ( $80.5 \pm 37.3$  mm Hg and ( $128.7 \pm 22.6$ ) mm Hg (P = 0.000) in patients with LSA covered completely and were ( $115.8 \pm 25.7$ ) mm Hg and ( $125.5 \pm 27.4$ ) mm Hg in those with LSA covered partially (P = 1.805). No statistics differences occurred between two groups referring to the mean aortic diameters, incidences of endovascular leakage, post-implantation syndrome (transient elevations of body temperature, C-reactive protein and mild leukocytosis) and incision infection. Transient movement disorder of both lower extremities occurred in two patients in the LSA-uncovered group within the first 24 hours postoperatively, while paraplegia developed in neither group during hospital stay. Patients presented with cooling, discoloration, pain and weakness of left upper extremity and pulselessness of left brachial artery were more often seen in LSA-covered group during perioperative and follow up period. The incidence of cooling, discoloration, pain and weakness of left upper extremity and stroke, together with the mortality had no statistics differences between patients with LSA covered completely or partially. The pulselessness of left brachial artery presented more often (P = 0.000) while the weakness of that presented less often (P = 0.001) in patients with LSA covered completely compared with those with LSA covered partially. No blood vessel by-pass grafting was performed on account of severe left arm ischemia.

**Conclusion** It is safe and feasible to cover LSA for managing the insufficiency of proximal landing zone in patients with Stanford B AD during TEVAR. Better long-term efficacy could be achieved in this way.

## Correlation between blood uric acid level and severity of coronary lesions

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**Background** To investigate the characteristics of intravascular ultrasound (IVUS) image of target borderline lesion in the proximal anterior descending artery (LAD) for finding the basement to treating these patients with the lesions.

**Methods** The borderline lesions with 30% – 70% dimension stenosis in the proximal LAD were found in 10 patients from Jun. 2010 to Oct. 2011. All the 10 patients had some discomfort in the precordium, including 7 males, 1 with diabetes, 3 with hypertension, 2 smokers and 2 with infarct history. The intervention was done in the patient with the typical syndrome after IVUS. For the atypical patients, the exercise test was done. The intervention was done in the positive patient after IVUS.

**Result** The discomfort in the precordium disappeared in all the 10 patients. The minimal lumen area (MLA) of them in the proximal LAD was  $4.85 \pm 1.49$  mm<sup>2</sup>. MLA in the 7 patients was more than 4 mm<sup>2</sup>. The



area stenosis (AS) of them in the proximal LAD was  $69.99\% \pm 7.07\%$ . AS in the 4 patients was less than 70%.

**Conclusion** It is questionable that the  $4 \text{ mm}^2$  of MLA or 70% of AS was considered to be the cut-off value for the intervention therapy. The suitable strategy to the patients with borderline lesion in the proximal LAD should come from the combination of IVUS and clinical condition.

### Efficacy and safety of fondaparinux during thrombolytic therapy in acute ST-elevation myocardial infarction patients

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**Background** To assess efficacy and safety of Fondaparinux during thrombolytic therapy in acute ST-elevation myocardial infarction patients.

**Methods** From Nov. 2011 to Apr. 2012, patients with acute ST-elevation myocardial infarction and pain to hospital time within 6 hours were received thrombolytic therapy by recombinant tissue-type plasminogen activator (rt-PA). Before thrombolytic therapy, patients were randomly assigned to Fondaparinux group (2.5 mg,  $n = 30$ ) or standard heparin group (60 U/kg, maximum 4000 U,  $n = 32$ ). Coronary angiography or PCI were performed at 90min after initiating study drugs. Primary endpoints of the trial were the rate of TIMI grade 3 flows at 90minutes. Other endpoints included incidence of all cause mortality at in-hospital, 30 days and 6 months, major bleeding and minor bleeding at in-hospital, 30 d and 6 months.

**Result** (1) There were no difference of primary endpoints (Fondaparinux group vs heparin group, 64.6% vs 62.5%,  $P = 0.158$ ). (2) PCI procedure: Successful rate of immediate post-procedure was 100%. The average number of stents per patient was  $1.1 \pm 0.4$  and the average diameter and length of stent were ( $3.0 \pm 0.7$ ) and ( $21.2 \pm 3.1$ ) mm. (3) Safety: No significant difference existed between fondaparinux group and heparin group in major bleeding (in-hospital, 30 d and 6 months,  $p > 0.05$ ). However, the fondaparinux group had a lower prevalence of mild bleeding than heparin group (in-hospital and 30 d,  $p < 0.05$ ). (4) In-hospital and all cause mortality at 30 d and 6 months: Average follow up time was  $6.8 \pm 2.1$  months. Fondaparinux group had a lower mortality of in-hospital but has no statistical difference ( $P > 0.05$ ). Mortality at 30 d and 6 months were all similar in Fondaparinux treated patients compared to heparin treated patients ( $P > 0.05$ ).

**Conclusion** Fondaparinux, which can reduce the time of reperfusion with decreasing mortality and mild hemorrhage, is feasible and safe for the patients with STEMI during thrombolysis therapy

### The efficacy and security analysis of interventional therapy supported by intra-aortic balloon pump for patients with high risk coronary heart disease

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**Background** To evaluate the efficacy and security of percutaneous coronary intervention (PCI) supported by intra-aortic balloon pump (IABP) for patients with high risk coronary heart disease.

**Methods** We retrospectively reviewed immediate success rate of PCI, in-hospital survival rate and complications of 624 patients with high risk coronary heart disease who underwent PCI supported by IABP in our institution from January 2000 to October 2011.

**Result** Out of all the 624 patients, 71% were ST-elevation myocardial infarction (STEMI), 21% were none ST-elevation myocardial infarction (NSTEMI) and 8% were unstable angina pectoris (UAP). The patients (averagely aged 68 years and 71% were males) suffered from hypertension (78%), family history of coronary heart disease (34%), abnormal metabolism of serum lipids (69%) and diabetes (45%). The latter two seemed presenting more frequently in patients with acute myocardial infarction (AMI). The incidence of major adverse cardiovascular events (MACE) in STEMI and NSTEMI group was significantly higher than that in UAP group (3.1% and 2.9% vs 0.01%,  $P < 0.01$ ). So was the mortality rate (1.7% and 1.1% vs 0.4%,  $P < 0.01$ ). Before hospital discharge, a majority of patients received antiplatelet therapy and evidence based drug therapy, including angiotensin converting enzyme inhibitor (ACEI)/angiotensin receptor blockers (ARBs), beta-blockers, calcium channel blockers and statins. With the support of IABP, immediate success of PCI was achieved in 323 cases with an immediate success rate up to 97.6% (609/624); in-hospital survival in 576 cases with a survival rate up to 92.3% (576/624); IABP success rate was 100%; total incidence of IABP complications needed to be handled was 4.5% (28/624).

**Conclusion** The success rate of PCI for patients with high risk coronary heart disease is extremely high when IABP support was applied, with an ideal prognosis and decreased complications. This method is clinically safe and efficient with high feasibility. The advantages become more evident when treating patients with AMI complicated by high risk of cardiogenic shock.

### Cardioprotective effects of single oral dose of nicorandil before selective percutaneous coronary intervention

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**Background** Nicorandil, an opener of ATP-sensitive  $K^+$  channels, was used to treat angina in patients with coronary artery disease. In this study, we aim to investigate the cardioprotective effects of single oral dose of nicorandil in patients undergoing selective percutaneous coronary intervention (PCI).

**Methods** One hundred and thirty-eight patients with acute coronary syndrome undergoing PCI from Jul. 2011 to Oct. 2012 were randomly divided into control group (group 1,  $n = 47$ ), 10 mg oral nicorandil group (group 2,  $n = 45$ ), and 20 mg oral nicorandil group (group 3,  $n = 46$ ) about 2 hours before procedure, respectively. Cardiac troponin I (cTnI) levels were determined at 20–24 hours after PCI.

**Result** There was a significant difference in the rate of any cTnI elevation among the three groups (group 1: 36.17%, group 2: 20.00%, group 3: 15.22%,  $P = 0.0176$ ). With respect to the frequency of cTnI elevation  $\geq 3$  and  $5 \times$  the upper limit of normal (ULN), there also had statistical difference among the three groups (17.02% in group 1, 8.89% in group 2, and 4.35% in group 3, respectively for cTnI elevation  $\geq 3 \times$  ULN,  $P = 0.0428$ ; 12.77% in group 1, 6.67% in group 2, and 2.17% in group 3, respectively, for cTnI elevation  $\geq 5 \times$  ULN,  $P = 0.0487$ ). Logistic regression analysis showed that

LVEF (OR = 0.915, 95% CI = 0.856 – 0.978) and the use of nicorandil (OR = 0.519, 95% CI = 0.295 – 0.912) before PCI were independent protective factors of myocardial injury.

**Conclusion** Single oral dose of nicorandil (10 mg, 20 mg) 2 hours before the PCI procedure could decrease the incidence of peri-procedure myocardial injury and PCI-related myocardial infarction.

### Comparative performance of different warfarin pharmacogenetic algorithms in Chinese patients

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**Objective** To compare the clinical value of different algorithms to predict the warfarin maintenance dose in Chinese Han population.

**Methods** A total of 488 Chinese Han patients from Fuwai hospital were recruited, who had stable dose of warfarin and target INR ranged from 1.5 to 3.0, and the indications for warfarin included prosthetic heart valve, atrial fibrillation and pulmonary embolism. These patients were divided into derivation group (n = 323) and validation group (n = 165) randomly. In derivation group we developed a warfarin maintenance dose algorithm based on genetic information, demographic characteristics and concomitant medications by multiple linear regression. In the validation group, we evaluated the accuracy of our algorithm, IWPC (The International Warfarin Pharmacogenetics Consortium) recommended algorithm, Miao's and Huang's algorithm by comparing the predicted dose with the actual dose. The performance of each algorithm was evaluated by calculating the percentage of patients whose predicted dose fell within 20% of their actual therapeutic dose (Percentage within 20%).

**Result** Our algorithm to predict warfarin maintenance daily dose included VKORC1-1639G > A, CYP2C9\*3 and CYP4F2 genotype, age, height, body weight, application of amiodarone and digoxin ( $R^2 = 0.652$ ,  $P < 0.001$ ). In the validation group, the average predicted dose by our algorithm had no statistical difference with the actual dose ( $3.51 \pm 1.03$  mg vs  $3.53 \pm 1.41$  mg,  $P = 0.779$ ); however, the predicted doses by IWPC, Miao's and Huang's algorithms were lower than the actual dose ( $3.10 \pm 0.83$  mg,  $2.68 \pm 1.71$  mg,  $2.95 \pm 0.75$  mg,  $P < 0.001$ ). Our algorithm identified 60.6% patients, whose predicted dose of warfarin were within 20% of the actual dose, 17.6% patients, whose predicted dose of warfarin were lower than 20% of the actual dose, and 21.8% patients, whose predicted dose of warfarin were higher than 20% of the actual dose; IWPC, Miao's and Huang's algorithm identified 52.7%, 25.4% and 46.7% patients, who predicted dose of warfarin fell within 20% of the actual dose, respectively; meanwhile the percentage of patients whose predicted dose of warfarin were underestimated by these 3 algorithms were higher than our algorithm (32.7%, 67.3%, 40%,  $P < 0.05$ ).

**Conclusion** Our algorithm is more accurate to predict the warfarin maintenance dose in Chinese Han Population, but prospective validation study in large population are needed.

### Is being an elderly woman a risk factor for worse outcomes after percutaneous coronary intervention? A large cohort study from one center

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**Background** Females, as compared to males have more risk factors and comorbidities, whose severity increases with age. While it has remained undefined because of conflicting Result in previous studies whether female gender is a risk factor for worse outcomes after percutaneous coronary intervention (PCI), the combination of being elderly (i.e., > 75 years old) and female may be a risk factor. There are thus far no solid data in this area.

**Methods** 29211 consecutive patients who underwent PCI [521 elderly females (> 75 years old); 5 666 young females (< 75 years old); 1 098 elderly males and 21 926 young males) at the Fu Wai Hospital in Beijing, were analyzed.

**Result** During hospitalization, elderly females had significantly higher rates of cardiac death and MACE ( $P < 0.05$ ). Kaplan-Meier estimated 3-year rate of cardiac death was significantly higher in elderly females in comparison with all other groups ( $P < 0.05$ ). Using Cox proportional hazard models, being an elderly female was a significant risk factor for cardiac death, cardiac death/MI in comparison with being a young female [OR (95% CI): 2.53 (1.15 – 5.59), 2.26 (1.27 – 4.03)] or young male [OR (95% CI): 2.22 (1.26 – 3.91), 2.25 (1.44 – 3.51)]; however, it was not a significant risk factor in comparison with being elderly male [OR (95% CI): 1.30 (0.97 – 1.71), 1.21 (0.94 – 1.55)].

**Conclusion** Elderly females had worse in-hospital and long-term outcomes after PCI therapy than other gender and age groups, but being an elderly female not an independent risk factor for worse PCI outcomes.

### Long-term efficacy of PCI vs CABG for patients with multiple coronary chronic total occlusions

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**Background** Data on the efficacy of percutaneous coronary intervention (PCI) for treatment of multiple coronary chronic total occlusion (CTO) lesions are scanty. The optimal revascularization strategy for multiple coronary CTO disease in the era of drug-eluting stents (DES) has become more controversial between coronary artery bypass grafting (CABG) and PCI. The aim of the present study is to compare the long-term outcomes of DES implantation for multiple coronary CTO lesions compared with CABG.

**Methods** We analyzed 261 patients who underwent coronary angiography for at least two de novo CTO lesions in our center from Nov. 2000 to Nov. 2006. Among them, 118 patients (45.2%) received DES implantation after recanalization for CTO lesions and 143 patients (54.8%) received CABG. Major adverse cardiac and cerebrovascular events (MACCE: death, acute myocardial infarction, stroke and repeat revascularization) and hospitalization costs were compared. Long-term

survival rates were estimated with the Kaplan-Meier method.

**Result** Patients in the CABG group were likely to have hyperlipidemia, diabetes mellitus, multivessel disease and higher euroSCORE. The mean follow-up was  $4.2 \pm 0.7$  years in the CABG group and  $4.3 \pm 0.5$  years in the DES group. Total hospitalization costs were lower ( $P = 0.017$ ) in the CABG group (median: 107 thousand Yuan) than in the DES group (median: 156 thousand Yuan). Rates of MACCE at 12 months were higher in the PCI group (16.9% vs 11.2% for CABG;  $P = 0.179$ ), but not statistically significant, in large part because of an increased rate of repeat revascularization (15.3% vs 7.0%,  $P = 0.016$ ). The overall survival rate (CABG: 73.4% and DES: 76.2% at 5 years,  $P = 0.599$ ) and the TVR-free survival rate did not differ between the groups.

**Conclusion** This study demonstrates the long-term (up to 5 years) efficacy and safety of DES for treatment of multiple coronary CTO lesions. The long-term survival rate of PCI with DES was comparable to that of CABG for the treatment of multiple coronary CTO. PCI with DES was more costly than CABG. PCI using DES might be an alternative to CABG in selected patients with multiple coronary CTO disease.

### The efficacy and safety of ivabradine hydrochloride tablets vs atenolol tablets in patients with chronic stable angina pectoris – a randomized, double-blind, double-dummy, multicentered active-controlled, parallel-arm phase II clinical trial

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**Objective** To evaluate the efficacy and safety of Ivabradine Hydrochloride Tablets in patients with chronic stable angina pectoris.

**Methods** This is a randomized, double-blind, double-dummy, multicentered, active-controlled, parallel-arm phase II clinical trial, conducted between Oct. 2009 and Jul. 2012. We compared Ivabradine Hydrochloride with Atenolol in patients with evidence of coronary artery disease (CAD) and chronic stable angina pectoris for at least 3 months before study entry. Briefly, we included 334 male and female patients aged between 18 and 70 years. All the patients in accordance with the inclusion criteria should withdrawal the medicine that can affect heart rate. After -7 – 0 days the patients with positive Exercise tolerance test (ETT) were randomized into two groups (if had not treated with similar drugs can be directly tested ETT): IVA-HCL group (treated with Ivabradine Hydrochloride tablets 5 mg bid) or Atenolol group (treated with Atenolol 12.5 mg bid) for 4 weeks. Adjusted the dose according to ETT test Result and heart rate after 4 weeks, either continued to use the original dose (IVA-HCL group, 5 mg bid; Atenolol group, 12.5 mg bid) or increased the dose (IVA-HCL group, 7.5 mg bid; Atenolol group, 25 mg bid) and then continue the treatment for 8 weeks. Compare the ETT value changes at three time points (before taking the medicine, just 4 weeks and 8 weeks after) between the two groups. Meanwhile, evaluated the drug related mortality, cardiac death, myocardial infarction and other adverse events in the process of drug use and within 7 days of medicine treatment.

**Result** Actually 334 patients enrolled in this study, but 2 persons in the IVA-HCL group did not take medicine. Therefore, there were 332 patients (IVA-HCL group  $n = 166$ ; Atenolol group  $n = 166$ ) included in the final

statistics. Clinical and ETT characteristic at baseline were similar between patients randomized to the IVA-HCL and Atenolol group ( $P > 0.05$ ). After 4 weeks of treatment, the primary efficacy criterion, change in total exercise duration (TED), increased by  $54.28 \pm 120.11$  s ( $P < 0.05$ ) in the IVA-HCL group compared with  $58.77 \pm 114.67$  s ( $P < 0.05$ ) in the Atenolol group ( $P > 0.05$ ). Patients experienced an improvement in TED of  $84.12 \pm 174.42$  s ( $P < 0.05$ ) in the IVA-HCL group after 8 weeks of treatment. There were also improvements with Atenolol treatment, relative to baseline, in TED value (increased by  $77.76 \pm 126.60$  s,  $P < 0.05$ ) at the end of 8<sup>th</sup> week. The TED had increased in both groups but there was no difference ( $P > 0.05$ ). There were small, non-significant changes in adverse events between the two groups ( $P > 0.05$ ). In the IVA-HCL group the number was 66, and 73 in the Atenolol group. Phosphenes (luminous phenomena described as increased brightness in limited areas of visual field) and blurred vision, which have been associated with Ivabradine treatment in previous studies, were reported by 9 patients (5.42%) in the IVA-HCL group ( $P < 0.05$ ). And one patient (0.6%) experienced moderate bronchospasm in the Atenolol group with none in the IVA-HCL group.

**Conclusion** Coronary patients can enjoy a number of clinical benefits from pure heart rate reduction. Ivabradine Hydrochloride Tablets have similar efficacy and safety in treat of patients with chronic stable angina pectoris vs Atenolol, as reported previously. Ivabradine is well tolerated in the study.

### Angiographic features of patients with atherosclerosis in the segments proximal to the myocardial bridge

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**Background** By studying the clinical and imaging features of myocardial bridge and severe atherosclerosis lesions in the segments proximal to the myocardial bridge, compared with that of pure myocardial bridge retrospectively, to analyze the clinical and imaging characteristics of these patients.

**Methods** The study population consisted of 2 groups (192 patients). The CHD Group included 92 patients with severe atherosclerosis lesion of luminal narrowing of  $\geq 70\%$  in the segments proximal to the myocardial bridge. The bridge group included 100 patients with symptomatic myocardial bridge lesion of systolic luminal narrow. All lesions were successfully treated with stent by standard interventional techniques. Quantitative coronary angiography was performed before and immediately after stent deployment.

**Result** The mean age and systolic pressure in the CHD patients were more than that in the pure bridge group ( $58 \pm 11$  vs  $42 \pm 10$  vs and  $157.8 \pm 9.8$  vs  $146.1 \pm 10.2$  mm Hg, respectively),  $P < 0.05$ . No significant difference was found between two groups such as gender, DM, smoking, hyperlipidemia, old myocardial infarction percentage. There was a significant difference in the extent of diameter stenosis during systolic stage between CHD and bridge groups ( $95 \pm 5\%$  vs  $90 \pm 7\%$ ). But the average length from the proximal end of myocardial bridge to the ostium of LAD and the average length of myocardial bridge had no difference between two groups.

**Conclusion** The patients with severe atherosclerosis lesion in the segments proximal to the myocardial bridge has more risk factors of CHD, the extent of diameter stenosis during systolic stage has some



promotive effect on CHD.

### Features and treatments of hypertension in elderly patients with Stanford B aortic dissection

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**Background** To summarize the features and treatments of hypertension in elderly patients with Stanford B aortic dissection.

**Methods** Retrospectively analyzed the features and treatments of hypertension between the elderly patients ( $\geq 60$  years,  $n = 91$ ) and the non-elderly patients ( $< 60$  years,  $n = 187$ ) who were suffered from Stanford B aortic dissection and hospitalized between April 2002 and July 2011.

