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Guest Editor
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Contents

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Program

POA 2017 Daily Program

May 5, 2017 (Friday)		
10:30–12:00		**Room VIP, 4F**
Oral Session Chair: *Jeong Bae Park* (Korea); *Wei-Chuan Tsai* (Taiwan)		
10:30–12:00		**Exhibition & Moderated Poster Area, 4F**
Coffee Break		
Moderated Poster Session I Chair: *Akira Yamashina* (Japan); *Tzung-Dau Wang* (Taiwan)		
13:00–13:30		**Room VIP, 4F**
Opening Ceremony		
13:30–14:00		**Room VIP, 4F**
Plenary Lecture Chair: *Jiunn-Lee Lin* (Taiwan); *Byung-Hee Oh* (Korea)		
13:30	PL-01	So! What's Aging? Is Arterial Aging a Disease? *Edward G. Lakatta* (USA)
14:00–15:30		**Room VIP, 4F**
Symposium 1 – Vascular Aging and Heart Damage/Dysfunction Chair: *Wen-Jone Chen* (Taiwan); *Gary F. Mitchell* (USA)		
14:00	SY1-01	Cardiac Remodeling in the Aging Process *Ernst Rietzschel* (Belgium)
14:20	S Y1-02	Vascular Aging and Heart Failure *Michael F. O'Rourke* (Australia)
14:40	SY1-03	Fitness and Cardiovascular Aging *James E. Sharman* (Australia)
15:00	SY1-04	Effects of Seasonal Variation and High-altitude on Cardiovascular Hemodynamics *Ta-Chen Su* (Taiwan)
15:30–16:00		**Exhibition & Moderated Poster Area, 4F**
Coffee Break		
Moderated Poster Session II Chair: *James Sharman* (Australia); *Lian-Yu Lin* (Taiwan)		
16:00–16:30		**Room VIP, 4F**
Plenary Lecture Chair: *Edward G. Lakatta* (USA); *Kuo-Liong Chien* (Taiwan)		
16:00	PL-02	The Interplay between Heart and Brain *Gary F. Mitchell* (USA)
16:30–18:00		**Room VIP, 4F**

Symposium 2 – Vascular Aging and Brain Damage/Dysfunction
Chair: *Alberto Avolio* (Australia); *Pei-Ning Wang* (Taiwan)

16:30	SY2-01	The Brain as a Target Organ of the Heart and the Ageing Vasculature: Role of Arterial Pulsatile Haemodynamics *Alberto Avolio* (Australia)
16:50	SY2-02	Preventive Geriatrics the Cross-talk between Arterial and Brain Aging: A Lifelong Condition *Angelo Scuteri* (Italy)
17:10	SY2-03	Management of Asymptomatic Carotid Artery Stenosis? On Vascular Cognitive Impairment I-Hui Lee (Taiwan)
17:30	SY2-04	Similarity and Disparity of Its Development of Carotid Intima and Media Thickness with Aging *Jeong Bae Park* (Korea)

18:30–20:00 **Room Elegant, 4F**

Welcome Reception

May 6, 2017 (Saturday)

08:30–10:00 **Room VIP, 4F**

Feature Lecture
Chair: *Hirofumi Tomiyama* (Japan); *Tzung-Dau Wang* (Taiwan)

08:30	F-01	PARADIGM-HF – New Analyses *John McMurray* (UK)
08:50	F-02	A Critical Role of Cellular Senescence in Metabolic and Cardiovascular Disease *Tohru Minamino* (Japan)
09:05	F-03	Calcifying Progenitor Cells with Decalcifying Potential to Reverse Atherosclerotic Vascular Calcification *Hyun-Jai Cho* (Korea)
09:20	F-04	Effect of Inter-individual Blood Pressure Variability on the Progression of Atherosclerosis in Carotid Arteries *Sung-Ha Park* (Korea)
09:35	F-05	Arterial Stiffness Contributes to Coronary Artery Disease Risk Prediction beyond the Traditional Risk Score (RAMA-EGAT Score) *Teerapat Yingchoncharoen* (Thailand)

10:00–10:30 **Exhibition & Moderated Poster Area, 4F**

Coffee Break

Moderated Poster Session III
Chair: *Jeong Bae Park* (Korea); *Tsung-Hsien Lin* (Taiwan)

10:30–12:00 **Room VIP, 4F**

Symposium 3 – Vascular Aging and Kidney Damage/Dysfunction
Chair: *Kazuomi Kario* (Japan); *Der-Cherng Tarng* (Taiwan)

10:30	SY3-01	Hemodynamic Biomarker-initiated Anticipation Medicine in the Future Management of Hypertension: Renal Protection *Kazuomi Kario* (Japan)
10:50	SY3-02	Mechanisms of Kidney Injury and Dysfunction due to Large Artery Stiffening *Junichiro Hashimoto* (Japan)

11:10	SY3-03	Association among Arterial Stiffness, Endothelial Dysfunction and Kidney Arteriosclerosis in Chronic Kidney Disease; Possible Role of Inflammation *Yusuke Ohya* (Japan)
11:30	SY3-04	Cardiorenal Syndrome in Acute Heart Failure Patients *Shih-Hsien Sung* (Taiwan)

12:00–13:30 **Room VIP, 4F**

Lunch Symposium-AUDICOR Technology – A Clinical Approach to Evaluate and Manage of Cardiac Function
Chair: *Chen-Huan Chen* (Taiwan)