**Result** The proportion of male in elderly group was higher than that in non-elderly group ( $P < 0.05$ ). Smoking was similarly common in both groups. The proportions of patients accompanied with diabetes mellitus, hyperlipidemia, hypertension and renal inadequacy had no statistics differences between two groups. Coronary artery disease, atherosclerotic ulcer and cardiac insufficiency were more often seen in elderly group ( $P < 0.05$ ). Histories of hypertension were more often given while the first-time diagnosis of hypertension were made less frequently in elderly group ( $P < 0.05$ ). Isolated systolic hypertensions were seen with greater frequency in the elderly group ( $P < 0.05$ ). The courses of hypertension were longer in the elderly group than those in the non-elderly group ( $P < 0.05$ ). The proportions of family history of hypertension and hypertension of grade 1, grade 2 and grade 3 had no statistics differences between two groups. The highest systolic pressures, diastolic pressures and pulse pressures of the patients on admission and the average systolic pressures, diastolic pressures and pulse pressures after treatments had no statistics differences between two groups. The combined treatments were applied frequently in both groups. The usages of intravenous drugs had no differences between two groups. Combinations of 2 antihypertensive drugs were more often used in the elderly group than those in the non-elderly group ( $P < 0.05$ ). Combinations of 3 antihypertensive drugs were used most frequently in both groups. Calcium-channel blocker,  $\beta$ -receptor blocker, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, diureticum, angiotensin receptor blocker+diureticum and  $\alpha_1$ + $\beta$  receptor blocker were adopted in turn as hypotensive drugs in elderly group.  $\alpha_1$ + $\beta$  receptor blocker was less used in the elderly group ( $P < 0.05$ ).

**Conclusion** The awareness rate of hypertension was higher and the highest blood pressures on admission were lower in elderly patients with Stanford B aortic dissection. The types of anti-hypertension drugs were less and  $\alpha_1$ + $\beta$  receptor blocker was less used in the elderly group.

### Features and treatments of hypertension in elderly female with Stanford B aortic dissection

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**Background** To summarize the features and treatments of

hypertension in elderly female with Stanford B aortic dissection.

**Methods** Retrospectively analyzed the features and treatments of hypertension in the elderly male group ( $\geq 60$  years,  $n = 67$ ) and the elderly female group ( $\geq 60$  years,  $n = 41$ ) who were suffered from Stanford B aortic dissection and hospitalized between April 2002 and July 2011. The average ages were ( $66.8 \pm 5.3$ ) and ( $65.5 \pm 4.6$ ) respectively.

**Result** The average ages were similar in the two groups. The proportions of patients accompanied with smoking history, diabetes mellitus, coronary artery disease, hyperlipidemia, hypertension, atherosclerotic ulcer, cardiac insufficiency, renal inadequacy and hypoxemia had no statistics differences between two groups. The histories of hypertension were less aware of while the first-time diagnosis of hypertension were made more frequently in elderly female group ( $P < 0.05$ ). The proportions of grade 1, grade 2 and grade 3 hypertension and the courses of the disease had no statistics differences between two groups. The highest systolic pressures and pulse pressures on admission and the average systolic pressures, diastolic pressures and pulse pressures after treatments had no statistics differences between two groups. The highest diastolic pressures on admission were higher in elderly female than those in elderly male ( $P < 0.05$ ). The combined treatments were applied frequently in both groups. The usages of intravenous drugs and types of oral hypotensive drugs had no differences between two groups. Calcium-channel blocker,  $\beta$ -receptor blocker, angiotensin-converting enzyme inhibitor, diureticum, angiotensin receptor blocker, angiotensin receptor blocker+diureticum and  $\alpha_1$ + $\beta$  receptor blocker were adopted in turn as hypotensive drugs in elderly female group. Diureticum was used more often in the elderly female group ( $P < 0.05$ ). The rates of reaching standard blood pressure, total mortalities and mortalities related to aortic dissection during follow up had no differences in two groups.

**Conclusion** The elderly female with Stanford B aortic dissection were characterized with less awareness of hypertension and higher diastolic pressures on admission. Ideal blood pressures reaching the standard could be achieved after normal anti-hypertension therapy. Emphasis should be put on the early diagnosis of elderly female population. Hypotensive drugs should be applied reasonably and blood pressures should be controlled strictly in order to lower mortalities and improve prognosis.

### Effect of deanxit on patients with heart failure secondary to valvular heart disease combined anxiety and depression

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**Background** To investigate the effect of deanxit on subjects with heart failure secondary to valvular heart disease combined anxiety and depression.

**Methods** After 60 patients being evaluated by HAMA and HAMD, the positive subjects were followed up for 2 weeks. According to baseline assessments, the patients were randomly divided into experimental group (basic drug therapy and Deanxit) and control group (only basic drug therapy). Cardiac function parameters and score of HAMA and HAMD were compared.

**Result** Compared with control group, Cardiac function improved markedly, the scores of HAMA and HAMD in experiment groups were significantly lower than those before treatment while little changes in the scores of HAMA and HAMD were found in those of the control group.

**Conclusion** To use Deanaxit combined anti-heart failure drugs could gain better synergic effect in the patients of heart failure secondary to valvular heart disease with anxiety and depression.

### Effect of CYP2C19\*2 and \*3, ABCB1 C3435T, and PON1 Q192R alleles on platelet reactivity and adverse clinical events in Chinese people treated with clopidogrel after percutaneous coronary intervention

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**Objective** Chinese people carry more often CYP2C19 loss-of-function alleles than Caucasian. Effect of the ABCB1 and PON1 variants on platelet reactivity and clinical outcomes of clopidogrel has not been reported in Chinese patients after percutaneous coronary intervention. The aim of this study was to investigate the effect of the CYP2C19, ABCB1, and PON1 variants on pharmacodynamics and clinical outcomes of clopidogrel in these patients.

**Methods** 670 Patients after angioplasty and stenting were enrolled in a single-center registry. The antiplatelet effect of clopidogrel was assessed by thrombelastography and the CYP2C19, ABCB1, and PON1 genotypes were detected by the ligase detection reaction. Primary clinical endpoints included cardiovascular death, nonfatal myocardial infarction, target vessel revascularization, and stent thrombosis. The secondary clinical endpoints were TIMI major or minor bleeding. The follow-up period was 12 months.

**Result** The frequency of the CYP2C19 LOF alleles was relatively high (57.3%,  $n = 384$ ; \*2/\*17 = 2, \*3/\*17 = 1, \*1/\*2 = 249, \*1/\*3 = 56, \*2/\*2 = 60, \*2/\*3 = 15, and \*3/\*3 = 1), and the CYP2C19 gain-of-function allele frequency was relatively low (0.925%; \*1/\*17 = 10). Platelet reactivity increased proportionally with the number of CYP2C19 LOF alleles. The risk of clopidogrel low response (CLR) also increased with the number of CYP2C19 LOF alleles [1 LOF allele: odds ratio (OR) 1.9, 95% confidence interval (CI) 1.2 – 3.0,  $P = 0.008$ ; 2 LOF alleles: OR 3.7, 95% CI 2.0 – 6.8,  $P < 0.001$ ]. Platelet reactivity and the rate of CLR did not differ between the CYP2C19\*2 and \*3 alleles. In addition, primary clinical events increased with the number of CYP2C19 LOF alleles: compared with noncarriers, carriers of 1 LOF allele [hazard ratio (HR) 2.7, 95% CI 0.96 – 7.42,  $P = 0.061$ ] and 2 LOF alleles (HR 5.2, 95% CI 1.64 – 16.35,  $P = 0.005$ ) were associated with primary clinical events. The clinical impacts of the CYP2C19\*2 and \*3 alleles were not different. The ABCB1 C3435T and PON1 Q192R alleles were not related to clopidogrel response and primary clinical events. Bleeding was not significantly different across the CYP2C19, ABCB1, and PON1 genotype groups.

**Conclusion** The CYP2C19 loss-of-function alleles had a gene – dose effect on the pharmacodynamics and adverse clinical events of clopidogrel in Chinese population after percutaneous coronary intervention. Neither ABCB1 nor PON1 genotypes significantly influenced on antiplatelet effect or clinical outcomes of clopidogrel in these patients.

### Clinical feature of cor triatriatum in 23 cases

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**Background** To summarize the data of clinical feature, accompanied abnormalities and imaging diagnosis of cor triatriatum in 23 cases enlisted in the study.

**Methods** From Jan. 1993 to Jun. 2005, twenty-three patients, 13 males and 10 females with a mean age of ( $9.6 \pm 10.0$ ) years (range 0.3 from 38 years) were studied. All cases were cor triatriatum laevis. Twenty-one of 23 patients were identified in surgery. Complete cor triatriatum in 15 case and incomplete cor triatriatum in 6. Electrocardiogram show that right unsymmetrical cardiac axis was in 18 patients and normal cardiac axis in 4. Eight cases had lung congestion in x-ray.

**Result** Echocardiogram diagnosed 12 in 23 cases before surgery. Heart catheter exam diagnosed 4 in 10 cases. Sixteen of 21 cases accompanied other abnormalities. Main malformations included atrial septal defect ( $n = 14$ ), partial anomalous pulmonary venous drainage ( $n = 6$ ), pulmonary stenosis ( $n = 3$ ), persistent left superior vena cava ( $n = 3$ ). Seven of 21 patients had no atrial septal defect.

**Conclusion** Cor triatriatum had great variation in clinical feature and complicated other malformations in high ratio. Color doppler imaging has high worthiness of diagnosis of cor triatriatum, but misdiagnosis and missed diagnosis rate is high in cor triatriatum accompanied other malformations. Heart catheter exam have missed diagnosis to cor triatriatum, but have higher diagnosis rate to accompanied abnormalities. Surgical exploration is very important in cor triatriatum accompanied other malformations.

### Effect of coexisting polymorphisms of CYP2C19 and P2Y12 on pharmacodynamics and adverse clinical events of clopidogrel in Chinese patients with acute coronary syndromes after percutaneous coronary intervention

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**Background** CYP2C19 G681A single polymorphism had been proved to effect on clopidogrel responsiveness. However, the effect of coexisting polymorphisms of the genes has not yet been reported in Chinese population. The present study investigated the effect of coexisting polymorphisms of CYP2C19 and P2Y12 on clopidogrel pharmacodynamics and adverse clinical events in Chinese patients with acute coronary syndromes (ACS) undergoing percutaneous coronary intervention (PCI).

**Methods** 577 Chinese Han patients with ACS undergoing PCI were enrolled in a single-center registry. The platelet reactivity was assessed by thrombelastography and the CYP2C19 G681A and P2Y12 C34T polymorphisms were detected by the ligase detection reaction. Primary clinical endpoints included cardiovascular death, nonfatal myocardial infarction, target vessel revascularization, and stent thrombosis. The secondary clinical endpoints were thrombolysis in myocardial infarction bleeding. The follow-up period was 12 months.

**Result** Genotyping revealed 194 carriers of the wild GG genotype of

CYP2C19 and the wild CC genotype of P2Y12 (group 1), 102 carriers of the wild GG genotype of CYP2C19 and the mutational T allele of P2Y12 (group 2), 163 carriers of the mutational A allele of CYP2C19 and the wild CC genotype of P2Y12 (group 3) and 118 carriers of the mutational A allele of CYP2C19 and the mutational T allele of P2Y12 (group 4). Group 4 had the lowest ADP-inhibition ( $49.74 \pm 32.61$ ) and the highest prevalence of clopidogrel low response (29.7%) than other groups. The rate of the composite primary endpoints increased more significantly in group 4 (8.5%) than in other groups; the rate of composite primary endpoints in group 2 (2.9%) and 3 (3.7%) had no significant compared with group 1 (1.5%).

**Conclusion** Coexisting, better than single polymorphisms of different genes affected on clopidogrel pharmacodynamics and adverse clinical events in Chinese patients with ACS undergoing PCI.

### Initial experience of occluding special type patent ductus arterioses using the Amplatzer vascular plug I

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**Background** Occluders licensed for clinical use are not fit for some special Krichenko E patent ductus arterioses (PDA). The Amplatzer vascular plug I (Plug I) has not been licensed for use for closure of PDA. We report our initial experience to occluding special type PDA with the Plug I.

**Methods** Patients referred with small and long Krichenko E PDA 1-3 mm in diameter underwent occlusion using this Plug I, this is a single lobe device of single layer Nitinol mesh for short vessel landing zones. All cases underwent pre-, intra- and post-procedural echocardiography at the completion of the procedure the next day and at a 30-day follow-up visit. Device sizing for device waist diameter and length was based on aortography.

**Result** 26 patients with a median age of 5 years (range 6 months – 32 years) and a median weight of 19 kg (range 7 – 67 kg) underwent successful PDA closure. The median ductus diameter was 2.2 mm (range 1 – 3 mm). Both transpulmonary (22/26) and transaortic approaches (4/26) were used. No persistent patency was observed after 24 hours and one month.

**Conclusion** The Plug I makes it easy to close some Krichenko E PDAs. Smaller delivery catheter profile and symmetric cylindrical device shape allow for use for small and long Krichenko E PDA 1 – 3 mm in diameter and small patients through transaortic approaches. Broader experience is required to further delineate device and patient selection as well as to document its long-term efficacy and safety.

### Clinical analysis of treatment for 1149 cases of membranous ventricular septal defect by interventional therapy in children

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**Background** To assess the characteristics and clinical experience of

treatment for pediatric ventricular septal defect by interventional therapy.

**Methods** We collected 1149 children with Vs D who received interventional therapy from 2001 June to 2012 February. There were 578 males and 571 females, age 2.5 – 16 ( $6.8 \pm 3.1$ ) years old and weight 8-54 ( $24.7 \pm 10.6$ ) kg. III – IV systolic regurgitant murmur could be heard at left sternal border between 3-4 intercostal space, pulmonic second sound enhanced or split. UCG showed the diameter of Vs D was 2 – 8 ( $4.3 \pm 1.1$ ) mm. Left ventricular angiography showed the left ventricular surface is 4 – 20 ( $6.38 \pm 3.17$ ) mm, right ventricular surface is 3 – 10 ( $3.81 \pm 1.75$ ) mm and the distance from upper Vs D margin to aortic valve is 0 – 6 ( $2.67 \pm 1.61$ ) mm. 464 patients combined with membranous ventricular septal aneurysm, 15 patients combined with patent ductus arteriosus, 16 patients combined with atrial septal defect and 4 patients combined with muscular Vs D.

**Result** The closure was successful conducted in 1125 patients and the success rate was 98.2%. The diameters of occluder were 4-16 ( $7.56 \pm 2.12$ ) mm. The patients who combined with PDA or ASD, Vs D was first closed and then PDA or ASD. The patients combined with muscular Vs D received occlusion simultaneously. 1061 patients (94.3%) had no shunt instantly, 38 patients (3.4%) had a small shunt and 26 patients (2.3%) had a trace of shunt. 1 cases of postoperative occluder shedding and the occluder was removed and patient received surgical repair of ventricular septal defect. 11 cases of postoperative III degree AVB, 1 patient underwent surgical operation and the rest recovered. 1 patient had III degree AVB 3 years after the occlusion and returned to normal after treatment. 75 cases of complete left bundle branch block, 3 patients did not recovered in the follow up and the rest became normal or not complete left bundle branch block. 1 cases of postoperative hematuria and the symptom disappeared after treatment.

**Conclusion** Strictly indications, standardized operation, proficient skill are the keys to reduce complications and improve the success rate in interventional therapy of Vs D. Occlusion of pediatric membrane Vs D is a safe, reliable, effective treatment. But its long-term efficacy still need long-term follow-up.

### Association between P2Y12 platelet receptor (C34T and G52T) polymorphisms and risk of cardiovascular events in coronary heart disease with clopidogrel in Chinese

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**Background** Recent data have implicated a haplotype of P2Y12 platelet receptor, as potential risk determinant for atherothrombosis. We wanted to investigate whether the platelet P2Y12 receptor polymorphisms affected long-term prognosis of Chinese patients who were treated with clopidogrel after percutaneous coronary intervention (PCI).

**Methods** Between Nov. 1, 2008 and Nov. 31, 2009, 268 Patients who received PCI and were exposed to clopidogrel treatment for almost 12 months, were enrolled in Hospital and underwent P2Y12 (G52T and C34T) determination. Follow-up was 12 months. The primary endpoint was a composite of death, myocardial infarction, urgent coronary revascularisation and stent thrombosis occurring during exposure to clopidogrel.

**Result** The patients were grouped H1/H1 (n = 195) and H2 carriers (H1/H2 and H2/H2, n = 73) by P2Y12 G52T genotype. Baseline characteristics were balanced between the two groups, except the proportion of H1/H1 is higher than H2 carriers in two vessel lesions ( $P < 0.05$ ). The combined end points also occurred more frequently in H2



carriers than in H1/H1 (10 vs 9,  $P < 0.05$ ). There were no significant difference between two groups with myocardial infarction, stent thrombosis, Urgent coronary revascularization and death ( $P > 0.05$ ). During the following time, cumulative survival of H2 carriers was lower than H1 (HR = 2.543, 95% CI: 1.033 – 6.259,  $P = 0.042$ ). The patients were also grouped CC genotype ( $n = 174$ ) and T carriers (CT and TT,  $n = 94$ ) by P2Y12 C34T genotype. Baseline characteristics were balanced between the two groups. There were no significant difference between two groups with the combined end points and cumulative survival (HR = 1.081, 95% CI: 0.426 – 2.746,  $P = 0.870$ ).

**Conclusion** P2Y12 platelet receptor H2 haplotype (G52T) is a major determinant of prognosis in Chinese patients with cardiac heart disease (CHD) who are receiving clopidogrel treatment after PCI. But there is not a strong association between C34T and an increased risk of cardiovascular events in patients with CHD receiving clopidogrel.

### Cytochrome P450 2C19 681G > A polymorphism in coronary heart disease patients treated with clopidogrel in Chinese

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**Background** The frequent genetic functional variant 681 G>A (\*2) of cytochrome P450 2C19 (CYP2C19) is an important contributor to the wide variability between individuals of the antiplatelet effect of clopidogrel. We wanted to investigate whether the CYP2C19\*2 polymorphism affected long-term prognosis of Chinese patients who were treated with clopidogrel after percutaneous coronary intervention (PCI).

**Methods** Between Jan. 1, 2008 and Dec. 31, 2009, 267 Patients who received PCI and were exposed to clopidogrel treatment for almost 12 months, were enrolled in Fu Wai Hospital and underwent CYP2C19\*2 determination. Follow-up was 12 months. The primary endpoint was a composite of death, myocardial infarction, urgent coronary revascularisation and stent thrombosis. Occurring during exposure to clopidogrel.

**Result** The patients were grouped CYP2C19\*1/\*1 ( $n = 130$ ), CYP2C19\*1/\*2 ( $n = 111$ ) and CYP2C19\*2/\*2 ( $n = 26$ ) by genotype, and baseline characteristics were balanced among the three groups. Urgent coronary revascularization occurred more frequently in CYP2C19\*2/\*2 and CYP2C19\*1/\*2 than in CYP2C19\*1/\*1 (3 vs 7 vs 2,  $P < 0.05$ ). There were no significant difference among three groups with myocardial infarction, stent thrombosis and death ( $P > 0.05$ ). The combined end points also occurred more frequently in CYP2C19\*2/\*2 and CYP2C19\*1/\*2 than in CYP2C19\*1/\*1 (4 vs 7 vs 3,  $P < 0.05$ ). During the following time, cumulative survival of CYP2C19\*2/\*2 was lower than CYP2C19\*1/\*1 (HR = 5.65, 95% CI: 1.63 – 19.49),  $P = 0.006$ ). Comparing Cumulative survival of CYP2C19\*1/\*2 with CYP2C19\*1/\*1, there were no significant difference (HR = 1.69, 95% CI: 0.53 – 5.36,  $P = 0.376$ ).

**Conclusion** CYP2C19\*2 genetic variant is a major determinant of prognosis in Chinese patients with cardiac heart disease (CHD) who are receiving clopidogrel treatment after PCI. CYP2C19\*2/\*2 (homozygous) brings a worse influence than CYP2C19\*1/\*2 (heterozygous).

### Menopause may aggravate symptoms of female apical hypertrophic cardiomyopathy patients

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**Purpose** Analyzing and summarizing the clinical and echocardiographic characteristics of female patients with apical hypertrophic cardiomyopathy.

**Methods** Female patients with apical hypertrophic cardiomyopathy who were diagnosed by echocardiography or magnetic resonance imaging between January 1994 and January 2009 at Fuwai hospital were consecutively enrolled in this study. Patients between 45 and 55 years old were classified as perimenopausal group, and the others were classified as non-perimenopausal group.

**Result** A total of 55 female patients with ApHCM were enrolled, and the average age is ( $54.89 \pm 14.15$ ) years. Interventricular septum thickness (IVST), left ventricular posterior wall thickness (LVPWT) and maximum apical thickness is lower in perimenopausal group than non-perimenopausal group ( $10.09 \text{ mm} \pm 2.51 \text{ mm}$  vs  $14.26 \pm 7.48 \text{ mm}$ ,  $P = 0.036$ ;  $8.73 \pm 1.10 \text{ mm}$  vs  $9.81 \pm 1.64 \text{ mm}$ ,  $P = 0.038$ ;  $17.82 \text{ mm} \pm 1.60 \text{ mm}$  vs  $19.74 \text{ mm} \pm 3.92 \text{ mm}$ ,  $P = 0.016$ ), indicating cardiac remodeling of patients in perimenopausal period are milder than the non-perimenopausal group. However, there was no significant difference in the frequency of clinical manifestations such as chest pain, palpitation, dizziness, dyspnea, and the NYHA functional classification among groups ( $P > 0.05$ , respectively).