12:00	LS-01	A Novel Device for Measuring Electromechanical Coupling: Hemodynamic Principles and Potential Application – An Overview *Michel Zuber* (Switzerland)
12:40	LS-02	Clinical Applications of Acoustic Cardiogram in Patients with Heart Failure *Shih-Hsien Sung* (Taiwan)

14:00–15:30 **Room VIP, 4F**

Symposium 4 – Measurement of Hemodynamics (Methods and Devices)
Chair: *James Sharman* (Australia); *Hung-I Yeh* (Taiwan)

14:00	SY4-01	The Steno-stiffness Chart Deriving from Simultaneous Measurement of Ankle Brachial Pressure Index (ABI) and Brachial-ankle Pulse Wave Velocity (baPWV) for the Wide Range Risk Stratification *Akira Yamashina* (Japan)
14:20	SY4-02	A Novel Device for Measuring Electromechanical Coupling: Hemodynamic Principles and Potential Application *Michel Zuber* (Switzerland)
14:40	SY4-03	Heart Rate Variability and Chronic Heart Failure *Cho-Kai Wu* (Taiwan)
15:00	SY4-04	National Prevalence of Hypertension Defined by A Central BP Monitor *Shao-Yuan Chuang* (Taiwan)

15:30–16:00 **Exhibition & Moderated Poster Area, 4F**

Coffee Break

16:00–17:30 **Room VIP, 4F**

Symposium 5 – Arterial Hemodynamics
Chair: *Akira Yamashina* (Japan); *Lian-Yu Lin* (Taiwan)

16:00	SY5-01	The Clinical Utility of Ambulatory Blood Pressure Monitoring *Jiguang Wang* (China)
16:20	SY5-02	Effects of Antihypertensive Agents on Central Hemodynamics *Hae-Young Lee* (Korea)
16:40	SY5-03	Diurnal Blood Pressure Rhythmicity in Relation to Environmental and Clock Gene Variations *Yan Li* (China)
17:00	SY5-04	Pulmonary Arterial Hemodynamics Analyzed with the Reservoir-wave Model *Jiun-Jr Wang* (Taiwan)

17:30–18:00 **Room VIP, 4F**

Lifetime Achievement Award
Chair: *Michael F. O'Rourke* (Australia); *Chen-Huan Chen* (Taiwan)

17:30 PL-03 Systemic and Pulmonary Artery Compliance: Lessons Learned and Implications for the Treatment of HFpEF
David A. Kass (USA)

18:00–18:30 **Room VIP, 4F**

Award and Closing Ceremony

Poster Presentation

West Corridor, 4F

Poster No.	Abstract Topic
P-01	Age-associated Imbalance of MFG-E8 and SIRT1 in VSMC Proinflammation and Stiffening *Li Zhang* (China)
P-02	Impact of Very Old Age on Long Term Prognosis in Elderly Patients with ST Segment *Ji Young Park* (Korea)
P-03	Limits to Longevity: The Still-changing Face of Death *Michael O'Rourke* (Australia)
P-04	Metabolic Function in Ageing Red Blood Cells of Diabetic Animals *Ankur Gupta* (India)
P-06	Protective Effects of Sodium Orthovanadate in Diabetic Reticulocytes and Ageing Red Blood Cells of Wistar Rats *Bihari Gupta* (India)
P-07	Role of Vanadium, Trigonella and Vitamin C on Defensive Enzymes of Red Blood Cells of Diabetic Animals *Bihari Gupta* (India)
P-09	Brain-derived Neurotrophic Factor and Central Pulse Pressure after an Oral Glucose Tolerance Test *I-Te Lee* (Taiwan)
P-10	Central Aortic Pressures and Outcomes of Percutaneous Coronary Intervention in End-stage Renal Disease Patients *Mu-Yang Hsieh* (Taiwan)
P-11	Chronic Insulin Infusion Induces Reversible Glucose Intolerance in Lean Rats yet Ameliorates Glucose Intolerance in Obese Rats *Vikas Sharma* (India)
P-14	Secondary Polycythemia in Obstructive Sleep Apnea: The Prevalence and Cadiovascular Damages *Kazuki Shiina* (Japan)
P-15	Self-measured Home Pulse Pressure is An Independent Predictor of Arterial Stiffness in Hypertensive Patients: Results from The Taiwan Clinical Trial Consortium of Cardiovascular Diseases (TCTC-12 Registry) *Yen-Ting Yeh* (Taiwan)
P-19	Can Cerebral and Systemic Pulse Wave Analysis Explain Pulsatile Cerebral Haemodynamics in Raised Intracranial Pressure? *Susan Lim* (Australia)

P-20	Brachial Cuff Reservoir Characteristics and End-organ Markers of Cardiovascular Risk in Australian Adults: A Cross-sectional Study *Xiaoqing Peng* (Australia)
P-21	Estimation of Central Aortic Systolic Pressure from Cuff-based Brachial Arterial Pressure by Statistical Learning Methods *Hanguang Xiao* (China)
P-22	New Methods for Arterial Analysis in Patients with Primary Aldosteronism *Che Wei Liao* (Taiwan)
P-23	Non-invasive Estimation of Intracranial Pressure Based on Increased Wave Reflection in Arteries Which Enter the Cranium to Supply the Brain *Michael O'Rourke* (Australia)
P-24	The Impact of Endovascular Aneurysmal Repair on Left Ventricular Function in Patients with Abdominal Aortic Aneurysm *Chuan-Tsai Tsai* (Taiwan)
P-25	Usefulness of Arterial Velocity Pulse Index (AVI) as A Non-invasive Assessment for Severe Aortic Stenosis Screening *Yuichiro Toma* (Japan)
P-26	Vascular Elastovisicous Biomarkers Derived from Oscillometric Pulse Waveform Analysis Was Useful to Improve Risk Stratification for Cardiovascular Mortality *Hung-Ju Lin* (Taiwan)
P-27	Cyclic Stretch Frequency-modulated Response of Protein Expression Related to Nitric Oxide Release in Human Umbilical Vein Endothelial Cells *Alberto Avolio* (Australia)
P-30	Hypertension, Obesity, Diabetes, and Heart Failure-free Survival: The Cardiovascular Disease Lifetime Risk Pooling Project in New Delhi, India *Ankush Kumar* (India)
P-31	Target of Blood Pressure Treatment for the General Elderly Population: A Systematic Review and Meta-analysis *Chi-Jung Huang* (Taiwan)
P-32	The Associations with Target Organ Damage of Morning Hypertension by Various Definitions *Qian-Hui Guo* (China)
P-33	The Contribution of Inflammation to the Development of Hypertension Mediated by Increased Arterial Stiffness *Hirofumi Tomiyama* (Japan)
P-34	The Effect of Ambulatory Blood Pressure Monitoring on the Target Organ Damage among the Patients with Metabolic Syndrome *Chia-Te Liao* (Taiwan)
P-35	Albuminuria Is Independently Associated with Myocardial Diastolic Dysfunction in Patients with Early-stage Hypertension: Results from Taiwan Clinical Trial Consortium of Cardiovascular Diseases (TCTC-12 Registry) *Chi-Cheng Huang* (Taiwan)
P-36	Sag Mediated Therapy Leads to A Predominant TH1 During Visceral Leishmaniasis on Triggering CD2 Epitope Thereby Leading to Reduction in Vascular Aging and Organ Damage *Sukrat Sinha* (India)
P-37	The Association of Nighttime Thoracic Fluid Content and Outcomes in Patients with Acute Heart Failure *Yu-Lun Cheng* (Taiwan)

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P-38	Central Aortic Pressure Is Closely Positively Associated with Vascular Calcification Especially in Hemodialysis Patient Compared with Peritoneal Dialysis *Seonghoon Choi* (Korea)
P-39	Pulse Wave Analysis in Patients with Intradialytic Hypotension *Han-Kuei Wu* (Taiwan)
P-42	The Risk of Major Bleeding in Patients with Atrial Fibrillation and Vascular Diseases *Mei-Chuan Lee* (Taiwan)
P-43	Acute Bout of Exergaming Attenuates Endothelial Dysfunction Following Postprandial Lipemia in Persons with Spinal Cord Injury *Eun Sun Yoon* (Korea)
P-44	Association between Serum Uric Acid and Exaggerated Blood Pressure Response to Exercise in Normotensive Men *Sae Young Jae* (Korea)
P-45	Comparison of The Effects of Short-term Stair Climbing vs Treadmill Walking Exercise on Endothelial Function and Arterial Stiffness in Healthy Young Adults *Min Jeong Cho* (Korea)
P-48	Parkinson's Disease Risk Score (PDRS) for Parkinson's Disease Screening in Aging Population: Effect of Yoga and Meditation *Vinod Sharma* (India)
P-49	Blood Pressure Variability and Target Organ Indices: Results from the Taiwan Clinical Trial Consortium of Cardiovascular Diseases (TCTC-12 Registry) *Chung-li Wu* (Taiwan)
P-52	Behavioural and Psychological Symptoms in Poststroke Vascular Cognitive Impairment *Sonu Kumar* (India)
P-53	Biofortified Food with Vitamin B-6, B-12 and Folic Acid Increases Concentrations of Vitamin and Shorten Concentrations of Homocysteine: Study in North Indian District *Vinod Kumar* (India)
P-58	The Profile of Behavioral and Psychological Symptoms in Vascular Cognitive Impairment with and without Dementia *Sonu Kumar* (India)
P-59	Clues of Transthoracic Echocardiography into Rapid Diagnosis of Type A Aortic Dissection in Hypertensive Patients *Ji Yeon Hong* (Korea)
P-60	Association of Sodium Intake with Albuminuria in Obese Patients *Bae Keun Kim* (Korea)

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Abstracts

Plenary Lectures

PL-01

So! What's Aging? Is Arterial Aging a Disease?

Edward G. Lakatta
Baltimore, Md., USA

Inside every old person is a young person wondering what happened." So, what is aging?