**Conclusion** Dramatic changes in hormone levels may aggravate the symptoms of the perimenopausal female ApHCM patients which may get a certain degree of relief in postmenopausal period. The symptoms of ApHCM patients in perimenopausal period can not completely indicate the severity and the evaluation of the condition of the female ApHCM should be based on the combination of clinical manifestations and echocardiographic characteristics as well as women's special physiological period.

### A 5-year analysis on iodine contrast induced anaphylactic reaction occurred during Percutaneous coronary intervention

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**Objective** The goal of this study is to analyze the characteristics of iodine contrast induced anaphylactic reaction occurred during

percutaneous coronary intervention (PCI), so as to provide a reference to help reduce the risk of its use.

**Methods** By searching the clinical database of Beijing Fuwai Cardiovascular Hospital, we retrospectively investigated the incidence of iodine contrast induced anaphylactic reaction during PCI, including coronary angiography, in recent 5 years. We described the relationships between the use of the agent and gender, age, clinical manifestation, and the type of the agent, respectively.

**Result** In all of the 79 102 patients who received PCI, 48 patients (0.061%) ended up with anaphylactic reaction. Among them, 44 (0.056%) were males and 4 (0.02%) were females. The risk ratio between male and female was 11. In addition, among all the 5 commonly used non-iodinated agent, including Iohexol, Ioversol, Iopamidol, Iodixanol and Iopromide induced most of the anaphylactic reaction. The clinical manifestation of the anaphylactic reaction varied broadly; in which rash was the most observed and shock was the severest drug adverse reaction. Two patients eventually died of severe anaphylactic reaction.

**Conclusion** In general, non-iodinated contrast is safe to use in PCI. However, it is still necessary to carefully monitor the occurrence of its anaphylactic reaction. Early recognition and intervention of its manifestation is very critical to improve the safety of both drug use and PCI.

### Acute fluctuation in blood glucose has no effect on platelet aggregation rate

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Short-term acute blood glucose fluctuations are often found among patients with high risk of thrombosis. Influence of the phenomenon on platelet aggregation rate is of clinical importance and should be clearly evaluated. Twenty-seven cases of newly diagnosed type II diabetes patients and 31 cases of acute coronary syndrome (ACS) were recruited for this study. All subjects went through anthropometric measurements, including height, weight, and BMI. In a morning after fasting for 12 hours, plasma glucose was determined, and platelet aggregation rate was measured at the same time. The patient then orally took 75 g of glucose and blood was collected 30, 60, 120 and 180 minutes later. The plasma glucose level and platelet aggregation rate were measured for each time point. C-peptide and insulin levels were also measured in diabetic patients and glycated hemoglobin was also determined in ACS patients. Result showed that ADP and AA-induced platelet aggregation rate remained similar at different time points (30, 60, 120 and 180 minutes) in diabetes patients following glucose intake. Pearson correlation analysis showed that platelet aggregation rate induced by ADP had no correlation with BMI, blood glucose, C-peptide at both 0 and 120 min. Pearson correlation analysis showed that platelet aggregation rate induced by AA had no correlation with blood glucose, insulin, C-peptide at both 0 and 120 min. However, the 2-h platelet aggregation rate induced by ADP was positively correlated with insulin levels ( $r = 0.477$ ,  $P = 0.014$ ). AA-induced, but not ADP-induced, platelet aggregation was positively correlated with BMI ( $r = 0.619$ ,  $P = 0.024$ ). Similar Result were obtained for the 31 ACS cases. ADP-induced platelet aggregation rate was not statistically different among the time points. The average glycated hemoglobin was  $6.40 \pm 0.70\%$ . There was no correlation between platelet aggregation rates and glycated hemoglobin.

### Mid-term outcome of mitral valve repair in children

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**Objective** To study mid-term outcomes after mitral valve repair in children younger than 12 years.

**Methods** Medical records of patients who underwent mitral valve repair from 2000 to 2008 were reviewed. The clinical data of consecutive 47 children, 26 boys and 21 girls, aged 1.5 – 12 ( $6.6 \pm 3.7$ ) years old, with the underlying diseases of congenital diseases ( $n = 40$ ), rheumatic heart diseases ( $n = 3$ ), and infective endocarditis ( $n = 4$ ), with the preoperative cardiac function of NYHA class I or II in 12 patients and class III or IV in 35 patients, were analyzed. Different valvoplasty Methods were chosen according to different pathology, including edge-to-edge, modified Devega, commissuroplasty, commissurotomy, chordae tendinae transplantation, and resection of mitral ring. The follow-up period was  $8.3 \pm 3.7$  years, ranged from 5 to 13 years. The clinical heart function and echocardiogram data were analyzed during follow-up.

**Result** There was only one early postoperative death, owing to serious low cardiac output syndrome. The operative mortality was 2.1% totally. She was a 2 years old girl with class IV heart function and received emergency valve repair procedure. Three patients lost contact during follow-up. The rate of follow-up was 91.5%. In the 44 follow-up patients, there were no late postoperative deaths. Four patients underwent mitral valve replacement 3, 3, 6 and 7 years after valve repair respectively. The rate of freedom from reoperation was 95.5% at 5 years postoperatively and 90.9% at 10 years postoperatively respectively. The 44 surviving follow-up patients showed good cardiac function. 35 were in NYHA class I and 9 patients in class II.

**Conclusion** Mortality and redo valve operation are uncommon after mitral valve repair in children younger than 12 years due to proper patient selection criteria and valve repair technique.

### Hybrid technology in treatment of Stanford type B aortic dissection: Short-term Result

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**Objective** To evaluate the short-term Result of hybrid procedures in the treatment for aortic arch lesions.

**Methods** From 2008 to 2012, 37 consecutive patients with the above dissections were retrospectively analyzed. Inclusion requirement: aortic landing zone proximal to the left subclavian artery of less than 15 mm. Hybrid, endovascular stent grafts were selected based on dissection characteristics. Annual follow-up visits included computed tomography angiography. End points include progressive pathology, complications and survival rates.

**Result** Surgery was successful in all patients. One patient died in hospital and one patient died within 30 days after surgery, No paraplegia, and cerebral infarction and left upper limb ischemia. Thrombosis formed in the aortic false lumen of the graft exclusion segment in all patients. Patency was seen at Short-term follow-up, without proximal end leak, graft displacement.

**Conclusion** Endovascular repairing combined with prosthesis bypass was a safe and effective method for complex Stanford type B aortic dissection involving the distal arch.

### The role of secreted protein NBL1 in pulmonary arterial hypertension associated with systemic-to-pulmonary shunts

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**Background** Proteins mainly expressed in normal lungs and characteristically changed in lungs suffering from systemic-to-pulmonary shunts will be useful research targets for pulmonary arterial hypertension in patients with congenital heart diseases (PAH/CHD). Thus, this study aimed to identify secreted proteins that significantly altered during the genesis and progression of PAH/CHD.

**Methods** An antibody microarray procedure was performed to detect proteins Whose plasma levels specifically changed in patients with congenital intracardiac shunts. Then, significantly changed proteins were identified and the target protein NBL1 was determined. Real-time quantitative PCR (RT-PCR), western-blot analysis and immunohistochemistry were performed to further examine the expression changes and location of NBL1 in lungs from patients and rats with systemic-to-pulmonary shunts; the potentially biological role of NBL1 on HPASMCs and HPAECs proliferation were also explored. The plasma NBL1 concentration in a set of 120 patients with or without PAH was assessed by a commercially available enzyme-linked immunosorbent assay.

**Result** The antibody microarray procedure derived several proteins with statistically significant differences between patients with or without PAH. Secreted protein NBL1, which appeared as a valuable candidate for molecular markers of PAH, was selected for validation. Quantitative RT-PCR analysis revealed that NBL1 was expressed with much higher specificity in normal lung tissues than in other systemic organ tissues, and the mRNA level was down regulated in a time-related modus in lungs suffering from systemic-to-pulmonary shunts; Western blot analysis revealed that NBL1 was highly expressed in normal lung tissues and similarly a time-related reduction was also observed in pulmonary hypertensive lungs; Immunohistochemical analysis showed that NBL1 was highly detected in normal lung tissues and was significantly down-regulated with the progression of PAH. Furthermore, NBL1 could specially reverse the inhibitory effect of BMP2/4 on HPASMCs and HPAECs proliferation; Elisa-kit also determined a detectable level of NBL1 in the supernatants of culture media of the HPASMCs and HPAECs. Finally, plasma NBL1 concentration was significantly down regulated according to the PAH/CHD stage.

**Conclusion** NBL1 is a secreted protein that is highly and mainly expressed in lungs. Down regulation of NBL1 correlated with the severity of PAH. NBL1 might be a candidate biomarker and a novel therapeutic target for PAH/CHD.

### Preoperative evaluation of 50 children with anomalous origin of the left coronary artery from the pulmonary artery and follow-up after surgery

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**Objective** To study retrospectively 50 children with anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) and try to find the practical indexes that may predict myocardial viability and the possible risk factors that may affect the choice of operation and the recovery after surgery.

**Methods** A retrospective study was performed in 50 children with ALCAPA between April 1999 and March 2013. The extent of myocardial viability was classified by myocardial <sup>18</sup>F-FDG imaging and the global clinical scores calculated by the deviations of clinical manifestations at 15 patients with myocardial <sup>18</sup>F-FDG imaging. The relationships between them were evaluated. Then all patients were divided into two groups by the global clinical scores and the pre-, peri- and post operative clinical manifestations were compared between them.

**Result** The extent of myocardial viability of 15 patients with myocardial <sup>18</sup>F-FDG imaging was classified into four grades. Meanwhile, the global clinical scores were calculated and their relationship was analyzed. The global clinical scores showed high correlation with the extent of myocardial viability. All patients then were divided into two groups (group 1: scores ≤ 3, group 2: scores > 3), and the pre-, peri- and post operative clinical manifestations were compared between them. More infants and toddlers, abnormal Q waves, ICC dysplasia, RCA/AO.

**Conclusion** In children with ALCAPA, the extent of myocardial viability evaluated by myocardial <sup>18</sup>F-FDG imaging is related closely to the global clinical scores. Even in young children with severely depressed left ventricular function, higher global clinical scores, median and long-term follow-up showed satisfactory recovery of cardiac function after successful restoration of a dual coronary arterial system.

### Children with 230 cases of arterial switch operation surgical Methods and Result analysis

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**Objective** To summarize the arterial switch operation surgical Methods and Result analysis.

**Methods** Retrospective analysis between August 2008 and October 2008, 230 underwent arterial switch operation, male 172 cases, 58 cases were female. 3 d – 11 years old; 2.1 – 25 kg weight. Simple arteries transposition of 75 cases, 105 cases complicated arteries transposition, Taussing - Bing deformity 50 cases. Using Leiden coronary artery method, 1LCx2R as coronary artery normal distribution, a total of 198 cases, and other types of coronary artery anomaly distribution, a total of 32 cases, including 4 cases of Intramural course of coronary artery. In most patients the "open trap door" and "double button" technique for coronary ostia transfer. Children are applying The Lecompte maneuver was used in all cases.



**Result** 20 cases (8.7%) died operation mortality. Normal coronary death 15 cases (7.6%, 15/198), coronary artery anomalies distribution in 5 cases died (15.6%, 5/32). Simple TGA death 6 cases, 4 cases of coronary events, including 2 cases of coronary artery variation and complex TGA died 9 cases, 7 cases of coronary events, including 2 cases of coronary artery variations, Taussing - Bing malformation in 4 of 5 cases died coronary events, including 1 case of coronary artery variation.

**Conclusion** With the progress of surgical technique and experience accumulation, improve surgical mortality compared with the previous, but complex coronary artery type is still the independent risk factors of surgical death.

### Clinical characteristics of patients with left ventricular thrombus after acute myocardial infarction

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**Purpose** To investigate clinical outcome of left ventricular thrombus (LVT) after acute myocardial infarction (AMI).

**Methods** We retrospectively assessed all cases with LVT after AMI in Fuwai Hospital from January 2007 to February 2012. During this period, 8 220 patients were diagnose with STEMI, 82 of which had a definitive diagnosis of LVT, detected by imaging or operative findings. Adverse events were followed-up by phone calls (69.2%).

**Result** LVT was detected in 82 of 8 220 AMI patients (0.998%). Those 82 patients, of which 76 were men and 6 were women, were averagely aged  $54.68 \pm 11.63$  y. Killip II to IV occupied 41.5% of the 82 cases. 51 patients (50.6%, 81) were survived from extensive anterior wall while 15 patients (18.3%, 75) were with triple vessel lesion. Emergency thrombolytic therapy were received by 25 patients (30.5%, 82) while emergency PCI were received by 11 patients (13.4%, 82). Patients who accompanied with underlying diseases, such as hypertension, diabetes mellitus, hyperlipidemia, old myocardial infarction, fibrillation atrial, old cerebral apoplexy were account for 40.2% (33, 82), 17.1% (14, 82), 51.2%, (42, 82), 18.3% (15, 82), 4.9% (4, 82) and 8.5% (7, 82), respectively. 19 cases had a LVT detected in the first week of acute phase of AMI, 13 of which were occur in the first 48 hours, while the farthest we could detect was at the 101 day after AMI. The shapes of LVT were all dense mural mass or trabs, except for 1 was rarefaction, and 1 was moyamoya. All of the thrombus (95.6%, 68) was located in apex of heart, except for 1 in left ventricular cavity, 1 in lower segment of left ventricle anterior wall, and 1 outside the inferoposterior wall. 40% (24, 60) patients with a LVEF lower than 40%. Among the 82 patients, 80 received dual ant platelet therapy, 58 were combined with low molecular weight heparin, while 10 of these 58 patients were additionally using warfarin. This three kind of therapy didn't accelerate the disappearance of LVT ( $P > 0.05$ ). Ventricular aneurysmectomy were conducted among 15 patients. 71 patients (86.6%, 82) were effectively followed-up with a median period of 23.2 week. LVT reoccurrence were appeared in 5 patients during the follow-up period, 3 of which had Ventricular aneurysmectomy during this time ( $P = 0.04$ ). Arterial embolism occurred in 4 patients (4.88%, 82). Among the embolized patients, 1 died of acute abdomen causing by mesenteric arterial embolism, and 1 had an OMI history and received emergency thrombolytic therapy, considering inappropriate emergency thrombolytic therapy may cause emboli

abscission. Additionally one more patient died of heart failure after 3 months of discharge.

**Conclusion** The incidence of LVT in this retrospective study is much lower than other prospective researches, which may imply that clinicians' attention on LVT is not enough. This study also suggests that clinicians should focus on early LVT formation after AMI, and that such patients ought to do regular follow-up after their discharges. Cosmically clinical trails are still needed to purchase an effective way to safely use thrombolytic and anticoagulation therapy, maybe especially for those who had received ventricular aneurysmectomy

### Thyroid status, cardiac function and mortality in patients with idiopathic dilated cardiodomyopathy

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**Background** Previous studies claiming the relationship between thyroid dysfunction and poor prognosis of heart failure had a major limitation that they included patients with different etiology. With full information of thyroid function profile from four hundred and fifty eight consecutive patients with idiopathic dilated cardiomyopathy, we tested the hypothesis that thyroid status can independently influence the mortality in patients with heart failure.

**Methods** The original cohort consisted of 532 consecutive patients with idiopathic dilated cardiomyopathy. All the patients took thyroid function test and other regular examinations in hospital, and we perform the follow-up through phone contact with patients, examining patients' hospital records or periodically review of patients in outpatient clinic. The risk of mortality was evaluated based on fT3, TSH, and the whole thyroid function profile, respectively.

**Result** At the end of follow-up, 458 patients remained in the cohort. The most frequent thyroid dysfunction was subclinical hypothyroidism (ScHypo,  $n = 41$ ), followed by subclinical hyperthyroidism (ScHypo,  $n = 35$ ), euthyroid sick syndrome (ESS,  $n = 17$ ), and hypothyroidism (Hypo,  $n = 12$ ). Compared with NYHA class II group, FT3 was lower in class III - IV group ( $2.89 \pm 0.45$  vs  $2.67 \pm 0.55$ ,  $P = 0.035$ ) and log-TSH was higher ( $2.17 \pm 0.36$  vs  $2.30 \pm 0.45$ ,  $P = 0.005$ ). Logistic analysis showed log-TSH and fT3 as independent predictors of exacerbated cardiac function (NYHA III - IV vs NYHA I - II). During the follow-up (17  $\pm$  8 months), there were 111 cumulative deaths. Hypothyroidism was the strongest predictor of mortality (HR, 4.189; 95% CI, 2.118 - 8.283), followed by ESS (HR, 3.147; 95% CI, 1.558 - 6.355) and ScHypo (HR, 2.869; 95% CI, 1.817 - 4.532). ScHyper showed no significant impact.

**Conclusion** We found clear association between an increased risk of death in HF caused by IDCM and thyroid dysfunction (ESS, ScHypo, and Hypo). These Result suggest that monitoring thyroid function in HF patients is necessary and further study about treatment is warranted.

## Effects of statin on serum markers and cardiac dyssynchrony in patients with nonischemic chronic heart failure

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**Objective** To explore a new treatment of heart failure, we investigated the effects of statin on serum markers and parameters of cardiac dyssynchrony in patients with chronic nonischemic heart failure.

**Methods** 85 patients with chronic nonischemic heart failure were enrolled in this study and were randomized into statin group (29 males and 13 females) and control group (31 males and 12 females). All of the patients received conventional treatment with digitalis, diuretic, nitrates,  $\beta$ -blocker and angiotensin converting enzyme inhibitor according to heart failure treatment guideline. Patients in statin group were additionally given simvastatin 40 mg or atorvastatin 10 mg when they met the inclusion criteria. N-terminal pro-brain natriuretic peptide (NT-proBNP), C-reactive protein (CRP), and echocardiography parameters including left ventricular ejection fraction (LVEF), left ventricular end-diastolic dimension (LVEDd) and ventricular dyssynchrony were evaluated at baseline, 1<sup>st</sup> month and 6th month after enrollment.

**Result** Statin therapy exerted no effects on the concentrations of NT-proBNP and CRP after 6 months follow up. Systolic velocities (Sm) and early diastolic mitral annulus velocities (Ea) at lateral annulus in statin group were significantly higher compared with those in control group at 6th month ( $P < 0.05$ ). Interventricular mechanical delay (IVMD), differences of time to peak myocardial systolic velocity ( $\Delta$  Ts) and the standard deviation of time to peak myocardial systolic velocity of all 12 left ventricular segments (Ts-12SD) in statin group were significantly lower than those in control group at 6th month ( $P < 0.05$ ).

**Conclusion** Statin therapy can improve the long-term effects on synchronization of inter-and intra-ventricular in patients with chronic nonischemic heart failure.

## The efficacy and safety of transradial approach PCI Vs femoral approach PCI for coronary heart disease

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**Objective** To evaluate the efficacy and safety of transradial approach PCI Vs femoral approach PCI for coronary artery disease.

**Methods** We searched PubMed, Embase, Cochrane Library, CNKI, VIPH and Wanfang database, the deadline of retrieval time is March 2013. We include the RCT trials that report transradial approach PCI Vs femoral approach PCI for acute myocardial infarction. Two researchers included extracted data and evaluate the quality of the included studies according to the Cochrane Handbook 5.0.2 Quality evaluation criteria.

The RevMan 5.0 software were used for quantitative data merging.

**Result** we finally included 26 English RCT (total 678 175 patients, covering 54 322 cases of radial PCI and 623, 853 cases of femoral PCI. Meta-analysis shows: In the index of PCI success rate (OR = 1.46, 95% CI: 0.60 – 3.58), all-cause mortality (OR = 1.01, 95% CI: 0.58 – 1.75), the recurrence of myocardial infarction within one year after PCI (OR = 0.68, 95% CI: 0.44 – 1.03), PCI operative time [radial PCI group means (40.5  $\pm$  19.3) min, femoral PCI group means (51.3  $\pm$  28.7) min, OR = -1.29, 95% CI: -2.95 – 0.38], and stroke (OR = 0.87, 95% CI: 0.73 – 1.03), the incidence of thrombosis (OR = 0.60, 95% CI: 0.33 – 1.09), the radial PCI group is similar with femoral PCI group. However, in the index that the postoperative vascular complications (OR = 0.52, 95% CI: 0.36 – 0.76) and hospital stay [radial PCI group means (3.0  $\pm$  1.6) days, femoral PCI group means (6.1  $\pm$  3.1) days, OR = -3.32, 95% CI: -6.52 – -0.13], the radial PCI group is better than the femoral PCI group, with a statistically significant difference ( $P < 0.05$ ).