Aging is a manifestation of progressive, time-dependent failure of molecular mechanisms that create disorder within a system of DNA and its environment (nuclear, cytosolic, tissue, organ, organism, other organisms, society, terra firma, atmosphere, universe). Continuous signaling, transmitted with different kinetics across each of these environments, confers a "mutual enslavement" that creates ordered functions among the components within the system. Accrual of this molecular disorder over time, i.e. during aging, causes progressive changes in the structure and function of arteries that are quite similar in humans, non-human primates, rabbits and rats that compromise cardiovascular reserve function, and confer a marked risk for incident cardiovascular disease. Nearly all aspects of signaling within the DNA environment system within the heart and arteries become disordered with advancing age: Signals change, as does sensing of the signals, transmission of signals and responses to signals, impaired cell renewal, changes in the proteome due to alterations in genomic transcription, mRNA translation, and proteostasis. The density of some molecules becomes reduced, and post-translational modifications, e.g. oxidation and nitration phosphorylation, lead to altered misfolding and disordered molecular interactions. The stoichiometry and kinetics of enzymatic and those reactions which underlie crucial cardiac and vascular cell functions and robust reserve mechanisms that remove damaged organelles and proteins deteriorate.

Arterial cells generate an inflammatory defense in an attempt to limit the molecular disorder. The resultant proinflammatory milieu is not executed by "professional" inflammatory cells (i.e. white blood cells), however, but by activation of renin-angiotensin-aldosterone endothelin signaling cascades that leads to endothelial and vascular smooth muscle and cardiac cells' phenotype shifts, resulting in production of inflammatory cytokines. Progressive molecular disorder within the arteries over time leads to an excessive allostatic load on the Cardiovascular (CV) system, that results in an increase and "overshoot" in the inflammatory defense signaling. This age-associated molecular disorder-induced inflammation that accrues in the heart and arteries does not, itself, cause clinical signs or symptoms of CV Disease (CVD). Clinical signs and symptoms of these CVDs begin to emerge, however, when the age-associated inflammation in the heart and arteries exceeds a threshold.

Thus, an emerging school of thought is that accelerated age-associated alterations within the arteries, per se, ought to be considered to be a type of CVD, because the molecular disorder and the inflammatory milieu it creates within the arteries with advancing age are the roots of the pathophysiology of the major chronic cardiovascular diseases, e.g. atherosclerosis and hypertension. Because many effects of aging on the CV system can be delayed or attenuated

by changes in lifestyle, e.g. diet and exercise, or by presently available drugs, e.g. those that suppress Ang II signaling, CV aging is a promising frontier in preventive cardiology that is not only ripe for, but also in dire need of attention! There is an urgency to incorporate the concept of cardiovascular aging as a disease into clinical medicine. But, sadly, the reality of the age-associated molecular disorder within arteries has, for the most part, been kept outside of mainstream clinical medicine.

References

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Lakatta EG[1], Levy D. Part I: Aging Arteries: A "Set Up" for Vascular Disease Arterial and Cardiac Aging: Major Shareholders in Cardiovascular Disease Enterprises: Circulation 2003;107: 139–146.
Wang Mingyi, Liqun Jiang, Robert E. Monticone, Edward G. Lakatta. Proinflammation: the key to arterial aging. Trends Endocrinol Metab 2014;25:72–79.

PL-02

The Interplay between Heart and Brain

Gary F. Mitchell
Cardiovascular Engineering, Inc., USA

With advancing age, the aorta stiffens markedly in many people whereas muscular artery stiffness remains largely unchanged. As a result of disproportionate aortic stiffening, the normal impedance gradient from central aorta to peripheral arteries is reduced. A reduction in impedance mismatch reduces wave reflection and thereby allows additional pulsatility to be transmitted distally into peripheral conduit arteries. Transmission of excessive pulsatility into conduit arteries is particularly problematic in high flow organs such as the brain and kidneys because high flow organs necessarily have low resistance, meaning that pulsatility that enters the conduits will be transmitted forward into the microcirculation, where it may cause damage. This lecture will examine the evidence supporting the role that aortic stiffness plays in the microvascular brain pathology that contributes to cognitive impairment and dementia in older people.

PL-03

Systemic and Pulmonary Artery Compliance: Lessons Learned and Implications for the Treatment of HFpEF

David A. Kass
Abraham and Virginia Weiss Professor of Cardiology, Professor of Medicine, Biomedical Engineering, and Pharmacology and Molecular Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, USA

The heart provides a given stroke volume with each beat, and to dampen its pulsatile impact on circulatory pressure and flow, arteries are compliant. More than a half a century ago, researchers realized that declines in systemic vascular compliance with aging was common, particularly in Westernized societies. This augments pulsatile perfusion to organs and imposes high late-systolic loads on the heart. The mechanical and energetic consequences of vascular stiffening were then identified, and with respect to the heart, recognition came

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that ejecting into a stiff arterial system reduces cardiac efficiency and requires countering ventricular systolic stiffening to preserve ventricular-vascular coupling. This combination, observed with aging and more in women, leads to acute load and heart function instability. Other studies assessed the effects of pulsatile pressure/flow on vascular tone and endothelial regulation. A critical role of both nitric-oxide dependent and independent signaling on resistance artery tone from cyclic arterial stretch was revealed and shown to be separate from established shear stress mediated effects. However, pulsatile perfusion in vessels unable to stretch – e.g. aged, stiff – led to defects in these vasoactive signals, suppressing endothelial protection against oxidative stress.

The pulmonary circulation also imposes pulsatile load, and more recent studies have examined this load, how it differs from the systemic circulation, and the impact of pulmonary hypertension. Unlike the systemic circulation, where the arteries that stiffen are not the same ones responsible for resistance, both properties reside principally in the same peripheral vessels in the lung. While aging stiffens systemic arteries, its impact on lung vessels is much less. This results in tight coupling of resistance and compliance and has implications for the treatment of PAH. Also unlike the systemic circulation, the downstream pressure for the pulmonary circulation, left atrial pressure (or PCWP), is much higher relative to mean artery pressure, and so itself impacts the net pulsatile load.