**Conclusion** Compared with the traditional femoral PCI, radial PCI have less postoperative vascular complications, shorter hospital stays, and at the same time, have similar effects in PCI success rate, all-cause mortality and less cardiovascular events incidence than femoral PCI. So radial PCI can be effective and safe method in the treatment of coronary heart disease. Taking into account the limitations of the meta-analysis, multi-center, double-blind and large sample RCTs are needed to provide a higher level of evidence.

## Efficacy and safety of clopidogrel added proton pump inhibitors vs clopidogrel in the treatment of cardiovascular patients after PCI

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**Objective** To evaluate the efficacy and safety of clopidogrel added proton pump inhibitors vs clopidogrel in the treatment of cardiovascular patients after PCI.

**Methods** We search MEDLINE, EMBASE, Cochrane Library and conference databanks, the retrieval time is ended until October 2012. We selected the clinical trails which is evaluated efficacy and safety of clopidogrel added proton pump inhibitors vs clopidogrel in the treatment of cardiovascular patients after PCI, and evaluate the quality of clinical trails following the Cochrane Handbook 5.0.2 the quality evaluation criteria of evaluation included in the research quality. And the datas are solved by the RevMan 5.0 software.

**Result** Our review included 13 RCT covering 55592 patients. meta-analysis Result show there is no statistical difference among incidence of MACE (OR = 1.19, 95% CI: 0.92 – 1.55), the rate of All-cause mortality (OR = 1.13, 95% CI: 0.83 – 1.52), and the rate of gastrointestinal bleeding (OR = 1.11, 95% CI: 0.48 – 2.55) in clopidogrel added Proton Pump Inhibitor (PPI) group or clopidogrel group. While there is low incidence rates of myocardial infarction, stent thrombosis, Target Vessel Revascularization (TVR).

**Conclusion** The incidence rate of MACE, stent thrombosis, and gastrointestinal bleeding is similar in added or not added PPI patients. Considering population limitations of our research, better evidence

should be offered by multicenter, large sample and double blind RCT researches in the future.

### Infective endocarditis caused by a heart-breaking needle: a case report

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Endocarditis is often caused by severe infection and defect structure of heart, which is difficult to control and most of the patients need surgical treatment. Here is infective endocarditis caused by foreign body, developing cerebral infarction, which have many clinical contradictions in the therapeutic process.

A 48 years old female patient was admitted complaining of persistent productive cough with fever in 3 months. She was diagnosed by local hospital with upper respiratory tract infection, and was administered with anti-virus and anti-bacterium drug. She had lose consciousness in a short time with encopresis and left skewing lips 20 days ago, and regained consciousness in 4 minutes.

Cerebral CT were repeat to determine a enlarging infarction area. Chest CT performs a foreign body in the base of lobus inferior pulmonis sinister and left ventricle, inflammation of lobus inferior pulmonis sinister. She had a history of sporadic encephalitis and a foreign body piercing history of prothorax. Echocardiogram shows medium echogenic mass in left ventricle, 21 × 11 mm, attaching to the anterolateral papillary muscle attachment points, without a clear border but uneven echo and some calcifications, which have a big mobility. Chest X ray shows a metal short rod-like foreign body in left inferior pulmonary and heart shadow. Chest CT scan shows stick-like metal shadow in left inferior pulmonary beside the border of the heart. During hospitalization, the patient present a numbness of left arm and left skewing lips. Cerebral CT shows multiple new infarction areas.

5 days after the infarction, surgery was taken to take off the foreign body. In the process, the metal foreign body was showed to present at the bottom of the anterior papillary muscle and go throw the left ventricular free wall to the lung, performing a calcified sinus. Vegetation located at the bottom of papillary muscle and the pericardium side of the heart. There were 3 segments of metal foreign body totally. The patients have a difficulty in anesthesia recovery, which took three days to regain consciousness. The antibiotic therapy continued after 1 month of the surgery. The patient had a satisfied recovery and was discharged.

### The effects of fractional flow reserve guided percutaneous coronary intervention: a systematic review and meta-analysis from comparative studies

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**Background** Myocardial fractional flow reserve has performed more and more popular at present. Clinicians use it to guide the percutaneous coronary intervention. The effect of FFR in the therapy of coronary artery disease needs to evaluate. We intend to perform a systematic review and meta-analysis of studies reporting clinical

outcomes of FFR-guided PCI vs angiography-guided PCI.

**Methods** We searched PubMed from the beginning of this century to March, 20, 2103, and also identified abstracts published at this period. Prospective and retrospective studies were all included in for analysis if data for two strategies guided PCI were available.

**Result** In published data from 4 trials (9 203 patients, 1 874 for FFR-guided PCI, 7 329 for angiography), we could conclude that the FFR-guided strategy of PCI could reduce the rate of MACE (OR = 0.53, 95% CI, 0.39 – 0.73)) and its components such as death (OR = 0.71, 95% CI, 0.45 – 1.12), myocardial ischemia (OR = 0.51, 95% CI, 0.36 – 0.71), and repeat revascularization (OR = 0.53, 95% CI, 0.39 – 0.73). We could conclude that the FFR-guided strategy of PCI could also limit the usage of stents and reduce the cost of hospitalization relatively.

**Conclusion** The FFR-guided strategy performs much better than angiograph-guided. Being the examination guiding the myocardial revascularization at present, although it has several aspects to improve and refine, FFR has opened a new era of incomplete revascularization of the interventions to coronary artery disease. And its systematic use will make PCI more effective and appropriate than at present.

### Distribution of clopidogrel metabolism related gene polymorphisms among Chinese ACS patients

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**Objective** To detect distribution clopidogrel metabolism related gene polymorphisms CYP2C19, ABCB1 and PON1 in Chinese ACS patients.

**Methods** Patients admitted to Fuwai Hospital from 2005 to 2008 with ACS within 4 weeks (30 days) were enrolled. All had informed consents for gene samples. The detection of gene polymorphisms was performed by Taqman Systems through PCR-RFLP. The alleles genotyped were CYP2C19 \*2-\*8, \*17, ABCB1 and PON1. Patients were classified as one of the 5 categories by metabolizer phenotypes as Extensive [without any “loss-of-function” (LOF) allele \*2-\*8 or “gain-of-function” (GOF) allele \*17], Intermediate (with only one LOF allele), Poor (with two or more LOF alleles), Ultra (with one or two GOF alleles) or Unknown (with one LOF allele and one GOF allele).

**Result** A total of 2800 Chinese ACS patients were enrolled with age of 59.0 ± 12.3 years and 79.9% males. The diagnosis proportion was STEMI in 74% enrolled patients, NSTEMI in 22.0% and UA in 4.0%. The minor allele frequency (MAF) for each genotype of CYP 2C19 \*2, \*3, \*4, \*17 were 28.7%, 4.6%, 0.1% and 1.2%, respectively. No LOF allele \*5-\*8 were found in this population. The MAF for ABCB1 and PON1 Q192R were 39.4% and 37.8%. Patient clopidogrel metabolizer groups were defined as Extensive in 41.7% enrolled patients, Intermediate in 45.6%, Poor in 10.3%, Ultra in 1.9% and Unknown in 0.6%, respectively. There were no significant differences for all genotypes between males and females. Total LOF carriers of CYP 2C19 were 56.4% and GOF carriers were 2.5%.

**Conclusion** Our study reflected the distribution of CYP 2C19, ABCB1 and PON1 gene polymorphisms in Chinese ACS patients. Compared to the Caucasians, it seems LOF genotypes of CYP 2C19 alleles more common in Chinese. Further exploration is needed to clarify the relation between genotypes and clinical outcomes in Chinese patients.



### Case report: takotsubo cardiomyopathy

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**Case report:** A 71-year-old woman presented to the emergency department with a 2 day history of chest pain. An electrocardiogram of local hospital showed elevated ST-segment of  $V_2 - V_5$  leads. Cardiac enzymes were negative. She was diagnosed of “acute myocardial infarction of anterior wall” by local hospital and was transferred to ER. The patient had a 20 years history of hypertension and 10 years history of type 2 diabetes mellitus. ECG showed sinus tachycardia with frequent ventricular premature beat and 1 – 3 mm ST elevation in leads  $V_2$  through  $V_5$ . Emergent CAG was normal. Left ventriculography was hypokinesis of apical segments with anterior and inferior wall in a Takotsubo pattern. LVEF was 36.2%. Repeat left ventriculography 4 weeks later showed improvement of previously-noted wall motion abnormalities with a normal ejection fraction of 63.6%. Takotsubo cardiomyopathy, or stress cardiomyopathy, a seemingly rare but in fact underrecognized transient left ventricular dysfunction, is a clinical entity mimicking an acute coronary syndrome. The clinical picture and electrocardiographic findings usually are indistinguishable from those of an acute coronary syndrome. Cardiac imaging studies usually reveal extensive apical and mid-ventricular akinesis or hypokinesis with basal sparing, discordant with minimally increased cardiac enzymes. These wall motion abnormalities typically extend beyond the vascular territory of a single coronary artery. Coronary angiography is necessary to differentiate ACS. The prognosis of TTC is good, with full recovery of cardiac function within 2 – 4 weeks in most of the cases.

### External carotid artery stenting in patients with ipsilateral internal carotid artery occlusion: early and long-term Result

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**Objective** External carotid artery (ECA) remains one of the most important sources of collateral circulation to brain in patients with ipsilateral carotid artery occlusion (ICA) and the impairment of this collateral due to atherosclerotic stenosis may exacerbate preexisting neurological ischemia. ECA revascularization to normalize ECA collaterals to cerebralis could alleviate neurological symptoms and provide conditions for subsequent additional procedures. The purpose of this study was to evaluate the safety and clinical efficacy of ECA stenting in patients with ipsilateral ICA.

**Methods** From January 2008 to December 2012, the clinical data of 16 patients [mean age ( $66.0 \pm 7.8$ ) years, 12 (75.0%) male] with ipsilateral ICA underwent ECA stenting was collected and analyzed. In them, thirteen (81.3%) patients had symptomatic external carotid stenosis and 6 (37.5%) patients planned to underwent CABG within 30 days after ECA stenting. The end points comprised hyperperfusion syndrome and hemodynamic depression at 30 days and transient ischemic attack, stroke, death and myocardial infarction, restenosis measured by carotid ultrasonography within 30-day and 4-year follow up.

**Result** All 16 patients underwent ECA stenting successfully.

In ECA stenting procedures, 2 (12.5%) patients suffered from hemodynamic depression during balloon dilation and recovered completely within 2 days after receiving additional fluids and vasopressor drugs. 10 (62.5%) patients underwent percutaneous intervention of other arteries, including 7 (43.8%) contralateral internal carotid arteries, 4 (25.0%) vertebral arteries, 5 (31.3%) renal arteries simultaneously. There were no severe adverse events occurring in perioperative period. After ECA stenting, 5 patients underwent CABG within 30 days with no sequelae. During an average of 46 months follow-up, one patient suffered from contralateral minor stroke and the other 15 patients remain asymptomatic. There were no other adverse events occurring at follow up. In addition, carotid ultrasonography was examined in all patients and showed that two patients developed a 50% in-stent restenosis in ipsilateral ECA, which did not result in recurrent neurological symptoms.

**Conclusion** ECA stenting may improve neurological symptoms including signs of transient ischemic attack, stroke, and amaurosis fugax in a follow-up of 46 months, and provide conditions for subsequent cardiac surgery, with a favorable mortality and morbidity. ECA stenting may be a promising therapeutic strategy for patients with ipsilateral ICA occlusion.

### Safety and feasibility of carotid artery stenting in patients with coexistent carotid and coronary artery disease

Hui Dong, Xiongjing Jiang, Yu-bao Zou, Ting Guan, Tuo Liang, Meng Peng, Yuejin Yang, Runlin Gao  
Safety and feasibility of carotid artery stenting in patients with coexistent carotid and coronary artery disease

**Objective** To evaluate the safety and feasibility of carotid artery stenting (CAS) for treating patients with coexistent carotid and coronary artery disease.

**Methods** The clinical data of 237 consecutive patients with coexistent carotid and coronary artery disease undergoing CAS in Fuwai hospital from January 2005 to June 2010 were collected and analyzed retrospectively. Indication for CAS was defined as carotid artery diameter reduction of > 60% (symptomatic) or > 80% (asymptomatic). 30-day rates of stroke, death and myocardial infarction after CAS were assessed.

**Result** The patients were 43 – 82 ( $66.1 \pm 7.7$ ) years old, there were 189 (79.7%) male. All patients suffered from coronary artery disease, of whom 87 (36.7%) had unstable angina pectoris and 82 (34.6%) had recent myocardial infarction (< 30 d). The procedural success rate of CAS was 99.2% (235/237). Cerebral protection devices were used in 234 patients (99.6%). Among them, 36 (15.2%) patients received simultaneous bilateral CAS and 79 (33.3%) patients underwent simultaneous percutaneous intervention of other arteries. Within 30 days after CAS, 127 (53.6%) patients underwent coronary revascularization, including 118 (49.6%) coronary artery bypass grafting and 9 (3.8%) percutaneous coronary intervention. The rate of major stroke, minor stroke, death and MI from time of CAS to 30 days was 2.1%, 3.0%, 0.4% and 0.4% respectively.

**Conclusion** This study indicated that CAS was safe and effective with a low incidence of periprocedural complications in patients with coexistent carotid and coronary artery disease, comparable to reported Result from carotid endarterectomy.

## Transcatheter renal denervation for resistant hypertension after transfemoral and transradial approach failure

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**Renal** sympathetic hyperactivity plays a crucial pathogenetic role in the maintenance and progression of arterial hypertension. As a novel device-based approach targeting the renal sympathetic nerves, renal denervation (RDN) has been shown to be effective and safe in reducing sympathetic nerve activity, norepinephrine spillover as well as blood pressure. Currently, the femoral artery is the most widely used as an access site for RDN. However, this approach may be difficult or impossible in certain patients with an acute angle between the infrarenal aorta and the renal arteries, the aorta-iliac occlusive disease and severe tortuosity of abdominal aorta and (or) iliac arteries. In a case report, Goncalves et al reported the feasibility of transradial RDN in a short female guided by a “Customized” Judkins right catheter. However, due to the unavailability of longer radiofrequency ablation catheter, RDN via forearm access was difficult and even impracticable in relative tall people. Here, we describe a case of RDN for resistant hypertension by a longer radiofrequency ablation catheter after transfemoral and transradial approach failure due to an acute aorto-renal angle and severe tortuosity of the radial artery respectively. Transcatheter RDN was performed successfully with no any complications. Transcatheter access might represent a technical alternative for RDN in certain patients after transfemoral and transradial approach failure when longer ablation catheter is available.

## Prognosis of clinical outcomes in Chinese patients receiving XIENCE V everolimus-eluting stent with baseline and residual syntax score: one-year Result from the prospective multicenter SEEDS study

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**Background** Previous studies demonstrated the safety and efficacy of everolimus-eluting stent in patients with simple to complex coronary lesions. The Syntax score has been proposed as a valuable tool to characterize the coronary anatomy prospectively with respect to its complexity. However, the safety and efficacy of XIENCE V stent in patients with small vessel, long lesion or multivessel disease stratified by Syntax score in Chinese population hasn't been addressed yet.

**Methods** This was a prospective, multicenter registry designed to enroll up to 1 900 patients with small vessel (reference vessel diameter

≤ 2.75 mm), long lesion (length ≥ 25 mm.), or multivessel disease (≥ 2 target vessels) suitable for treatment with XIENCE V at 48 centers in China mainland, Macao and Taiwan. The primary outcome was ischemia-driven target vessel failure (ID-TVF), defined as the composite of cardiac death, MI (Q and non-Q wave), or ID-TVR) at 12 months. The baseline Syntax score (bSSlow ≤ 6, 6 < bSSmid ≤ 12, bSShigh > 12) and residual Syntax score (rSSlow ≤ 0, 0 < rSSmid ≤ 4, rSShigh > 4) were applied in all enrolled patients.

**Result** A total of 368 (19.37%) small vessel patients, 807 (42.47%) long lesion patients, and 725 (38.16%) multivessel patients with 2849 lesions were treated. The primary outcome ID-TVF at 1 year was 5.57% in all patients, and 2.89%, 4.59% and 8.00% in patients with small vessel, long lesion and multivessel disease, respectively. ARC defined definite or probable stent thrombosis in all patients through 1 year was 0.58%. ID-TVF and each component were all significantly higher in patients in the highest bSS or rSS tertile. The cumulative ID-TVF at 1 year was 9.16% in bSShigh patients, 4.33% in bSSmid patients and 2.68% in bSSlow patients (Log-rank, P < 0.0001). When patients stratified by rSS, the primary endpoint was 8.94% in bSShigh patients, 6.10% in bSSmid patients and 4.15% in bSSlow patients (Log-rank, P = 0.0008).

**Conclusion** Low rates of ID-TVF and stent thrombosis were observed in this large-scale, multicenter, “real-world” study of XIENCE V stent on Chinese population, which demonstrated its safety and effectiveness in high risk cohorts with small vessel, long lesion, and multivessel disease. A significantly higher rate of 1 year ID-TVF was observed in the highest baseline and residual Syntax score groups, indicating that baseline and residual Syntax Score might be a useful tool to predict clinical outcomes in complex patients treating with 2nd generation XIENCE V stent.

## Policosanol attenuates statin-induced increasing in serum proprotein convertase subtilisin/kexin type 9 when combination with atorvastatin

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**Objective** It has been demonstrated that statin treatment alone significantly increases plasma proprotein convertase subtilisin/kexin type 9 (PCSK9) levels, which limited its lipid-lowering effect. Policosanol is a natural nutritional supplement used primarily for cholesterol lowering which has little side-effects. The effect of policosanol combined with statin on lipid profile as well as PCSK9 in Chinese patients with atherosclerosis is still unknown.

**Methods** This is a randomized, open-label controlled study with 2 protocols. In protocol I, 27 patients with atherosclerosis were enrolled and randomly divided to atorvastatin 20 mg/d (n = 13) and atorvastatin 20 mg/d + policosanol 20 mg/d (n = 14) for 8 weeks. Serum PCSK9 and lipid profile were determined at day 0 and week 8 respectively. In protocol II, 14 healthy volunteers were randomized to policosanol 20 mg/d (n = 7) and blank control group (n = 8) for 12 weeks. Serum PCSK9 and lipid profile were determined at day 0 and week 12 respectively.

**Result** In protocol I, upon 8 weeks of treatment, LDL-C was decreased by 38% with atorvastatin 20 mg/d and by 37% with atorvastatin 20 mg/d + policosanol 20 mg/d. There was no significant difference in the percent of LDL-C lowering between the two treatment

groups. Atorvastatin 20 mg/d significantly increased serum PCSK9 by 35% ( $255 \pm 81$  ng/mL vs  $345 \pm 97$  ng/mL,  $P = 0.002$ ). However, atorvastatin 20 mg/d + policosanol 20 mg/d increased serum PCSK9 only by 17% ( $264 \pm 60$  ng/mL vs  $310 \pm 86$  ng/mL,  $P = 0.184$ ). In protocol II, upon 12 weeks of treatment, there is a trend of decreasing serum PCSK9 level by 19% in policosanol group but it doesn't reach the statistical significance yet ( $289 \pm 71$  ng/mL vs  $235 \pm 46$  ng/mL,  $P = 0.069$ ).

**Conclusion** Policosanol combined with statin attenuated statin-induced increasing in serum PCSK9 levels, however, the combination treatment didn't further lower serum cholesterol levels. It indicated that policosanol might have a modest effect of lowering serum PCSK9, and this might be a more attractive effect than its lipid lowering effect.

### Perioperative fondaparinux vs nadroparin in non-ST-elevation acute coronary syndrome patients receiving higher-dose unfractionated heparin during percutaneous coronary intervention

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**Background** Current guidelines gave fondaparinux a class I recommendation for use in non-ST-elevation acute coronary syndromes (NSTEMI-ACS) undergoing invasive strategies. Nadroparin is still one of the most common anticoagulants used in NSTEMI-ACS and crossover anticoagulation regimens are common in patients undergoing percutaneous coronary intervention (PCI) in China. This study compared the safety and efficacy between perioperative fondaparinux and nadroparin in patients with NSTEMI-ACS who received higher-dose unfractionated heparin (UFH) during PCI.

**Methods** A total of 340 patients with NSTEMI-ACS were randomized to receive either fondaparinux (2.5 mg/d) or nadroparin (0.1 ml/10 kg/12 h) upstream of PCI. We excluded 42 patients not receiving PCI. For the two groups, the dose of UFH during PCI was 7 000 – 10 000 units (120 – 140 units/kg) or 5 000 – 7 000 units (85 – 100 units/kg) with tirofiban. The primary safety endpoint was the composite of major or minor bleeding at 9 days and major vascular access-site complications within 48 hours after PCI. The primary efficacy endpoints included death, myocardial infarction, or target vessel revascularization at 9 days.

**Result** The primary safety endpoint occurred in 5.5% of the patients in fondaparinux group and 7.2% in nadroparin group (hazard ratio [HR], 0.63; 95% confidence interval [CI], 0.30 – 1.30;  $P = 0.67$ ). All bleeding events occurred during PCI or within 24 hours after PCI, and the majority occurred within 6 hours after PCI. The incidence of major (2.7% vs 2.6%, HR 1.04, 95% CI 0.27 – 4.98;  $P = 0.96$ ) or minor (2.7% vs 4.6%, HR 0.51, 95% CI 0.25 – 2.02;  $P = 0.39$ ) bleeding was similar between the two groups. Fondaparinux group had similar incidence of the primary efficacy endpoints compared with nadroparin group (2.7% vs 4.6%, HR 0.68, 95% CI 0.21 – 2.64;  $P = 0.59$ ).

**Conclusion** Perioperative fondaparinux was comparable to nadroparin in patients with NSTEMI-ACS receiving higher-dose UFH during PCI. Reduced dose of UFH during PCI may decrease perioperative bleeding events and vascular access-site complications.

### Association between CYP2C19 gene polymorphisms and short-term clinical endpoints of Chinese ACS patients

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**Objective** To investigate associations between clopidogrel metabolism related genes CYP2C19 \*2, \*3, \*4, \*17 and short-term adverse clinical endpoints like death, myocardial infarction and stent thrombosis among Chinese patients with ACS (acute coronary syndrome).

**Methods** Based on previous parts about genotyping Result and prespecified inclusion and exclusion criteria, we collected clinical information of enrolled patients such as age, gender, past history of disease, in-hospital medications and reperfusion Methods, and then combined them with gene Result to analyze associations between different gene polymorphism and short-term ischemic clinical events like death, myocardial infarction, stent thrombosis. First we analyze impact of single gene on single clinical endpoint and composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina, subsequently we integrate CYP2C19 \*2-\*4 as a whole gene (CYP2C19 LOF gene) to evaluate associations between CYP2C19 LOF gene and single clinical endpoint and composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina. We use Cox regression models as statistical Methods and the Result were presented as HR as well as 95% confidence intervals.

**Result** 2569 patients entered this part of study about impact of different gene polymorphisms on short-term prognosis eventually. Among them 485 females (18.9%), median age 58 years. Multivariable regression models had disclosed only CYP2C19 \*3 and \*4 were associated with repeated revascularization (HR 8.86, 95% CI 1.76 – 44.76 and HR 0.003, 95% CI 0.000 – 0.13). CYP2C19 \*17 was not associated with risk of bleeding, other genes were not associated with single endpoint and composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina (all with  $P > 0.05$ ). CYP2C19 LOF gene were not associated with single endpoint and composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina (all with  $P > 0.05$ ).

**Conclusion** There were no significant associations between clopidogrel metabolism related genes CYP2C19 \*2, \*3, \*4, \*17 and short-term adverse clinical endpoints like death, myocardial infarction and stent thrombosis. Only CYP2C19 \*3 and \*4 were associated with repeated revascularization. These Result reminded us that there were no associations between gene polymorphisms and short-term ischemic clinical endpoint, routine genotyping of above genes are not recommended in clinical practice.



## Association between ABCB1, PON-1 gene polymorphisms and short-term clinical endpoints of Chinese ACS patients

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**Objective** To investigate associations between clopidogrel metabolism related genes ABCB1 C3435T and PON-1 Q192R and short-term adverse clinical endpoints like death, myocardial infarction and stent thrombosis among Chinese patients with ACS (acute coronary syndrome).

**Methods** Based on previous parts about genotyping Result and prespecified inclusion and exclusion criteria, we collected clinical information of enrolled patients such as age, gender, past history of disease, in-hospital medications and reperfusion Methods, and then combined them with gene Result to analyze associations between different gene polymorphism and short-term ischemic clinical events like death, myocardial infarction, stent thrombosis. First we analyze impact of single gene on single clinical endpoint and composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina, subsequently we integrate CYP2C19, ABCB1 and PON-1 as a whole gene to evaluate associations between CYP2C19 LOF gene and single clinical endpoint and composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina, last we evaluate associations between multiple genes and single clinical endpoint and composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina. We use Cox regression models as statistical Methods and the Result were presented as HR as well as 95% confidence intervals.

**Result** 2569 patients entered this part of study about impact of different gene polymorphisms on short-term prognosis eventually. Among them 485 females (18.9%), median age 58 years. Multivariable regression models had disclosed only ABCB1 associated with composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina (HR 1.97, 95% CI 1.09–3.55), other genes were not associated with single endpoint and composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina (all with  $P > 0.05$ ). CYP2C19, ABCB1 and PON-1 LOF gene were not associated with single endpoint and composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina (all with  $P > 0.05$ ). Multiple genes were not associated with single endpoint and composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina (all with  $P > 0.05$ ).

**Conclusion** There were no significant associations between clopidogrel metabolism related genes ABCB1 C3435T and PON-1 Q192R and short-term adverse clinical endpoints like death, myocardial infarction and stent thrombosis. Only ABCB1 associated with composite endpoint of death, myocardial infarction, stroke, stent thrombosis, repeated revascularization and recurrent angina. These Result reminded us that ABCB1 can predict short-term risk of MACE.

## Evaluate the effects of APACHE II in intensive care patients of heart specialist hospital

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**Objective** To evaluate the effects of APACHE II in intensive care patients of Heart specialist hospital and analyse its deficiencies.

**Methods** A retrospective study was performed in 345 patients admitted into ICU from December 1, 2009 to April 31, 2010. Calculate their APACHE II score and in hospital mortality rate. Compare it with the actual mortality rate, and to explore the parameters which correlate with the in hospital mortality of intensive care patients.

**Result** The actual death rate was 4.93% ( $n = 17$ ), the predicted death rate was 7.85%, and there was no significant difference between them ( $P > 0.05$ ). The area under the ROC curve is 0.832. The analysis of model fitting index shows good ( $P = 0.794$ ). But the SMR value (the actual death rate/the predicted death rate) is 0.63, meaning that the predicted death rate needs to be calibrated by a factor of 0.63 to give an accurate representation of actual death rate. Through the comparison between survival and unsurvival group, we found that: except for WBC ( $P = 0.004$ ) and Cr ( $P < 0.01$ ), other acute physiology parameters have no difference between the two groups. Other commonly used parameters comparison shows that Big-ET, NT-proBNP and mechanical ventilation have significantly difference between the two groups ( $P < 0.05$ ). Univariate regression analysis shows that, for the acute physiology parameters, BR, Na, Cr, WBC were correlated with death, and for other commonly used parameters: TB, ALB, AST, ALT, NT-pro BNP, big-ET, mechanical ventilation were correlated with death. And the multivariate regression analysis shows that Na (OR 0.846, 95% CI 0.74–0.968,  $P = 0.015$ ), Mechanical ventilation (OR 358.7, 95% CI 27.2–4 731.7,  $P < 0.01$ ) correlated with death. After the acute physiology parameters were transformed into APACHE II score, then do the Univariate regression analysis shows that BR, WBC were not any longer correlated with mortality, but K, which wasn't correlated with mortality before transforming, was correlated with mortality.

**Conclusion** APACHE II can be continuous to predict cardiac intensive care patients' prognosis, but still exist some deficiencies.

## The effect of fructose consumption on plasma cholesterol in adults: a meta-analysis of controlled feeding trials

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Fructose is widely used as a sweetener in production of many foods, yet the relation between fructose intake and cholesterol remains uncertain. We performed a systematic review and meta-analysis of human controlled feeding trials of isocaloric fructose exchange for other carbohydrates to quantify the effects of fructose on total cholesterol (TC), LDL cholesterol (LDL-C), and HDL cholesterol (HDL-C) in adult humans. Weighted mean differences were calculated for changes from

baseline cholesterol concentrations by using generic inverse variance random-effects models. The Heyland Methodological Quality was used to assess study quality. Subgroup analyses and meta-regression were conducted to explore possible influence of study characteristics. Twenty-four trials (with a total of 474 subjects) were included in our meta-analysis. In an overall pooled estimate, fructose exerted no effect on TC, LDL-C and HDL-C. Meta-regression analysis indicated that fructose dose was positively correlated with the effect sizes of TC and LDL-C. Subgroup analyses showed that isocaloric fructose exchange for carbohydrates could significantly increase TC by 12.97 mg/dL (95% CI: 4.66 – 21.29;  $P = 0.002$ ) and LDL-C by 11.59 mg/dL (95% CI: 4.39 – 18.78;  $P = 0.002$ ) at  $> 100$  g fructose/d but had no effect on TC and LDL-C when fructose intake was  $\leq 100$  g/d. In conclusion, very high fructose intake ( $> 100$  g/d) could lead to significantly increase in serum LDL-C and TC. Larger, longer and higher-quality human controlled feeding trials are needed to confirm these result.

### Admission high blood pressure can predict short-term prognosis of patients with ST-segment elevation myocardial infarction without cardiogenic shock and history of hypertension

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**Introduction** Several studies have demonstrated an inverse relationship between systolic blood pressure at admission and mortality in patients presenting with acute myocardial infarction (AMI). However, data on the relation between admission blood pressure and short-term prognosis in AMI patients without cardiogenic shock are still lacking.

**Methods** ST-segment elevation myocardial infarction (STEMI) patients without cardiogenic shock enrolled in this study were divided into 4 groups based on history of hypertension and admission blood pressure values (140/90 mm Hg as the cut-off value). The primary endpoint was incidence of all-cause mortality at day 7 and 30 after admission to emergency department. After baseline adjustment with Cox proportional hazards regression model, we explored whether high admission blood pressure was a risk factor that influence the short-term prognosis for the cohort.

**Result** A total of 7 298 patients without cardiogenic shock at admission were enrolled in our study. The risk of mortality at day 30 increased in patients with high admission blood pressure ( $\geq 140/90$  mm Hg) but without history of hypertension or cardiogenic shock at admission compared with patients with normal admission blood pressure ( $< 140/90$  mm Hg) (HR 1.41, 95% CI 1.03 – 1.94). The same findings were not seen in patients with a history of hypertension. History of hypertension was not associated with short-term prognosis for the entire cohort.

**Conclusion** Attention should be paid to AMI patients with admission blood pressure beyond 140/90 mm Hg and without history of hypertension as well as admission cardiogenic shock in order to improve the short-term survival for the subpopulation.

### Surgical procedures after failure of catheter interventions in the congenital heart diseases

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**Objective** Review the patient data that underwent surgical procedures which after interventional failure or occurred serious complications. Summarize open heart surgical Methods, especially rare complications.

**Methods** Collect 24 patients of age 3 – 67 yrs ( $19.9 \pm 18.3$  yrs) and weight 11 – 70 kg ( $39.3 \pm 20.7$  kg) who underwent open heart surgery treatment which after interventions failure with atrial septal defect, ventricular septal defect, and patent ductus arteriosus during 1999.6 – 2011.11 in Fu Wai Hospital. Analyze clinical data, interventional failure reasons, complication types, intraoperative findings, surgical skills, and surgical Result of these patients.

**Result** These 24 cases include ASD (14 cases), VSD (7 cases), and PDA (3 cases). Interventional complications involve occluder shedding (8 cases), residual shunt (6 cases), pericardial tamponade with perforation (3 cases), occluder shifting (2 cases), hemolysis (2 cases), severe tricuspid insufficiency (1 case), noncoronary sinus fistula to RA (1 case), and cAVB (1 case). Time interval surgical intervention after intervention is 1 hour to 5 Years ( $7.4 \pm 14.5$  months). 24 cases were removed occluders and surgically repaired cardiac anomalies simultaneously. All patients were discharged, no additional complications cases and no death cases.

**Conclusion** There are rare complications after catheter interventions, such as CoA caused by occluder shedding, except residual shunt, cAVB, and valve injury. Early Surgery is necessary, once the surgery indication is clear after interventions. Although the complications are complex, the intervention advantage of minimally invasive, easy to operate and safety should be affirmed. Regular follow-up after interventions is recommended. In case of interventional failure or complications, remove the occluder while correct cardiac anomalies underwent surgical procedures is safe and effective remedies.

### Long-term Result of tetralogy of fallot and treatment for the Complications

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**Purpose** Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart disease in China. The reported early-Result of treatment for the disease are satisfactory. However, more and more surgeons are increasingly concerned about their long-term postoperative Result, while the research related to this is rarely reported in China. Based on the retrospective study of TOF after radical operation, the long-term Result of and complications of treatment are discussed.

**Methods** We have retrieved articles reported within 10 years on long-term postoperative result of TOF after radical operations. Moreover, the patients of TOF who have received radical operations at Fu Wai Hospital over 10 years have been followed up by telephone or face-to-face interview. The follow-up result were analyzed statistically.

**Result** The survival rates of TOF after radical operations at 10, 20, and 25 years are 94.8%, 92.8% and 92.8%, respectively, 5-, 10- and 20-year freedom from reoperation rates are 81.5%, 68.9% and 46.6%.

The main issues include: pulmonary valve regurgitation and right ventricular dilatation, tricuspid regurgitation, right ventricular outflow tract/pulmonary residual stenosis, heart failure and decreased activity, arrhythmias and sudden death. For pulmonary valve regurgitation, pulmonary valve replacement surgery or percutaneous pulmonary valve replacement approach can be taken. If right ventricular outflow tract aneurysm is large enough, complete removal of the original patch and the akinesis myocardial fibrosis surrounding the area is necessary. Reconstruct the right ventricular outflow tract, if combined with moderate to severe pulmonary regurgitation and cardiac dysfunction, implanted valved conduit at the same time. Right ventricular outflow tract obstruction can be removed by secondary surgery, balloon dilatation and stent implantation, or self-expanding stents. Severe tricuspid regurgitation, should be actively treated, the preferred approach is tricuspid valvuloplasty, If it is repaired difficultly or badly, possible tricuspid valve replacement surgery should be taken. The basic treatment strategy of TOF at Fu Wai Hospital is that, for children less than six months, if there are no symptoms, clinical observations may be the best choice. if there are symptoms, palliative surgery should be taken for the children with poor developed pulmonary arteries. If the pulmonary artery development is good, some experts prefer to immediately perform radical surgery, while the other experts prefer to perform the surgery later. For the children six months or more, according to their preoperative assessment Result to determine radical surgery or palliative surgery.

**Conclusion** The early surgical Result of TOF are good. And for the pulmonary valve ring and pulmonary artery well developed cases, reserving the right ventricular outflow tract intact can lead to satisfactory long-term Result. But for transannular patch or external conduit repair, its long-term Result and complications should be aware by the surgeons. And these patients may need lifelong follow-up and repeated surgical or interventional therapy intervention. Besides, the treatment strategies of TOF need further clinical studies.

### Increased plasma levels of erythropoietin after renal denervation in patients with resistant hypertension

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**Objective** Erythropoietin (Epo) plays a crucial role in the formation and maturation of erythrocytes and is produced primarily by peritubular cells in the renal cortex. Previous studies suggest that renal sympathetic nerve activity (RSNA) may influence Epo regulation. Catheter-based renal denervation (RDN) has been shown to reduce renal noradrenaline spillover and blood pressure in patients with resistant hypertension. We therefore aimed to investigate whether RDN influences Epo levels.

**Method** 33 patients with resistant hypertension (age  $61 \pm 12$  yrs; baseline office blood pressure (BP)  $165 \pm 16/85 \pm 18$  mm Hg despite treatment with an average of  $4.9 \pm 1.7$  antihypertensive medications)

underwent bilateral RDN. Plasma levels of Epo, office blood pressure, twenty-four hour ambulatory blood pressure monitoring (ABPM), muscle sympathetic nerve activity (MSNA), renal function and haemoglobin were measured before the procedure and at 3 months follow-up. Antihypertensive medication was not changed during the first 3 months after RDN.

**Result** Office blood pressure was reduced by  $15 \pm 19/5 \pm 12$  mm Hg at 3 months after denervation ( $P < 0.001$  for systolic BP;  $P = 0.033$  for diastolic BP). 24 h-mean systolic and diastolic BP were also reduced (from  $145 \pm 16$  to  $140 \pm 18$  mm Hg;  $P = 0.036$ , and from  $80 \pm 11$  to  $77 \pm 12$  mm Hg;  $P = 0.024$ ), respectively. While haemoglobin levels remained unchanged, a significant increase in plasma Epo levels was observed at 3 months after RDN ( $7.81 \pm 3.68$  vs  $9.88 \pm 5.06$  mIU/mL;  $P = 0.025$ ). Changes in Epo levels correlated with baseline MSNA ( $r = 0.580$ ,  $P = 0.004$  for burst frequency;  $r = 0.471$ ,  $P = 0.023$  for burst incidence), such that the increase in Epo was most pronounced in patients with high baseline MSNA. The RDN induced changes in MSNA tended to correlate inversely with changes in Epo levels ( $r = -0.402$ ;  $P = 0.064$ ).

**Conclusion** Our findings suggest that RDN is associated with increased plasma levels of Epo in the absence of changes in hemoglobin, and that these effects are possibly mediated via a reduction in sympathetic nerve activity.

### Admission high blood pressure can predict short-term prognosis of patients with ST-segment elevation myocardial infarction without cardiogenic shock and history of hypertension

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**Introduction** Several studies have demonstrated an inverse relationship between systolic blood pressure at admission and mortality in patients presenting with acute myocardial infarction (AMI). However, data on the relation between admission blood pressure and short-term prognosis in AMI patients without cardiogenic shock are still lacking.

**Methods** ST-segment elevation myocardial infarction (STEMI) patients without cardiogenic shock enrolled in this study were divided into 4 groups based on history of hypertension and admission blood pressure values ( $140/90$  mm Hg as the cut-off value). The primary endpoint was incidence of all-cause mortality at day 7 and 30 after admission to emergency department. After baseline adjustment with Cox proportional hazards regression model, we explored whether high admission blood pressure was a risk factor that influence the short-term prognosis for the cohort.

**Result** A total of 7 298 patients without cardiogenic shock at admission were enrolled in our study. The risk of mortality at day 30 increased in patients with high admission blood pressure ( $\geq 140/90$  mm Hg) but without history of hypertension or cardiogenic shock at admission compared with patients with normal admission blood pressure ( $< 140/90$  mm Hg) (HR 1.41, 95% CI 1.03 – 1.94). The same findings were not seen in patients with a history of hypertension. History of hypertension was not associated with short-term prognosis for the entire cohort.

**Conclusion** Attention should be paid to AMI patients with admission blood pressure beyond  $140/90$  mm Hg and without history of hypertension as well as admission cardiogenic shock in order to improve



the short-term survival for the subpopulation.

### Comparison of procedural and long-term outcomes between transradial and transfemoral approach for triple vessel coronary artery disease intervention

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**Objective** The aim of the present study was to evaluate the safety, feasibility, procedural variables and long-term outcome by transradial (TR) approach compared with the transfemoral (TF) access in triple vessel coronary artery disease undergoing percutaneous coronary intervention.

**Background** The feasibility, safety and efficacy between TR and TF approach for coronary interventional treatment have been compared in some complicated situations including AMI, unprotected left main coronary artery disease. However, in terms of triple vessel disease intervention, there is still no comparison regarding procedural and long-term outcomes between TR and TF approach.

**Methods** Totally 4 974 consecutive patients (TR: 3856, TF1118), who were diagnosed as triple vessel disease without LM involved by angiography and underwent percutaneous revascularization, were prospectively enrolled in the study. Procedural Result (including success rate, hospitalization duration, fluoro time, bleeding event etc) were recorded specifically in database. Over a mean follow-up period of 22 months, we obtained clinical outcome including death, myocardial infarction (MI), thrombosis, target lesion revascularization (TLR), target vessel revascularization (TVR), and major adverse cardiac events (MACE, the composite of death, MI, and TVR). In order to diminish the selective bias between the two groups, we used propensity score matching method and got 930 pairs of patients with comparable baseline data to compare the procedural and long-term outcome between TR and TF group.

**Result** After propensity score matching, clinical and angiographic characteristics were similar between the two groups. No significant difference was observed between the two groups for procedural success rate (TR 99.8% vs TF 99.9%,  $P = 0.62$ ), total fluoro time (TR  $14.54 \pm 10.99$  min vs TF  $15.35 \pm 10.36$  min,  $P = 0.11$ ), contrast volume (TR  $166.34 \pm 94.97$  min vs TF  $171.60 \pm 96.86$  min,  $P = 0.40$ ). However, duration of hospitalization (TR  $7.49 \pm 4.46$  days vs TF  $8.63 \pm 6.23$  days,  $p < 0.0001$ ), in-hospital occurrence of TIMI bleeding (TR 1.0% vs TF 2.9,  $P = 0.003$ ) were significant lower with TRI. According to clinical follow-up, cumulative rates of MI (TR 2.9% vs TF 3.3%,  $P = 0.68$ ), TVR (TR 6.1% vs TF 7.7%,  $P = 0.16$ ), all thrombosis (TR 4.3% vs TF 4.7%,  $P = 0.64$ ) did not statically differ in the two groups. However, all-cause mortality (TR 1.8% vs TF 3.7%,  $P = 0.01$ ) and MACE (TR 10.2% vs TF 13.7%,  $P = 0.02$ ) were significant lower with TRI.