All of this pathobiology is particularly relevant to the syndrome of heart failure with a preserved ejection fraction (HFpEF), impacting over 15 million patients worldwide. This syndrome is really a compendium of co-morbidities, some of the heart, but also of other organs, including the lung as PAH is common. No targeted treatments have yet been successful, but new insights into signaling pathways, and understanding the interaction of vascular stiffening, ventricular remodeling, and inflammatory and metabolic defects common in affected patients, is leading to new therapy efforts. Alas, directly de-stiffening systemic vessels has proven very difficult, and it may be too late once this has settled in, while the lung presents different challenges. However, approaches to molecularly reverse the negative impacts from vascular stiffening may work, and exciting times lie ahead.

Feature Lectures

F-01
PARADIGM-HF – New Analyses

John McMurray

Professor of Medical Cardiology, British Heart Foundation Glasgow Cardiovascular Research Centre, University of Glasgow, and Queen Elizabeth University Hospital, Glasgow, Scotland, UK

The Prospective comparison of ARNi with ACEi to Determine Impact on Global Mortality and morbidity in Heart Failure trial (PARADIGM-HF), showed that a strategy of simultaneously blocking the renin-angiotensin system and the enzyme neprilysin (thereby augmenting natriuretic and other vasoactive peptides) with sacubitril/valsartan 97/103 mg bid (LCZ696 200 mg bid) was superior to blocking the renin-angiotensin system alone with enalapril 10 mg bid in reducing mortality and morbidity in patients with heart failure and reduced ejection fraction (HFrEF).[1] Since the publication of PARADIGM-HF, the largest trial ever in heart

Table 1. (for Abstract F-01)

Title	Journal
Angiotensin receptor neprilysin inhibition compared with enalapril on the risk of clinical progression in surviving patients with heart failure.	Circulation
A putative placebo analysis of the effects of LCZ696 on clinical outcomes in heart failure.	Eur Heart J
Effect of the angiotensin receptor neprilysin inhibitor LCZ696 compared with enalapril on mode of death in heart failure patients.	Eur Heart J
Efficacy and safety of LCZ696 (sacubitril/valsartan) according to age: Insights from PARADIGM-HF	Eur Heart J
Comparing LCZ696 with enalapril according to baseline risk using the MAGGIC and EMPHASIS-HF risk scores: an analysis of mortality and morbidity in PARADIGM-HF.	JACC
Estimating the long-term treatment benefits of sacubitril/valsartan.	NEJM letter
Influenza vaccination in patients with chronic heart failure: The PARADIGM-HF trial	JACC-HF
Risk related to pre-diabetes and diabetes in heart failure with reduced ejection fraction: Insights from PARADIGM-HF.	Circ-HF
Influence of ejection fraction on outcomes and efficacy of sacubitril/valsartan (LCZ696) in heart failure with reduced ejection fraction: The PARADIGM-HF trial.	Circ-HF
Influence of sacubitril/valsartan (LCZ696) on 30-day hospital readmission after heart failure hospitalization.	JACC
Importance of clinical worsening of heart failure treated in the outpatient setting: Evidence from the PARADIGM-HF trial.	Circulation
Factors associated with non-completion during the run-in period prior to randomization and influence on the estimated benefit of LCZ696 in the PARADIGM-HF Trial.	Circ-HF
Efficacy of sacubitril/valsartan relative to a prior decompensation: The PARADIGM-HF trial.	JACC-HF
Cost-effectiveness analysis of sacubitril/valsartan vs. enalapril in patients with reduced ejection fraction.	JAMA Cardiol
Geographic variations in the PARADIGM-HF trial.	Eur Heart J
Effects of sacubitril/valsartan in the PARADIGM-HF trial according to background therapy.	Circ-HF
Dementia-related adverse events in PARADIGM-HF and other trials in heart failure with reduced ejection fraction.	Eur J HF
Prognostic implications of changes in N-terminal pro-B-type natriuretic peptide in patients with heart failure.	JACC
Efficacy of sacubitril/valsartan vs. enalapril at lower than target doses in heart failure with reduced ejection fraction.	Eur J HF
Reduced risk of hyperkalemia during treatment of heart failure with mineralocorticoid receptor antagonists by use of sacubitril/valsartan compared with enalapril.	JAMA Cardiol
Systolic blood pressure, cardiovascular outcomes and efficacy and safety of sacubitril/valsartan (LCZ696) in patients with chronic heart failure and reduced ejection fraction.	Eur Heart J

failure, a number of in-depth secondary analyses have provided more information on the actions of sacubitril/valsartan (summarized in the Table 1). In this presentation, I will review the highlights of some of these additional analyses.

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McMurray JJ, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, Rouleau JL, Shi VC, Solomon SD, Swedberg K, Zile MR; PARADIGM-HF Investigators and Committees. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med 2014;371:993–1004.