**Conclusion** As compared to TFI, TRI for triple vessel disease intervention is feasible, safe and associated with similar procedural success, abbreviated hospitalization, reduced bleeding, lower incidence of death and MACE, and comparable long term efficacy.

### Can “hybrid stent implantation” improve long-term safety without adversely affecting efficacy when treating multilesion coronary artery disease in the drug-eluting stent era?

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**Background** Though drug-eluting stent (DES) almost solved problem of restenosis, safety issues related to stent thrombosis are still the major concern of DES. We hypothesized that hybrid stent implantation may decrease the use of DES, probably improving the long-term safety but not affecting efficacy adversely when treating multilesion coronary artery disease in the DES era.

**Methods** From April 2004 to October 2006, 848 patients with multilesion disease underwent hybrid stent implantation. During the same period 5 647 patients with multilesion coronary heart disease were treated by exclusive DES implantation in Fu Wai Hospital. According to propensity score matching, we chose 823 pairs of patients with multilesion coronary artery disease for inclusion into our study. We obtained the 24-month clinical outcome including death, myocardial infarction (MI), thrombosis, target lesion revascularization (TLR), target vessel revascularization (TVR), and major adverse cardiac events (MACE, the composite of death, MI, and TVR). We used Cox's proportional-hazard models to assess relative risks of all the outcome measures after propensity match.

**Result** At 24 months, patients in the hybrid stent implantation group showed a significantly higher risk of TLR (8.39% vs 3.28%, HR 2.38, 95% CI: 1.50 – 3.70), TVR (11.07% vs 6.32%, HR 1.61, 95% CI: 1.15 – 2.27) and MACE (13.75% vs 8.75%, HR 1.37, 95% CI: 1.02 – 1.85). No significant difference was apparent in terms of mortality (1.22% vs 1.70%, HR 0.55, 95% CI: 0.24 – 1.25) MI (1.95% vs 2.31%, HR 0.73, 95% CI: 0.37 – 1.42), or thrombosis (definite+probable) (0.73% vs 1.58%, HR 0.40, 95% CI: 0.15 – 1.05).

**Conclusion** In patients with multilesion coronary artery disease, the exclusive DES implantation was associated with significantly lower risks of TLR, TVR and MACE, and the hybrid stent implantation did not result in any significant improvements regarding safety issues. Prospective studies are needed to confirm our Result.

### Clinical analysis of inpatients of systemic lupus erythematosus with coronary artery disease

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**Objective** In order to improve clinical practice and awareness, we analyze clinical characteristics of coronary artery disease (CAD) patients with systemic lupus erythematosus (SLE),

**Methods** Searching 2002 – 2013 year diagnosis of CAD patients

with SLE through Fuwai hospital electronic medical records management system, 25 CAD patients with SLE are found in all. The control groups are 50 cases matched randomly from FuWai Hospital diagnosis of CAD without connective tissue diseases. For each group, traditional coronary risk factors, blood biochemistry, chest X-ray, ultrasound, and Result of coronary angiography are analyzed retrospectively.

**Result** Compared to CAD patients without connective tissue diseases, CAD patients with SLE have earlier menopause [(47.80 ± 4.07) years vs (50.81 ± 2.98) years,  $P < 0.01$ ], have more unstable angina possibilities [92% (23/25) than 50% (25/50)], get more III and IV grade heart failure rate [28% (7/25) than 4% (2/50),  $P < 0.01$ ]. CAD patients with SLE have higher level of C-reactive protein [(12.46 ± 14.85) than (8.86 ± 6.21),  $P < 0.01$ ], creatinine [(77.39 ± 20.34) than (67.06 ± 17.02),  $P < 0.05$ ], urea nitrogen [(8.86 ± 7.17) than (6.21 ± 2.09),  $P < 0.05$ ] in blood than the control group. Results of Chest X-rays in the case group show more costophrenic angle blunting [36% (9/25) than 6% (3/50),  $P < 0.01$ ] and pulmonary congestion [28% (7/25) than 2% (1/50),  $P < 0.01$ ]. Coronary angiography showed CAD patients with SLE the rate of two coronary blockage [24% (6/25) than 4% (2/50),  $P < 0.01$ ] and three coronary artery disease [48% (12/25) than 26% (13/50),  $P < 0.05$ ] is significantly higher than the control group.

**Conclusion** CAD patients with SLE have earlier menopause than CAD patients without connective tissue disease. Traditional coronary risk factors are similar in these two groups. The case group patients' coronary pathological changes are extensive, with higher occlusion rate, easily combined with cardiac insufficiency. Tests and inspections like C-reactive protein, creatinine, urea nitrogen, chest X-rays, coronary angiography may be able to reflect CAD combined with SLE's severity and prevent cardiac events of CAD patients with SLE.

### Percutaneous balloon aortic valvuloplasty in the treatment of patients with severe aortic stenosis

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**Background** Patients who have aortic stenosis (AS) with severe heart failure or cardiogenic shock are considered unsuitable for surgical aortic valve replacement (AVR) or transcatheter aortic valve implantation (TAVI), and generally have a poor prognosis with conservative therapy. It has been shown that percutaneous balloon aortic valvuloplasty (PBAV) may transiently improve severe left ventricular dysfunction in patients with AS.

**Objective** To assess procedural and clinical outcomes in patients with severe AS undergoing PBAV, who are considered transiently unsuitable for either AVR or TAVI.

**Methods** Between March 2011 and January 2013, a total of 10 patients underwent PBAV. Pre- and post-procedure aortic valve gradients were measured by catheterization and echocardiography. Patients were assessed for symptomatic benefit and clinical outcomes.

**Result** Mean patient's age was 70 ± 8 years (52 – 87), 6 were male, and the logistic EuroScore was 26.1 ± 6.7%. All patients were severe heart failure with New York Heart Association (NYHA) class ≥ III, and 5 were in cardiogenic shock requiring inotropic support. Mean left ventricular fraction (LVEF) were 29 ± 6%, and LVEF ≤ 30% was in 6 patients. PBAV was successfully performed in all cases. Mean transaortic valve gradient fell from 50 ± 18 mm Hg to 33 ± 14 mm Hg ( $P = 0.028$ ). The most common complications were hypotension and minor bleeding

at the femoral puncture site. No patients died during procedure, and 2 died in hospital: one died of pulmonary infection 3 days after procedure; 1 died of repeated ventricular tachycardia. Three died post-discharge: 1 died of cardiogenic shock at 6-month; 1 had a sudden death at home at 16-month; 1 died of multiple organ failure at 5-month. Five patients underwent secondary successful TAVI ( $n = 2$ ) or AVR ( $n = 3$ ).

**Conclusion** In high-risk patients with AS and temporary contraindications to AVR or TAVI, PBAV can be safely used as a bridge to intervention with good outcomes.

### Transradial vs transfemoral method of percutaneous coronary revascularization for chronic total occlusion disease: comparison of procedural and late-term outcomes

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**Background** Transradial coronary intervention is a safe and effective method of percutaneous revascularization. Furthermore, the indications for transradial percutaneous coronary intervention (PCI) are expanding. However, the efficacy and the safety between TR and TF approaches of PCI for chronic total occlusion (CTO) have not been compared.

**Objective** This study sought to compare outcomes between transradial (TR) and transfemoral (TF) percutaneous revascularization in patients with chronic total occlusion (CTO).

**Methods** Among 2 352 consecutive patients with CTO disease treated with percutaneous revascularization by either TR ( $n = 1 858$ ) or TF ( $n = 494$ ) vascular access, procedural outcomes, resource use, in-hospital bleeding, and late clinical events were compared according to vascular access method.

**Result** Clinical and angiographic characteristic were similar in both groups. Duration of hospital stay (7.7 ± 4.9 vs 9.4 ± 5.4,  $P < 0.001$ ) and in-hospital occurrence of bleeding defined by Bleeding Academic Research Consortium (5.9% vs 1.9%,  $P < 0.001$ ) were significantly lower with TR access. Using propensity score modeling (421 matched pairs), over a mean follow-up period of 15 months, rates of death (0.5% vs 1.0%,  $P = 0.413$ ), nonfatal myocardial infarction (0.5% vs 0.5%,  $P = 1.000$ ), stent thrombosis (0.5% vs 0.5%,  $P = 1.000$ ), and any target vessel revascularization (4.0% vs 5.7%,  $P = 0.262$ ) did not statistically differ among TR and TF groups, respectively.

**Conclusion** In contrast to TF vascular access, TR percutaneous coronary revascularization for CTO disease is feasible and associated with similar procedural success, abbreviated hospitalization, reduced bleeding, and comparable late-term clinical safety and efficacy.

### Early alterations of red blood cell rheology in infective endocarditis patients with sepsis

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**Objective** Septic shock is one of the main causes of death of infective endocarditis (IE). Microcirculation plays a vital role in the

development of multiple organ failure in severe sepsis. The effects of red blood cell (RBC) rheology on these tissue and microcirculation variables in early severe sepsis are not well defined. The aim of the present study was to explore the red blood cell rheology in a intensive care unit population on admission.

**Methods** On the basis of the preliminary work, we investigated the erythrocyte deformability and aggregation, osmotic fragility and erythrocyte electrophoresis rate, among the three groups of IE patients with sepsis, non-septic critical ill patients and volunteers, in order to further clarify the pathogenesis of IE. Red blood cell rheology was assessed within the first 24 hrs after intensive care unit admission.

**Result** The whole blood viscosity was significantly altered in septic compared to non-septic patients and volunteers for the majority of shear stress rates studied. Red blood cell deformability and the aggregation index were significantly altered in septic compared to non-septic patients and volunteers. The erythrocyte electrophoresis rate was decreased significantly in septic compared to non-septic patients and volunteers. We also found that the osmotic fragility of RBCs at 145 mOsm/kg was greater increased in septic patients than the other groups, and non-sepsis critical ill patients was higher than the control group, but no statistical difference.

**Conclusion** Early alterations of red blood cell rheology are common in intensive care unit patients, especially in those with sepsis. These alterations could contribute to the microcirculatory alterations observed in critically ill patients.

### Transcatheter closure of coronary artery fistulae: initial human experience with the amplatzer duct occluder II

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**Purpose** Transcatheter device closure is an alternative treatment for selective patients with coronary artery fistulae (CAF). Currently available technology is limited for closure of CAF with tortuous coronary artery to the drainage. The purpose of this study was to evaluate the technical feasibility, safety, and efficacy of the new device Amplatzer duct occluder II (ADO II) for closure of coronary artery fistula (CAF).

**Methods** From April 1, 2011 to July 15, 2012, 5 patients (3 males, 2 females) aged from 3 years to 27 years (median age 5 years) underwent CAF closure with the ADO II. We evaluated early and short-term Result.

**Result** The devices (ADO II) were deployed via the femoral vein (3 cases), brachial artery (1 case) and radial artery (1 case). There were no complications during the procedures. Median fluoroscopy and procedural times were 20 and 39 min, respectively. Immediate trivial and mild residual shunt was present in one patient, respectively, but disappeared 24 hours after the procedure, and there was no recanalization at a median follow-up of 6 months.

**Conclusion** The new device ADO II was safely deployed with complete resolution of the CAF shunt with tortuous coronary artery to the drainage. The reduced sheath sizes and softer shape of this device allows for venous or arterial approach. The ADO II might be a preferable alternative for closure of small- tortuous CAFs.

### Digoxin and mortality in patients with atrial fibrillation

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**Background** Digoxin is frequently used for rate control in paroxysmal, persistent and permanent atrial fibrillation (AF). The relationship of digoxin and mortality was so different in recent studies, and it remains unclear how digoxin affected mortality. The objective of this study was to determine the relationship between digoxin and mortality in patients with AF.

**Methods** In this prospective observational multicentre registry study, all AF cases were confirmed by the electrocardiograms (ECGs) in the ED from November 2008 to October 2011 in China. Patients' demographics, medical history, type of AF, treatment, and outcome of emergency room visit were collected at baseline by the treating physicians using a standardized questionnaire. The main outcome measure was all-cause mortality at 1 year post-ED visit.

**Result** The association between digoxin and mortality was assessed in 2016 Chinese patients with AF enrolled in emergency department (ED) using multivariate Cox proportional hazards models. Of those, 722 received digoxin as initial therapy and 1 291 received no digoxin at baseline. Propensity scores for digoxin use were estimated for each of these 2016 patients and used to assemble a cohort of 359 pairs of patients receiving and not receiving digoxin, who were balanced on 49 baseline characteristics. Among pre-match patients, digoxin was associated with an increase in all-cause mortality (16.6% vs 12.6%,  $P = 0.014$ ). However, this association became non-significant after multivariable adjustment (HR: 1.03; 95% CI: 0.66 – 1.61;  $P = 0.911$ ) and adjustment for propensity scores (HR, 0.97; 95% CI: 0.63 – 1.50;  $P = 0.892$ ). All-cause mortality occurred in 15.2% and 14.7% of matched patients receiving and not receiving digoxin, respectively (HR: 1.21; 95% CI: 0.68 – 2.13;  $P = 0.519$ ).

**Conclusion** There was no significant increase in all-cause mortality in AF patients with digoxin as baseline initial therapy.



## A prospective, multicenter, randomized trial comparing paclitaxel-coated balloon with Paclitaxel-eluting stent for the treatment of drug-eluting stent restenosis: 9-month angiographic and 12-month clinical Result from PEPCAD China ISR

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**Background** Treatment of drug-eluting stent (DES) restenosis is still challenging with no established best strategy. The PEPCAD China ISR trial was to demonstrate the efficacy and safety of paclitaxel-coated balloon (PCB) Sequent Please (B Braun, Germany) compared to paclitaxel-eluting stent (PES) TAXUS Liberte (Boston Scientific, USA) in a Non-European patient population with DES restenosis.

**Methods** In this prospective, multicenter, randomized trial, we planned to enroll patients between 18 – 80 years old with at least one DES restenotic lesion stratified by Mehran classifications at 17 Chinese centers. Patients were 1: 1 randomly assigned to either receive PCB or PES treatment. The primary endpoint was in-segment late lumen loss (LLL) at 9-month, and the major secondary endpoints include percentage of diameter stenosis (%DS), binary restenosis at 9-month, target lesion failure (TLF) defined as the composite of cardiac death, target vessel myocardial infarction, or ischemia-driven target lesion revascularization at 12-month, and definite/probable stent thrombosis (ST).

**Result** 215 patients were randomized to PCB group (n = 109) and PES group (n = 106). In terms of the patient, lesion or procedural characteristics there were no significant differences between both treatment groups. Angiographic follow-up data at 9-month was available for 172 (80%) patients. The 9-month in-segment LLL in the PCB was non-inferior as compared to the PES group ( $0.46 \pm 0.51$  mm vs  $0.55 \pm 0.61$  mm, difference [95% CI]:  $-0.06$  mm [ $-0.23, 0.10$ ], P for non-inferiority = 0.0005). The 9-month in-segment %DS, binary restenosis, 12-month TLF, and definite/probable ST rates were no statistical differences between both treatment groups ( $29.0 \pm 21.3$  vs  $30.8 \pm 25.3$ , P = 0.59;  $18.6\%$  vs  $23.8\%$ , P = 0.38;  $16.5\%$  vs  $16.0\%$ , P = 0.92;  $0.9\%$  vs  $1.0\%$ , P = 1.00, respectively).

**Conclusion** PCB angioplasty was non-inferior to PES implantation in a Chinese population in need of revascularization after DES restenosis without the necessity of having additional metal layers for drug release. (ClinicalTrials.gov identifier: NCT01622075).

## The clinical characteristics and outcomes of Chinese NSTEMI-ACS patients in different time periods

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**Objective** To compare the clinical characteristics, treatment Methods and outcomes in Chinese non ST elevated acute coronary syndromes (NSTEMI-ACS) patients from two large clinical trials in different time periods.

**Methods** All Chinese NSTEMI-ACS patients from two large International clinical trials (OASIS registry and TIMACS) who accepted coronary artery angiography after first admission were recruited in our analysis. The current primary outcome was the combination of death, myocardial infarction, refractory ischemia, and stroke within 180 days. We compared the clinical characteristics, treatment Methods and outcomes between those two patient groups.

**Result** The total of 1 473 NSTEMI-ACS patients were recruited in our analysis, in which 749 from Organization to Assess Strategies for Ischemic Syndromes (OASIS REISTRY) that completed in 38 centers in China from April 1999 to December 2000, and the other 724 patients from The Timing of Intervention in Acute Coronary Syndromes (TIMACS) trial in 24 centers in China performed from April 2007 to June 2008. For baseline characteristics, comparing to TIMACS patients, OASIS group had older age ( $58.7 \pm 10.2$  y vs  $64.2 \pm 10.1$  y), more males ( $74.4\%$  vs  $66.3\%$ ), higher blood pressure at admission ( $136/83$  mm Hg vs  $131/78$  mm Hg), more myocardial infarction history ( $28.0\%$  vs  $12.0\%$ ), but less current smoking ( $30.0\%$  vs  $33.8\%$ ), less histories of previous PCI ( $6.4\%$  vs  $9.4\%$ ), stroke ( $5.1\%$  vs  $8.8\%$ ), hypertension ( $56.6\%$  vs  $62.8\%$ ) and diabetes ( $16.2\%$  vs  $23.3\%$ ). After admission, comparing to OASIS group, TIMACS patients had significant higher PCI proportion ( $74.9\%$  vs  $49.3\%$ , P < 0.001). In addition, for secondary prevention, TIMACS patients had significant higher medication treatment proportion in hospital, at discharge and at 180 days' follow up than OASIS group (P < 0.05 for  $\beta$ -blocker, ACEI/ARB and lower lipid drugs) and also higher compliance rate. The combined primary outcome event rate at 180 days was much lower in TIMACS than OASIS patients ( $13.0\%$  vs  $48.5\%$ , P < 0.001) in which the refractory angina reduction contributed most for it. By multivariable Logistic regression analysis for combined primary outcomes at 180 days, after adjusted for other factors, previous PCI (HR: 2.23; 95% CI: 1.17 – 4.24), medical history of diabetes (HR: 1.84; 95% CI: 1.22 – 2.79) or stroke (HR: 2.47; 95% CI: 1.19 – 5.13), calcium antagonists treatment during hospitalization (HR: 1.71; 95% CI: 1.25 – 2.33) were independent risk factors in OASIS group; while patient age (HR: 1.03; 95% CI: 1.01 – 1.06), previous MI (HR: 2.35; 95% CI: 1.21 – 4.58), IABP treatment during hospitalization (HR: 3.96; 95% CI: 1.52 – 10.31) were independent risk factors in TIMACS group.

**Conclusion** TIMACS population had higher rates on PCI treatment and secondary prevention medication administration but less integrated incidence of primary outcomes than OASIS group which reflected the big progress in Chinese medical care in the decades according to the updated guidelines.

## Stroke as the first and recurrent manifestation of takayasu arteritis: a case report.

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**Takayasu arteritis** is a chronic, idiopathic disease characterized by granulomatous vasculitis of medium and large arteries. In addition to constitutional symptoms, it causes various clinical morbidities, such as arm claudication, decreased arterial pulses, carotidynia and hypertension. Neurological involvement is reported in only a minority of patients and occurrence of stroke as the first and recurrent manifestation of disease has been rarely reported. The rarity of the disease and especially such a presentation can cause considerable delay in the diagnosis and treatment. We reported clinical, laboratory and imaging findings of an 18-year old boy with TA, who was initially presented by a stroke and suffered another two strokes within 10 months. CTA showed a serious coarctation of the descending aorta about 3.0 mm in width, occlusion of initial segment of right subclavian artery and left external carotid artery, and nearly occlusion of initial segment of right external carotid artery. BP right arm 143/85 mm Hg, right leg 116/79 mm Hg, left arm 210/110 mm Hg, and left leg 112/35 mm Hg. ABI right 0.55, and left 0.53. The angiography showed occlusion of right subclavian artery, and 90 percent stenosis of the middle part of the descending aorta. Patient was planted a stent in the descending aorta. He improved remarkably after two weeks of follow up.