F-02

A Critical Role of Cellular Senescence in Metabolic and Cardiovascular Disease

Tohru Minamino

Department of Cardiovascular Biology and Medicinem Niigata University Graduate School of Medical and Dental Sciences, Japan

Epidemiological studies have shown that age is the dominant risk factor for lifestyle-related diseases. The incidence and the prevalence of diabetes, heart failure, coronary heart disease and hypertension increase with advancing age. However, the molecular mechanisms underlying the increased risk of such diseases that is conferred by aging remain unclear. Cellular senescence is originally described as the finite replicative lifespan of human somatic cells in culture. Cellular senescence is accompanied by a specific set of phenotypic changes in morphology and gene expression including negative regulators of the cell cycle such as p53. Primary cultured cells from patients with premature aging syndromes are known to have a shorter lifespan than cells from age-matched healthy persons. It is also reported that the number of senescent cells increases in various tissues with advancing age. Interestingly, such accumulation of senescent cells in aged animals is attenuated by caloric restriction that regulates the lifespan regulatory system and delays age-associate phenotypes. I therefore hypothesize that cellular senescence in vivo contributes to the pathogenesis of age-associated disease. An important feature shared by several types of senescent cells is persistent up-regulation of inflammatory molecules and accumulating evidence has suggested a critical role of senescence-induced inflammation in metabolic and cardiovascular disease. Here I will present our recent data on the role of cellular senescence in age-related pathologies and will discuss the potential of anti-senescence as a novel therapeutic strategy for age-associated diseases.

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F-03

Calcifying Progenitor Cells with Decalcifying Potential to Reverse Atherosclerotic Vascular Calcification

Hyun-Jai Cho
Seoul National University Hospital, South Korea

Vascular calcification (VC) is a feature of advanced atherosclerotic plaque and often considered a passive consequence of inflammation and necrosis. However, the pathophysiology of VC involves an actively-regualated process that resembles bone formation and functions to maintain a balance between osteoblastic and osteoclastic cells. Experimentally, we would like to introduce the new concept that calcifying progenitor cells have the potential to become either osteoblasts or osteoclasts, and that a certain signal can push these cells towards becoming osteoclasts instead of osteoblasts.

We isolated progenitor cells from the aortas of mice using two markers (stem cell antigen-1 and platelet-derived growth factor receptor alpha). Sca-1+/PDGFRa+ cells were more committed to the osteoblastic lineage, whereas Sca-1+/PDGFRa-cells were bi-directional; they could also become osteoclast-like cells. The findings suggest that these bi-directional cells could be targeted by new therapies that shift their fate toward the osteoclastic lineage, thereby preventing calcium accumulation in blood vessels.

To test this idea, we treated the bi-directional cells with a drug that stimulates PPAR-gamma. The treated cells primarily turned into osteoclast-like cells, suggesting that the drug could prevent and reverse calcium accumulation in blood vessels. When we injected bi-directional cells (Sca-1+/PDGFRa-) into a mouse model of atherosclerosis, we found an increase in the severity of calcium build-up and calcified plaques in arteries. But this effect was prevented by simultaneous treatment with the PPAR-gamma-activating drug, which decreased the infiltration of osteoblasts into the plaques while increasing the infiltration of osteoclasts.

Taken together, these results offer new therapeutic targets for reversing calcium accumulation in blood vessels.

F-05

Effect of Inter-individual Blood Pressure Variability on the Progression of Atherosclerosis in Carotid Arteries

Sung-Ha Park
Yonsei University Health System, South Korea

Increase in visit to visit blood pressure has been shown to be associated with adverse cardiovascular outcomes independent from mean blood pressure. Post hoc analysis from previous hypertension outcome trials have consistently demonstrated the association of visit to visit blood pressure variability with increased risk in cardiovascular events. However, the mechanism by which increased blood pressure variability raises the risk of cardiovascular disease has yet to be elucidated. In this talk, we will discuss recent data regarding the association of blood pressure variability with cardiovascular disease and discuss a recent post hoc analysis from the CAMELOT and the PREVENT study.

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F-06

Arterial Stiffness Contributes to Coronary Artery Disease Risk Prediction beyond the Traditional Risk Score (RAMA-EGAT Score)

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Arterial stiffness as measured by the cardio-ankle vascular index (CAVI) is a widely available method in Thailand. Data from a large cross-sectional study revealed a significant correlation of CAVI and the presence of coronary artery disease as detected from 64-slice coronary computed tomography arteriography. Futhermore, CAVI was shown to predict long-term cardiovascular events in the patients with intermediate cardiovascular risk.

Invited Lectures

SY1-01

Cardiac Remodeling in the Aging Process

Ernst Rietzschel
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(Abstract not available).

SY1-02

Vascular Aging and Heart Failure

Michael F. O'Rourke
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In youth and young adults, the systemic arterial system is beautifully designed for its role of receiving blood in spurts from the left ventricle and delivering this in a near steady stream through the organs and tissues of the body. This is the period (15–30 years) of maximal fertility, which has determined human evolution over eons past.

Factors which contribute to optimal function have been emphasised by Michael Taylor in his observational and modelling studies, and are summarised in "McDonald's Blood Flow in Arteries" [1]. The system of branching pipes, with proximal distensibility and distal stiffness limits the volume of blood which is held in arteries while the junction of conduit arteries with resistance arterioles at the distal end creates wave reflection which excludes flow pulsations from the arterioles and capillaries while creating a pressure wave which moves back to the heart with such timing that its foot corresponds to aortic valve closure, so maintaining coronary flow without increasing aortic or Left Ventricular (LV) systolic pressure. Wave velocity is relatively low and so timed as to create maximal efficiency for the intermittently beating heart. Viscous energy loss in the resistance arterioles and capillaries is minimised through exclusion of pulsatile flow.

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This pattern of vascular-ventricular (and vascular-vascular) interaction at origin and end of conduit arteries is seen in most mammals, which live for shorter life spans than humans.

Beyond age 30 in humans, the proximal arteries which distend most with LV ejection, show signs of medial degeneration which progresses through the rest of life. These changes are attributable to fatigue and fracture of elastin fibres. This leads to transfer of pulsatile stresses from elastin fibres to less extensible collagen fibres. The proximal arteries (particularly the thoracic aorta) dilates and stiffens progressively. Such stiffening has two ill-effects – one irreversible and the other reversible. The local dilation and stiffening of the proximal aorta increases impedance, and causes a local increase in pulsatile pressure. This is irreversible (but suggests possibility of surgical correction in the future). The second and reversible factor is the increased Pulse Wave Velocity (PWV) which is the physical accompaniment of arterial stiffening. Increased PWV causes reflected waves from peripheral sites to return early to the heart, during systole, and boosting pressure, thus increasing LV load and causing LV hypertrophy, while increasing pulse pressure and predisposing to damage of conduit arteries at sites of weakness or damage – and leading to hemorrhage or thromboses.

Cardiac dysfunction, then failure, follows aortic stiffening like a shadow over many years. This is usually characterised by clinicians as hypertension – usually isolated systolic hypertension in older adults. But the increase in aortic and LV systolic pressures are underestimated by change in brachial systolic pressure. Far larger changes are seen from effects of arterial degeneration on aortic PWV, Young's modulus of the aortic wall, or from augmented pressure which is generated by early return of wave reflection, and can be estimated from the radial artery pulse waveform.

Cardiac dysfunction and failure are the inevitable result of arterial stiffening and elevated central aortic pressure, and develop over decades, initially manifest only as apparent deterioration in physical fitness. By the time that cardiac failure becomes apparent, the downhill course is swift, with average life expectancy in the Framingham cohort around 5 years.

Levy et al from Framingham [2] have pointed out that cardiac failure can develop from two different mechanisms – as "diastolic" failure with predominantly impaired delayed relaxation of the hypertrophied LV or as "systolic" failure where ventricular scarring from micro or macro infarction lead to LV dilation and impaired contractility. Both mechanisms can be present in one person. Poor life expectancy is similar in both.

Treatment of "systolic" or "diastolic" heart failure is similar in both and is based on reduction of wave reflection with drugs such as ACEIs, ARBs, dihydropyridine CCBs, nitrates and nitrate-like drugs. All have a predominant effect in reducing wave reflection while maintaining peripheral resistance and perfusion of vital organs [1,3].

Detailed studies of wave reflection in patients with heart failure do show different effects of wave reflection in patients with heart failure from predominantly systolic or diastolic dysfunction. With diastolic dysfunction, use of conduit arterial vasodilator drugs decreases augmentation pressure – i.e., the late systolic peak of the LV and aortic pressure waves [1,4]. This decreases LV systolic load and improves LV relaxation [4]. With systolic dysfunction, there is little or no apparent late systolic pressure boost (since the weakened LV cannot generate this). With reduction in wave reflection [5], the major change is with the aortic flow waveform where waveform is lengthened by prolonged duration of systole, and with flow wave showing a convexity to the right in consequence of increased late systolic flow and ejection duration [4,5]. Intermediate changes – reduction in pressure augmentation, increase in LV flow – are seen in patients with combined systolic/diastolic dysfunction as cause of cardiac failure.

This paper concentrates on mechanisms – aortic stiffening in older persons, increase in LV load, LV hypertrophy and impaired LV function, developing over decades and manifest at a later stage in life as "systolic" heart failure, "diastolic" heart failure, or a combination of both.

It logically deals with effects of wave reflection, its effects on pressure and/or flow waveform. It explains the logic of treatment, and how cardiac failure can be prevented or delayed by identification of aortic stiffening, and its ill-effects reduced before failure is manifest.

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SY1-03

Fitness and Cardiovascular Aging

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Cardiorespiratory fitness is associated with better quality of life and functional independence, and is one of the single most powerful predictors of all cause and cardiovascular mortality. Ageing is accompanied by a progressive decline in cardiorespiratory fitness as well as impairment of cardiovascular structure and function. Regular aerobic exercise reverses the ageing effects on cardiovascular function by improving structural remodelling and function of the heart and arteries. Similarly, the decline in cardiorespiratory fitness is lessened with regular physical activity, but this must be maintained at a high intensity, and appears to be less effective for women compared with men, and for older compared with younger people. There is some data to indicate that excessive endurance exercise may have adverse cardiovascular effects, but the benefits of regular physical activity throughout the lifespan markedly outweigh the risks.

SY1-04

Effects of Seasonal Variation and High-altitude on Cardiovascular Hemodynamics

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Cooling and high-altitude exposure are associated with major changes in cardiovascular function, which have been attributed as the mechanism of increased risk of cardiovascular morbidity and mortality. Seasonal variation in cardiovascular function is an important emerging issue in the area of human health. This study aims to investigate the seasonal variation of cardiovascular function.