An 18-year-old boy was admitted to our hospital with a 10-month history of coarctation of aorta. 10 month before admission, the patient suffered a sudden onset of impaired mobility of the left side body under no obvious predisposing causes, dysphagia and cough. The skull CT examination revealed cerebral infarction. It was detected that his left arm blood pressure (BP) was 180/90 mm Hg, but his BP in legs was not checkable. The cardiovascular CT angiography (CTA) presented that there is coarctation of the thoracic aorta (diameter 4.62 mm), calcification of the wall and collateral circulation. Six months ago, he was referred to the department of Cardial Surgery, Fuwai Hospital. The ultrasonic cardiogram at Fuwai Hospital suggested patent ductus arteriosus (3 mm) and a distal segment narrow (10 mm) of the descending aorta. CTA showed a serious coarctation of the descending aorta about 3.0 mm in width, occlusion of initial segment of right subclavian artery and left external carotid artery, and nearly occlusion of initial segment of right external carotid artery. BP right arm 143/85 mm Hg, right leg 116/79 mm Hg, left arm 210/110 mm Hg, and left leg 112/35 mm Hg. ABI right 0.55, and left 0.53. Takayasu arteritis was suspected, but the doctor didn't give him operation. Then he went to Xiehe Hospital. Basal laboratory examinations revealed erythrocyte sedimentation rate (ESR) 2 mm/h; IgG, IgA, IgM negative, and ANA negative, normal ASO, CRP and RF. During hospitalization, the patient suffered another infarct of brain with his left side body movement disturbance. So he was hospitalized in Jinan Military Region General Hospital. The skull CT suggested bilateral

multiple lacunar infarction. Prednisone, starting at 60 mg qd was given and was slowly reduced to 15 mg qd within four months. Aspirin 50 mg qd, Omeprazole 20 mg bid, Caltrate 2 pills qd and Naioxintong Capsule 4 pills tid were given. Patient was referred to the department of Peripheral Vascular, Fuwai Hospital in order to perform interventional treatment. Patient had history of cerebral infarction approximately three years ago with no sequelae. Patient had left-sided impairment of mobility and speech difficulties. The Bruit was audible over the right carotid artery and the back area. The right radial pulse and both femoral pulses were weak. The left arm BP was 180/110 mm Hg, while the right arm BP was 140/120 mm Hg. At Fuwai Hospital, the patients were administered Nifedipine Sustained Release Tablets (ii) 10 mg q8h and Metoprolol Tartrate Tablets 25 mg q8h to control BP. Prednisone was given 20 mg qd. Pantoprazole 40 mg qd was substituted for Omeprazole to protect the stomach. Calcitriol Soft Capsules 0.25ug qd and calcium carbonate tablet 0.5 g tid were given to prevent osteoporosis.

Patient was performed percutaneous peripheral vascular imaging via femoral artery, showing occlusion of right subclavian artery, 90 percent stenosis of the middle part of the descending aorta. A Wallstent 22 mm\*45 mm was planted in the descending aorta. The treatment was successful. Aafter the intervention, the patient still had high BP for his age (140/80 mm Hg) and the antihypertensive drugs should not be discontinued. Besides, he should receive dual antiplatelet therapy with aspirin 100 mg qd and clopidogrel 50 mg qd to prevent thrombotic events. After two weeks follow up, the patient recovered remarkably.

## Clinical profile and management of hospitalized patients with chronic heart failure in Xinjiang

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**Objective** Chronic heart failure (CHF) is a common cause for admission to hospital in the Chinese population. It remains one of the major cardiovascular diseases with an increasing hospitalization burden and an ongoing drain on health care expenditures. The purpose of this survey was to determine the epidemiological factors, the current status of treatment and prognosis in patients with a clinical diagnosis of CHF in Xinjiang.

**Methods** This was a prospective, multi-centre, hospital-based study conducted in 15 hospitals distributed throughout the major parts of Xinjiang from January 2010 and October 2012. CHF was diagnosed by clinical and echocardiography criteria according to the modified Framingham criteria. Follow-up information was obtained through outpatient examination or telephone contact.

**Result** A total of 5 357 patients of all ages were enrolled, 34.7% female and 65.3% male. Mean age was 64.60 ± 12.77 years. The number of patients with CHF dramatically increased with advancing age, 68.7% was aged > 60 years. The main risk factors or possible causes of CHF were coronary heart disease, hypertension, and idiopathic dilated cardiomyopathy, which accounted for 50.8%, 31.8% and 7.2% respectively. Rheumatic heart disease and pulmonary heart disease causing heart failure were scarce. In these patients, systolic function was reduced (left ventricular ejection fraction < 45%) in 2066 (38.6%) and normal (left ventricular ejection fraction ≥ 45%) in 3291 (61.4%). At discharge, conventional drugs, including diuretics and digitalis, were prescribed in 45.5% and 26.8%. 72.8% of patients were on blockers of

the rennin-angiotensin-system (including angiotensin-converting enzyme inhibitors or angiotensin-receptor-blockers) and 66.8% on beta-blockers. Spironolactone was prescribed in 46.6%. Among the participating hospitals, the prescription rates of neuroendocrine antagonists was much less in primary hospitals than teaching hospitals and district hospitals ( $P < 0.001$ ). One-year mortality rate of patients discharged alive in primary hospitals, district hospitals and teaching hospitals was 16%, 14% and 11% respectively ( $P < 0.001$ ).

**Conclusion** The present study reports the clinical profile and management of patients with CHF as it presents in Xinjiang. Standard treatment for CHF seems to be less than optimum, particularly in primary hospitals. Early identification, treatment and prevention of the CHF include lifestyle changes and management for controlling the components of the CHF, are major challenges in the general population in Xinjiang.

### The impacts of baseline alkaline phosphatase and other traditional biomarkers on the extent of coronary artery disease and early outcome in patients with angina-like chest pain

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**Objective** We compare the predictive value of alkaline phosphatase (ALP) C-reactive protein (CRP), neutrophil count, fibrinogen, hemoglobin A1C (HbA1c) and survival in patients with stable angina pectoris (SAP).

**Methods** Patients with SAP, 1433, scheduled for coronary angiography were prospectively followed up and were classified into tertiles according to values of serum ALP. The relationship between the five markers and clinical outcomes were evaluated.

**Result** ALP was correlated with hs-CRP, neutrophil count, fibrinogen and HbA1c. Area under the ROC curve ( $AUC = 0.57$ , 95% CI 0.53 – 0.63,  $P = 0.001$ ) and multivariate logistic regression models were consistently suggested that ALP, Fibrinogen and HbA1c were independent predictors of severity of coronary artery disease (CAD) for patients with SAP (ALP: OR = 1.01, 95% CI 1.00 – 1.02,  $P = 0.010$ ; Fibrinogen: OR = 1.49, 95% CI 1.15 – 1.93,  $P = 0.002$ ; HbA1c: OR = 1.53, 95% CI 1.23 – 1.89,  $P = 0.000$ ). During an average 12-month follow-up, 133 out of 1433 patients underwent pre-specified outcomes. In Cox regression models, HbA1c and neutrophil count, but not ALP, CRP and fibrinogen, were identified as the independent predictors of adverse prognosis (HR = 1.53, 95% CI 1.23 – 1.89,  $P = 0.000$ ; HR = 1.49, 95% CI 1.15 – 1.93,  $P = 0.002$ , respectively).

**Conclusion** High levels of ALP were correlated with CRP, neutrophil count, fibrinogen and HbA1c and that it was an independent predictor for extent of CAD but not for the early outcome of patients with SAP.

### Analysis of cardiopulmonary bypass status in China: eight-year development trends

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**Objective** Study the development of cardiopulmonary bypass (CPB) in the past 8 years to come up with predictions and recommendations in China.

**Methods** Domestic hospitals performing cardiovascular operations were inquired with questionnaires annually (between 2003 and 2008) upon the amount of on-pump and off-pump cardiovascular operations, oxygenators of different types and the amount of extracorporeal membrane oxygenations (ECMO). All the hospitals in this study were divided into 8 grades by the amount of cardiovascular operations. The market share of hospitals in each grade was analyzed.

**Result** The total amount of cardiovascular operations was 170 547 in 2010, of which 136 753 were performed under CPB. The ratio of imported membrane oxygenators increased from 43.22% in 2003 to 59.75% in 2010, while bubble oxygenator composition decreased from 43.78% in 2003 to 14.59% in 2010. 44 hospitals carried out 206 cases of ECMO in 2010. There were 32 hospitals that performed cardiovascular operations over 1, 000 cases and their market share was 43%. There were 255 hospitals that performed cardiovascular operations less than 50 cases and their market share was only 3%.

**Conclusion** CPB in China has gone through a rapid development in the past eight years. Medical resources for CPB should be concentrated and systematic train regulations should be established in future.

### The investigation of exercise tolerance changes of patients with essential hypertension

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**Objective** To investigate exercise tolerance changes of patients with essential hypertension through evaluating their exercising cardiorespiratory function.

**Methods** 84 subjects were selected and divided into two groups, essential hypertension group (EH,  $n = 60$ ) and Normal group (N,  $n = 24$ ). All subjects received cardiopulmonary exercise test.

**Result** The baseline SBP and DBP of EH group were significantly higher. Exercise time,  $VO_{2max}/kg$ ,  $VO_{2A1'}/kg$  and  $HR_{max}$  of EH group were significantly lower. During the recovery phase, HRR2, HRR3, 2 minrSBP and 3 minrSBP of EH group were significantly lower.

**Conclusion** Patients with essential hypertension who don't have obviously abnormal cardiopulmonary function may have lower exercise tolerance, however, during the recovery phase, no obvious difference was investigated compared to N group. It suggests that exercise tolerance and quality of life of patients with essential hypertension could be improved by proper exercise.



### Effect of desmopressin on platelet aggregation and blood loss in patients undergoing valvular heart surgery

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**Objective** To explore the effects of desmopressin on platelet aggregation and blood loss in patients undergoing cardiac surgery with cardiopulmonary bypass and to evaluate the function of desmopressin in hemostasis.

**Methods** For a randomized, double-blind, placebo-controlled trial, a total of 102 patients undergoing valvular heart surgery were divided into a desmopressin group ( $n = 52$ ) and a control group ( $n = 50$ ). A dose of desmopressin ( $0.3 \mu\text{g}/\text{kg}$ ) was administered intravenously 1 hour before the end of the cardiopulmonary bypass in the desmopressin group. At the same time, normal saline was given to the control group. Platelet aggregation was measured. Postoperative blood loss, blood transfusions and urine volumes were documented.

**Result** There was no significant difference in platelet aggregation between the two groups. The blood loss in the first 6 hours was reduced in the desmopressin group ( $202 \pm 119 \text{ ml}$  vs  $258 \pm 143 \text{ ml}$ ,  $P = 0.023$ ). Postoperative blood loss, blood transfusions and urine volumes were not different between the groups.

**Conclusion** A single dose of desmopressin can reduce postoperative blood loss within the first 6 hours in patients undergoing valvular heart surgery.

### The association study between hypertension combined metabolic syndrome with coronary disease

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**Objective** To study the relationship of EH combined MS and its metabolic components with the CHD.

**Methods** EH whether with MS can be divided into EH group and EH combined MS group, determine their BMI, FBG, TG, TG, HDL-C, LDL-C.

**Result** (1) Compared with EH group, EH with MS group of BMI, FBG, TG level increased significantly ( $P < 0.05$ ); HDL-C, LDL-C levels decreased significantly ( $P < 0.05$ ); (2) EH with the MS group coronary disease events is increased, but no statistical difference ( $P > 0.05$ ). (3) Logistic regression analysis showed that MS is independent risk factor for CHD. (4) Pearson analysis shows the elements of MS, TG and HDL were positively correlated.

**Conclusion** (1) MS is independent risk for CHD, and dangerous degree is higher than its single components. (2) EH with the MS has a certain effect on CHD. (3) MS in lipid metabolism may have its protection regulation mechanism between components.

### High dose Atorvastatin is associated with decreased C-reactive protein but not cardio- and renal-protective effect in patients undergoing coronary artery bypass grafting

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**Background** High dose statins were reported to have upstream effect in patients undergoing percutaneous coronary intervention, especially in terms of cardio and renal protection. However, the upstream effect of high dose atorvastatin in coronary artery bypass grafting patients is not clear. On the assumptions of that the cardio- and renal protective effect of high dose Atorvastatin are associated with the anti-inflammatory effect of statins, we conducted a double-blinded, randomized prospective study in our institute.

**Methods** 60 statin native patients undergoing coronary artery bypass grafting under CPB were enrolled in the study and randomized into two groups: Atorvastatin group and control group (30 patients each). Patients in Atorvastatin group received 80 mg Atorvastatin 12 hours before surgery and plus 40 mg 2 hours before surgery, control group received equal dose of placebo in the same regimen. Serum high sensitive CRP (hs-CRP), Cr and CK-MB were measured at baseline, before surgical incision, after surgery, and 6 hours, 12 hours, 24 hours and 48 hours postoperatively.

**Result** There were no significant differences between the two groups in baseline parameters. hsCRP increased significantly postoperatively compared with baseline values in both groups, and the hsCRP values in Atorvastatin group before surgical incision and after surgery were significantly higher than the controlled group ( $3.69 \pm 0.79 \text{ mg/L}$  vs  $6.42 \pm 1.48 \text{ mg/L}$ ,  $7.68 \pm 3.26 \text{ mg/L}$  vs  $11.01 \pm 3.64 \text{ mg/L}$  respectively,  $P < 0.05$ ), however the values in the other time points did not differ significantly. Serum Cr in both groups decreased after surgery point but increased in the following time points compared with baseline value. However there were no significant differences of serum Cr values in all time points between the two groups. CK-MB increased after surgery in both groups, but no significant differences were detected between the two groups. No liver failure case was reported during the study.

**Conclusion** High dose Atorvastatin is associated with decreased hsCRP after surgery in patients coronary artery bypass grafting, however the upstream effect of Atorvastatin in terms of cardio- and renal protective effects were not found in this study.

### Effect of orally single dose of hydrochloride ivabradine on heart rate and pharmacokinetics in healthy male volunteers

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**Objective** To evaluate the effect of single dose hydrochloride ivabradine on heart rate and pharmacokinetics in healthy Chinese volunteers.

**Methods** 66 volunteers were randomized to 3 groups: ivabradine 5 mg ( $n = 12$ ), 10 mg ( $n = 12$ ), 20 mg ( $n = 12$ ). Serum ivabradine concentrations were determined at 0.25 h, 0.5 h, 0.75 h, 1 h, 1.5 h, 2 h, 4 h, 6 h, 8 h, 12 h, 24

h, heart rate were collected at 2 h, 6 h, 12 h, 24 h after received single dose of ivabradine. The plasma concentrations of ivabradine were determined by the HPLC-MS/MS method.

**Result** After single dose administration, the  $C_{\max}$  was  $(9.67 \pm 4.55)$  ng/mL,  $(23.1 \pm 13.0)$  ng/mL,  $(46.9 \pm 18.5)$  ng/mL for 5 mg, 10 mg, 20 mg hydrochloride ivabradine respectively,  $t_{\max}$  was  $(1.0 \pm 0.5)$  h,  $(1.0 \pm 0.4)$  h,  $(0.9 \pm 0.5)$  h respectively. Resting heart rate was reduced at 2 hours and back to baseline after 6 hours. The maximum decreased of heart rate was  $(5.27 \pm 10.96)\%$ ,  $(5.86 \pm 12.50)\%$ ,  $(10.17 \pm 8.90)\%$ , respectively. There was a significant lag time between peak plasma concentrations of ivabradine maximum bradycardic effect. The peak plasma concentration of ivabradine appears in the 45 min – 1 h after administration, while the largest decline of heart rate appears in 2 h.

**Conclusion** This study shows that ivabradine could decrease the Chinese male healthy volunteer resting heart rate in a dose-dependent effect.

### The effects of slow breathing rate on heart rate variability and blood pressure variability

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**Objective** The objective of this study was to investigate the effects of slow breathing rate on heart rate variability (HRV) and blood pressure variability (BPV) in healthy subjects.

**Methods** 53 healthy volunteers underwent three periods of controlled breathing at 8, 12 and 16 breaths/min. ECG (RR), respiratory and blood pressure signal were continuously and simultaneously recorded. In our study, the influence of the respiration on RRI (RR interval) and BP were observed. Simultaneously, we studied the effects of slow breathing rate on RRI, amplitude of blood pressure oscillation, High-frequency (HF) power, low-frequency (LF) power and LF/HF ratio of HRV and BPV. Then we also corrected the effects of slow breathing rate on respiratory peak shifts.

**Result** RRI and BP cyclical change coincided with the respiratory cycle; As breathing rate reduced, amplitude of RRI and blood pressure oscillation increased, heart rate slowed ( $P < 0.05$ ), respiratory peak shifted towards left ( $P < 0.05$ ). Compared to 16 breaths/min, conventional spectral analysis showed increased LF and HF ( $P < 0.05$ ) power, decreased LF/HF ratio ( $P < 0.05$ ) of HRV, increased LF, HF power ( $P < 0.05$ ) and LF/HF ratio of BPV at a rate of 12 breaths/min; It also showed increased LF power ( $P < 0.05$ ) and LF/HF ratio ( $P < 0.05$ ), decreased HF power ( $P < 0.05$ ) of HRV and BPV at a rate of 8 breaths/min. As the respiratory frequency decreased gradually, correct spectral analysis showed increased HF power, decreased LF power and LF/HF ratio (Compared with 16 breaths/min, statistically significant respiratory rate effects were found in HF power, LF/HF ratio of HRV and BPV in 8, 12 breaths/min and LF power of HRV in 8 breaths/min,  $P < 0.05$ ).

**Conclusion** Reductions of respiration rate shifted the respiratory peak into the junction of HF and LF or even below LF range. In accordance with this shift, the effects of slow breathing rate on respiratory peak shifts should be corrected when we performed HRV and BPV spectral analysis; correct spectral analysis demonstrated that slow respiration can cause increase in HF power and decrease in LF power and LF/HF ratio. These demonstrated that slow breathing was indeed capable of increasing vagal activities and shifting sympatho-vagal balance towards vagal activities.

### Different $\alpha_1$ -antitrypsin levels between CHD and non-CHD groups

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**Background** Being abundant in circulation, the new biomarker of systemic inflammation,  $\alpha_1$ -antitrypsin (AAT) modulates immune and inflammatory process through its inhibition of the activity of several serine proteases. Atherosclerosis-based coronary heart disease (CHD) is generally known as an inflammation-mediated pathological process. However, whether AAT plays a role or not in the process of the disease is still not clear. To investigate the relationship between AAT and CHD, we initiate the following case-control trial.

**Methods** 460 participants were enrolled in this case-control study, including 274 CHD patients and 186 non-CHD patients diagnosed by coronary angiography. The basic characteristics of the two groups were recorded. Serum lipid markers and AAT level were measured in all participants and BMI was also calculated.

**Result** Compared with non-CHD group, the concentration of AAT was significantly higher in CHD group ( $150.92 \pm 27.195$  mg/dl vs  $143.97 \pm 19.680$  mg/dl,  $P = 0.003$ ). However, after adjusting traditional risk factors such as age, sex, HDL-C, LDL-C, and BMI, AAT level was of no statistical significance between the two groups ( $P = 0.232$ ).

**Conclusion** Studies have demonstrated the benefits of AAT, and gene mutations leading to AAT deficiency relates to severe disorders. However, in this study we found CHD patients had a higher AAT concentration. Although after adjusting other traditional factors, AAT was not an independent risk factor for CHD, it might play a role in the development of CHD. Large-scale prospective cohort studies and further basic researches are needed to confirm the causality and mechanisms related.

### Bisoprolol fumarate did not worsen plasma glycosylated hemoglobin level in type 2 diabetes mellitus patients associated with hypertension and/or coronary heart disease

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**Objective** The effect of beta-blockers on glucose metabolism

remains controversial. The aim of this study was to assess the effect of bisoprolol fumarate, a highly selective beta-1 adrenoceptor antagonist, on plasma glycosylated hemoglobin (HbA1c) levels in patients of type 2 diabetes mellitus (T2DM) associated with hypertension and/or coronary heart disease.

**Methods** A prospective, multicenter open-label clinical trial was conducted in T2DM patients, aged 18 – 80 years, associated with hypertension and/or coronary heart disease. Bisoprolol was given at doses of 2.5 – 10 mg/d for 20 weeks, and a periodic follow-up was conducted. The primary endpoint was the change in plasma HbA1c level, and the secondary endpoints included changes in fasting blood glucose (FBG) level, serum lipid level, blood pressure and heart rate. Any adverse reactions caused by bisoprolol treatment were recorded.

**Result** 392 subjects were enrolled in this study. After 20 weeks of bisoprolol treatment, the HbA1c level, FBG level and serum lipid level were not significantly different from corresponding values at baseline, while blood pressure and heart rate were significantly reduced after bisoprolol therapy. No severe adverse events were observed. There were no significant differences in plasma HbA1c levels following treatment with low-, medium- or high-doses of bisoprolol.

**Conclusion** In patients of T2DM associated with hypertension and/or coronary heart disease, treatment with bisoprolol fumarate for 20 weeks reduced blood pressure and heart rate, with no adverse effects on HbA1c.

### Lercanidipine can improve renal function in patients with atherosclerotic renal artery stenosis undergoing renal artery intervention

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**Purpose** To investigate the nephroprotective effect of lercanidipine in patients undergoing renal artery intervention.

**Methods** A prospective, single-center cohort study was conducted and the patients with atherosclerotic renal artery stenosis aged 30-75 year were consecutively enrolled between September, 2011 and October, 2012. Lercanidipine was regularly taken after the intervention. All patients were invited to present themselves at our institute at 3 and 6 months after the intervention. Serum creatinine, clinical blood pressure, 24-hour ambulatory blood pressure, pulse wave velocity, 24-hour urine protein were measured. Adverse events were recorded.

**Result** In term of renal function, estimated glomerular filtration rate ( $75.02 \pm 27.11$  ml/min/1.73 m<sup>2</sup> vs  $71.28 \pm 21.35$  ml/min/1.73 m<sup>2</sup>,  $P = 0.266$ ) or 24-hour urine protein [ $0.055$  (0.01-0.225) g vs  $0.03$  (0.01-0.28) g,  $P = 0.742$ ] at 3 months after the intervention was not statistically different compared with the baseline. At 6 months after the intervention estimated glomerular filtration rate significantly increased ( $78.03 \pm 23.12$  ml/min/1.73 m<sup>2</sup> vs  $71.28 \pm 21.35$  ml/min/1.73 m<sup>2</sup>,  $p = 0.021$ ), 24 hour urine protein decreased significantly [ $0.02$  g (IQR, 0.01 – 0.1) vs  $0.03$  g (IQR, 0.01 – 0.28),  $P = 0.042$ ]. Blood pressure was controlled better at 3 months and 6 months after intervention. At 3 and 6 months after intervention the number of antihypertensive drugs, clinical systolic blood pressure, diastolic blood pressure, 24-hour average systolic blood pressure, 24-hour average diastolic blood pressure significantly decreased. Pulse wave velocity decreased significantly at 3 and 6 months after intervention. At the end of follow-up, death, dialysis, myocardial

infarction or stroke occurred in none of the patients. Mild lower extremity edema occurred in only one patient. No other side effects occurred.

**Conclusion** The study showed that lercanidipine can improve renal function in patients undergoing renal artery intervention. It was safe and effective in control of hypertension.

### Early routine post-fibrinolysis angioplasty benefits more patients with acute ST-elevation myocardial infarction

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**Objective** Evaluate whether early routine post-fibrinolysis angioplasty represents a reasonable reperfusion option for victims of ST-elevation myocardial infarction (STEMI), So that we can calmly deal with these patients and patients can have better prognosis.

**Methods** A total of 936 STEMI patients were randomized to full Urokinase followed by stenting within 3-12 hours (early routine post-fibrinolysis angioplasty; 472 patients), or primary stenting within 12 hours (Primary angioplasty; 464 patients). The primary endpoints were the reperfusion time within 3 hours and the incidence of no-reflow or slow-reflow. The secondary endpoints were the acute incidence of bleeding, the extent of myocardial damage, determined by the 6-month left ventricular function and the 3 year composite incidence of death, reinfarction, stroke, or revascularization.

**Result** Early routine post-fibrinolysis angioplasty significantly increased the percentage of reperfusion treatment within 3 hours ( $P < 0.01$ ). The primary angioplasty group resulted in higher frequency of no-reflow or slow-reflow ( $P < 0.01$ ). Both groups were similar regarding major bleeding ( $P > 0.05$ ). The 6-month left ventricular function of early routine post-fibrinolysis angioplasty group was better than primary angioplasty group. Both groups were similar regarding reinfarction, stroke or revascularization ( $P > 0.05$ ), but the incidence of 3-year cumulative death is higher in the primary angioplasty group ( $P < 0.01$ )

**Conclusion** Early routine post-fibrinolysis angioplasty can significantly improve effective time window within effective reperfusion treatment percentage, Result in better myocardial perfusion, lower no-reflow and preserving left ventricular function and the prognosis of patients with STEMI than primary angioplasty.

### Effects of ventricular conduction block patterns and pulmonary hypertension on mortality in hospitalized patients with dilated cardiomyopathy

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**Objective** Ventricular conduction block (VCB) identified on a 12-lead electrocardiogram are associated with poor outcomes in patients with known cardiac diseases. The prognostic implications of VCB



patters in dilated cardiomyopathy (DCM) patients, however, need to be evaluated. The purpose of this study was to determine all-cause mortality in DCM with VCB.

**Methods and Result** An observational cohort study was undertaken of patients from 2003 to 2011, 1 119 patients were enrolled with median follow-up of 3.5 years. Standard demographics, echocardiography and routine blood tests were obtained shortly after admission. Outcome was assessed with all-cause mortality. All patients were then divided into LBBB, RBBB, intraventricular conduction delays (IVCD) and narrow QRS groups. Of those, 19.8% (n = 221) had LBBB, 7.3% (n = 82) had RBBB, 6.0% (n = 67) had IVCD, 66.9% (n = 749) had narrow QRS. All-cause mortality rates were highest in patients with IVCD (47.8%, n = 32), intermediate in those with RBBB (32.9%, n = 27) and LBBB (27.1%, n = 60), and lowest in those with narrow QRS (19.9%, n = 149), a significant difference in all-cause mortality risk among the VCB groups and narrow QRS group (log-rank  $\chi^2 = 51.564$ ,  $P < 0.001$ ). In addition, significant mortality differences were also demonstrated between the DCM patients with VCBs and pulmonary hypertension (PH) compared with those without PH (37.9% vs 20.9%, log-rank  $\chi^2 = 27.087$ ,  $P < 0.001$ ). Presence of RBBB, IVCD, PH, left atrium diameter and NYHA functional class were the independent predictors of all-cause mortality in DCM patients.

**Conclusion** VCB, in particular IVCD, predicts mortality in DCM, and that RBBB and IVCD but not LBBB are independent predictors of mortality.

### Hypertension: meta-analysis of randomized controlled trials

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**Background** Aliskiren is a novel renin-angiotensin aldosterone system (RAAS) inhibitor, the combination therapy of aliskiren and amlodipine for blood pressure control have been reported recently. The primary objective of this analysis is to review recently reported randomized controlled trials (RCTs) to compare antihypertensive effects and adverse events between mono (amlodipine or aliskiren alone) and combination therapy of both medicines.

**Methods** Databases for the search included Pubmed, embase and the Cochrane Central Register of Controlled Trials. Revman v5.0 statistical program was used to analyze the data. Weighted mean differences (WMD) with a 95% confidence interval (CI) were used for the calculation of continuous data, and relative risk (RR) with a 95% CI was used for dichotomous data.

**Result** We analyzed the data from 7 RCTs for a total of 6074 participants in this meta-analysis. We found that the aliskiren/amlodipine combination therapy had a stronger effect in lowering blood pressure as compared with the monotherapy using aliskiren (SBP: WMD = -10.42, 95% CI -13.03 - -7.82,  $P < 0.00001$ ; DBP: WMD = -6.60, 95% CI -7.22 - -5.97,  $P < 0.00001$ ) or amlodipine (SBP: WMD = -4.85, 95% CI -6.88 - -2.81,  $P < 0.00001$ ; DBP: WMD = -2.91, 95% CI -3.85 - -1.97,  $P < 0.00001$ ). No differences were found in terms of adverse events between combination therapy and monotherapy, except for the rates of peripheral edema and hypokalaemia which were significantly lower in the combination therapy than in the amlodipine monotherapy (RR = 0.78, 0.66 - 0.92,  $P = 0.004$ ; RR = 0.51, 0.27 - 0.97,  $P = 0.04$ ). Similar antihypertensive effects were found

in both obese (body mass index  $\geq 30$  kg/m<sup>2</sup>) hypertensive and non-obese hypertensive patients. Moreover, there was no difference with the blood pressure lowering or adverse effects with regards to the combination therapy in both subgroups.

**Conclusion** We found that aliskiren/amlodipine combination therapy provided a more effective blood pressure reduction than monotherapy with either drug without significant increase in the occurrence of adverse events.

### Sudden death of a 15-year-old boy: what's the etiology?

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**History** A male patient, 15 years old, complained of "fatigue for 1 day, and respiratory and cardiac arrest for 5 hours". Before admission, the patient was on the 5th day of military training. On the day of admission, after running, the patient suffered a sudden death and received CPR. A physical examination after CPR at admission showed the following: RR 22 times/min; P 113 bpm; blood pressure 92/59 mm Hg. At the bottom of both lung lobes, a slight amount of moist rales was heard. No wheezing or pleural friction rub was heard. The border of cardiac dullness was normal, and heart rate was 113 bpm, with a regular rhythm. No pathological murmurs, extra heart sounds, or pericardial friction rub was heard in each heart valve auscultation area. Laboratory test Result were as follows. A routine blood test showed: WBC,  $20.9 \times 10^9$ /L; GR, 85.7%; Hb, 172 g/L; and PLT,  $261 \times 10^9$ /L. Blood biochemistry was as follows: Cr, 199  $\mu$ mol/L; BUN, 5.6 mmol/L; Alb, 55.5 g/L; TBIL, 40.6  $\mu$ mol/L; IBIL, 11.9  $\mu$ mol/L; DBIL, 28.7  $\mu$ mol/L; ALT, 295 U/L; AST, 1129 U/L; LDH, 2062 U/L; CK > 300 ng/ml; and TnI > 50 ng/ml.

**Impression** Sudden cardiac death and severe myocarditis? Arrhythmia, atrial fibrillation, ventricular tachycardia, ventricular fibrillation, cardiopulmonary resuscitation postoperative state, acute enteritis, severe sepsis, septic shock, acute respiratory distress syndrome, acute liver injury, acute kidney injury. The patient was conscious when transferred into the ICU, with mild agitation. After admission, the next day, however, the patient suffered another SD and showed ventricular arrhythmia. After 1.5 h CPR, however, the patient's heart rate still could not be maintained. After approximately 3 hours of chest compression, clinical death was declared at 12:43 pm. At autopsy, we found atrioventricular node artery stenosis, obvious thickening of the arterial intima, and fatty infiltration around the atrioventricular node. We diagnosed the patient with congenital hypoplasia.

### Relationship of CTGF, HGF and atrial fibrosis in patients with atrial fibrillation during rheumatic heart disease

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**Objective** To investigate the possible molecular mechanisms of atrial fibrosis, the alteration of connective tissue growth factor (CTGF), hepatocyte growth factor (HGF) and the level of phosphorylation of MAPKs signaling pathway molecules in patients with atrial fibrillation during rheumatic heart disease was detected.

**Methods** About 200 g right arterial tissue was taken from 21 patients (11 sinus rhythm, SR), 10 atrial fibrillation (AF) with rheumatic heart disease during undergoing surgery. Masson staining was used to observe the degree of atrial fibrosis, and the protein expression of CTGF and HGF were measured by immunohistochemistry technique, and the level of phosphorylation of MAPKs signaling pathway molecules was detected by western blot.

**Result** Compared with SR group, the protein expression of CTGF, the level of phosphorylation of MAPKs signaling pathway molecules and collagen volume fraction are significant increased in AF group, but the protein expression of HGF is markedly reduced in AF ( $P < 0.001$ ).

**Conclusion** The expression of CTGF increased, but HGF reduced in the myocardial tissue of patients with rheumatic heart disease which may contribute to activate the MAPKs signal pathway. As a result, it can promote atrial fibrosis, and then participate in the incidence and maintain of atrial fibrillation.

### Impact of hemodynamics on in-stent restenosis after coronary bifurcation stenting

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**Objective** Stenting in coronary bifurcation has always been an important issue in cardiology, considering the higher procedural difficulties and the post-interventional risks like in-stent restenosis (ISR). The mechanism and causes of ISR are still not fully understood, however, a series of studies demonstrate that hemodynamic factors provoked by stent implantation affect the risk of restenosis. In the past decade, most of the numerical models carried out lack patient-specificity, simulating stenting interventions in idealized arterial geometries. Hence, the aim of this work is to implement a patient-specific virtual model, overcoming the limitations of the current state-of-the-art in numerical stenting procedures simulations.

**Methods** Four patients with LAD/D1 bifurcation lesions were divided into ISR ( $n = 2$ ) and non-ISR ( $n = 2$ ) groups. The pre-interventional geometry of a patient-specific atherosclerotic coronary bifurcation was generated from computed tomography angiography (CTA) images. Then stents were virtually implanted in the geometry model according to the follow-up CTA at 1 year. Numerical models were established to calculate the distribution of the hemodynamic factors and then to analyze the impact of hemodynamics on ISR after stenting compared with the follow-up CTA.

**Result** The wall shear stress (WSS) in all the segments of all patients was less than 0.7 Pa, and the WSS of the stented segment coronaries was less than the rest of the arteries. Comparing the calculated Result with the follow-up CTA, we found that the WSS of the restenosis group was lower than the nonrestenosis group.

**Conclusion** The presented work proves the feasibility of implementing a patient-specific virtual model replicating actual clinical cases. The model was investigated in terms of stresses and subsequently validated through a comparison with the actual post-intervention lumen. Such computational studies could be used prior to stenting implantation, comparing different clinical options and facilitating the intervention strategy planning. Also, the distribution of hemodynamic factors such as WSS can be evaluated as predictors of ISR.

### Effects of chronic kidney disease on platelet response to antiplatelet therapy in acute myocardial infarction patients

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**Objective** To elucidate effect of dual antiplatelet therapy on platelet response in acute myocardial infarction patients with chronic kidney disease.

**Methods** From Sep. 2011 to Jun. 2012, a total of 195 acute myocardial infarction patients undergoing drug eluting stent implanting were enrolled, among them, 133 cases with normal renal function, and 62 cases with chronic kidney disease (CKD). We examined platelet reactivity after clopidogrel 300 mg and aspirin 300 mg treatment for 24 h. High on treatment platelet reactivity (HPR) was defined as  $> 55\%$  for light transmission aggregometry.

**Result** The CKD patients had higher diabetes mellitus (24.8% vs 43.5%,  $P = 0.01$ ), anemia (5.6% vs 16.1%,  $P = 0.03$ ) and high on treatment platelet reactivity (28.6% vs 45.2%,  $P = 0.03$ ) than those with normal kidney function patients. Logistic regression analyses showed that CKD and diabetes mellitus were independent predictors of HPR. Prevalence of HPR was higher in CKD patients compared with normal kidney function patients ( $65.1\% \pm 10.2$  vs  $45.3\% \pm 7.8$ ,  $P < 0.01$ ). In subgroup analysis testing was done before and after antiplatelet treatment. At baseline there were no differences in platelet aggregation, however, absolute decrease in reactivity after antiplatelet treatment was significantly less in CKD patients compared to patients with normal kidney function ( $63.2\% \pm 8.6$  vs  $43.2\% \pm 5.2$ ,  $P < 0.01$ ).

**Conclusion** CKD is an important contributor to apparent HPR.

### Study on the molecular genetic correlation between atrial fibrillation and sodium channel gene SCN5A in Chinese population

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**Objective** Atrial fibrillation is the most common arrhythmia with high mortality and disability. It can lead to ventricular rhythm disorders, impaired heart function and atrial mural thrombosis. Atrial fibrillation has been considered as the result of various mechanisms and factors, and recent studies have shown that gene variations of ion channels, gap junction proteins, and nuclear pore proteins are closely associated with it. Sodium channel gene SCN5A is one of its virulence genes, but there is no such research between them in Chinese population yet. Our aim is to explore the molecular genetic relevance between SCN5A and atrial fibrillation in Chinese population.

**Method** We collected the clinical datum and blood samples of patients with atrial fibrillation in our hospital. All selected patients did routine examinations and echocardiography. Besides, we also collected patients with other cardiovascular diseases (hypertension, coronary heart disease, rheumatic heart disease and dilated cardiomyopathy) but without atrial fibrillation as control group. Do logistic regression analysis to find whether these factors (LAD and LVEF) may relate with the onset of atrial fibrillation. We extracted their DNA samples, and screening

SCN5A gene by direct DNA sequencing method, include the exons and exon-intron junction regions. Then DNA samples of 200 healthy individuals of the same race were also sequenced as control group to identify gene mutation or SNP.

**Result** Totally 125 Patients with atrial fibrillation is eligible. Among them, 12 cases are lone atrial fibrillation, 9.6% of the total number, other patients are combined with hypertension (68%), rheumatic heart disease (9.6%), coronary heart disease (15.2%) and dilated cardiomyopathy (4%). Logistic regression analysis showed that LAD ( $t = 6.360$ ,  $P < 0.001$ ) may have influence on atrial fibrillation development, the differences were statistically significant ( $P < 0.05$ ). Among aforementioned patients, a novel SCN5A gene heterozygosis missense mutation A364S was identified. This mutation is the nucleotide changed from G to T in the locus 1092 of SCN5A gene, lead to the 364th amino acid of Nav1.5 protein change from alanine to serine. We also identified 8 SCN5A SNPs, 2 novel SNPs are N1387N and M1486I, and the other 6 SNPs were once reported, they are A29A, H558R, P1089L, R1192Q, F1206F and D1818D, respectively.

**Conclusion** 1. We firstly report that SCN5A mutation is related with atrial fibrillation in Chinese population, SCN5A-A364S is a novel mutation. 2. LAD is associated with the occurrence of atrial fibrillation.

### Correlation of electrophysiological characteristics with genotype in arrhythmogenic right ventricular cardiomyopathy

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**Objective** Although mutations of several genes are associated with arrhythmogenic right ventricular cardiomyopathy (ARVC), the exact correlation between genotype and electrophysiological (EP) features remain unclear.

**Methods** Ninety Chinese ARVC patients who underwent intracardiac EP study were recruited and 9 known genes of ARVC including PKP2, DSC2, DSG2, DSP, JUP, TGFB3, TMEM43, DES and LMNA were screened.

**Result** A total of 53 mutations were identified in 57 patients (63%), among which 19 (33%) carried multiple mutations. Mutation carriers had more frequent clinical ventricular tachycardia (VT) (89% vs 55%;  $P < 0.001$ ) and negative T waves in  $V_1$  to  $V_3$  (61% vs 33%;  $P = 0.016$ ). So did patients with plakophilin-2 (PKP2) mutations than all others. Syncope occurred more often in multi-mutation carriers (58% vs 21%;  $P = 0.003$ ). VT was significantly more often induced in mutation carriers (75% vs 39%;  $P = 0.001$ ) and PKP2 mutation carriers (80% vs 48%;  $P = 0.002$ ). Furthermore, induced VT with a rate  $\geq 200$  bpm was also more often documented in mutations carriers (88% vs 54%;  $P = 0.013$ ), as well as PKP2 mutations carriers (91% vs 67%;  $P = 0.041$ ). Compared with non-carriers, the basal free-wall (90% vs 68%;  $P = 0.028$ ) and inferior wall (90% vs 12%;  $P = 0.026$ ) of right ventricle were more often the low voltage area in mutation carriers.

**Conclusion** Pathogenic gene mutations were found in nearly 2/3 of ARVC patients. Mutation carriers, especially PKP2, had a higher proportion of a history of VT and more inducible fast VT. They were also more frequently found to have substrates at basal free-wall and

inferior wall of right ventricle than non-carriers, supporting that they are more susceptible to VT.

### Screening of pathogenic genes in arrhythmogenic right ventricular cardiomyopathy

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**Objective** Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a heritable cardiac disease predominantly caused by mutations in desmosomal protein genes. Previous genetic analyses of Chinese ARVC population are limited to small size and single gene. This study was aimed to investigate the genotype in a large series of Chinese patients with ARVC through comprehensively screening nine ARVC-causing genes.

**Methods** A total of 100 unrelated ARVC patients and 300 age, gender and ethnicity-matched healthy controls were genetically tested for 9 previously reported ARVC-causing genes, including plakophilin-2 (PKP2), desmoplakin (DSP), desmoglein-2 (DSG2), desmocollin-2 (DSC2), and plakoglobin (JUP), transforming growth factor beta-3 (TGFB3), transmembrane protein 43 (TMEM43), desmin (DES) and Lamin A/C (LMNA), with multiplexing targeted resequencing. Clinical characteristics were compared between the two groups of mutation carriers and non-carriers.

**Result** Fifty-nine mutations were identified in 64% of the patients, among which, 93% were located in desmosomal protein genes. PKP2 mutation accounted for 54% of the total and 58% of the desmosomal mutations, with truncating mutation type occupied about 2/3 of the PKP2 mutations. Only 4 mutations were found in non-desmosomal genes: 2 in TMEM43 and 2 in TGFB3. Two of them (one of each gene) appeared as single missense mutation. No mutation was identified in DES or LMNA. Multiple mutations were found in 23% of the patients, with PKP2 being found in 57% of the multi-mutation carriers. Genotype-phenotype analysis showed that ventricular tachycardia history occurred more in mutation carriers than non-carriers (86% vs 58%,  $P = 0.003$ ), especially the clinical ventricular tachycardia shaped as left bundle-branch block with superior axis (72% vs 50%,  $P = 0.033$ ).

**Conclusion** PKP2 is the most common gene that identified in 64% of Chinese ARVC patients. Ventricular tachycardia history occurs more in mutation carriers than non-carriers. Non-desmosomal genes should be added to desmosomal protein genes when performing molecular genetic screening in patients with suspected ARVC.



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