We recruited 137 middle-aged (64 in Taipei and 73 in Xitou, Nanto) staff members who underwent a continuous health monitoring for at least three seasons to investigate the seasonal variation in cardiovascular function. We compared intra-individual changes in

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cardiovascular functions, complete blood counts, and biochemical examinations, which were continuously measured in the same subjects in autumn vs. winter and winter vs. summer. The cardiovascular function was assessed by measuring the arterial pressure waveform by a cuff sphygmomanometer using an oscillometric blood pressure device (DynaPulse 200A, Pulse Metric, San Diego, CA) and aortic stiffness was measured by brachial-ankle pulse wave velocity (baPWV) (Colin VP-1000; Colin, Komaki, Japan).

Results showed that the cholesterol level, white and red blood counts, and platelet counts in winter were higher than in summer and autumn. We observed not only higher vascular stress indicated by higher levels of brachial systolic blood pressure (SBP) and diastolic blood pressure (DBP), central end-SBP and DBP, systemic vascular resistance, and baPWV, but also lower cardiac activities including lower levels of heart rate and cardiac output in winter compared to summer and autumn in the study subjects.

High-altitude travel can cause altitude illness if you are going to destinations higher than 8,000 feet above sea level because development of low oxygen levels. We recruited 11 healthy subjects to attend the high-altitude travel study of health effects of high-altitude on cardiovascular function in Taiwan during Dec. 31, 2016–Jan. 2, 2017.

Low blood oxygen saturation was found in all participants when gradually went up the mountain about 8,000 feet above sea level. In addition, not only increased brachial and central BP, but also elevated heart rate, LV dp/dt max, and cardiac output were noted while participants were going uphill from 978 to 8,470 feet, and finally to 8,950 feet above sea level. The increased cardiovascular workload was recovered while participants were gradually going downhill to 32 feet above sea level.

In conclusion, this study provides evidence of higher vascular stress and susceptibility to athero-thrombosis during winter compared to autumn and summer. For high-altitude travel, the significant increase in cardiovascular workload and critical decrease in blood oxygen saturation noted in high-altitude mountain indicated caution should be taken because the potentially hazardous effects may induce cardiovascular events, particularly those with underlying cardiovascular and/or pulmonary diseases.

SY2-01

The Brain as a Target Organ of the Heart and the Ageing Vasculature: Role of Arterial Pulsatile Haemodynamics

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The pulsatile action of the heart is the sine qua non of the circulation of blood in the vascular system, and the pulse generated by ventricular ejection travels throughout the arterial vasculature at a speed determined by the stiffness of large arteries. Whereas the pulse amplitude of blood flow scales to vessel calibre and decreases with distance from the heart, the amplitude of the corresponding pressure pulse is determined by arterial stiffness and wave propagation phenomena and generally increases with travel towards the periphery. In youth, the central aorta is relatively more distensible than peripheral arteries, presenting a low impedance, thus buffering pulsatile energy. With increasing age and subsequent increase in aortic stiffness resulting in increased impedance, there is reduced buffering of central aortic pulsatility. The system becomes more uniformly stiff, thus enabling pulsatile energy to reach further into microcirculatory beds, affecting end organs.

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As the brain is contained in a rigid structure (skull), the pulsatility of pressure in flow in the cerebral vasculature can influence perfusion pressure through interaction with intracranial pressure as well as causing potential damage to the microcirculation. Increased mechanical stress on cerebral endothelial cells can also affect the mechanotransduction and cell signalling pathways resulting in modulation of protein expression. Experimental evidence will be presented that suggests that cyclic mechanical stretch on cerebral endothelial cells can potentiate expression of the amyloid precursor protein (APP), thus establishing a possible link between large artery function, vascular stiffness, pulse pressure and potential vascular causes of cognitive impairment and dementia, leading to Alzheimer's disease.

SY2-02

Preventive Geriatrics the Cross-talk between Arterial and Brain Aging: A Lifelong Condition

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To prevent disability and allow healthcare sustainability in the era of population aging a life-course approach to chronic disease is required. The life-course approach is aimed at the identification, assessment, and intense follow-up of subjects of ANY AGE with a "greater than average" rate of aging in one or more function(s).

Arterial aging – clinically evaluable noninvasively as carotid-femoral Pulse Wave Velocity (PWV), an index of arterial stiffness – has emerged as a risky condition for cardiovascular events and cognitive decline. With advancing age, arterial aging is less and less dependent on blood pressure levels. The cross-talking between arterial and brain aging will be discussed as a key factor to prevent disabling condition with advancing age, starting at younger ages when the alteration in large artery as well as in brain structure and function are detectable but "silent".

SY2-03

Management of Asymptomatic Carotid Artery Stenosis? On Vascular Cognitive Impairment

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Severe asymptomatic carotid stenosis over 70% increases the incidence of microembolism and chronic brain hypoperfusion, which may consequently impair neurocognition and brain connections. There are controversies in the interventional management of asymptomatic carotid stenosis because of contemporary advancement in medical therapy with regard to stroke prevention. Moreover, there is lack of controlled evidence for cognitive benefit of aggressive medical therapy with or without carotid revascularization. We longitudinally compared patients with asymptomatic carotid stenosis over 70% treated by either aggressive medical therapy alone or in combination with carotid artery stent placement, utilizing a battery of neuropsychological tests, structural MRI, diffusion tensor imaging (DTI), and resting-state functional MRI before and after treatment. I will review the current management of asymptomatic carotid stenosis, followed by report our findings on two-year functional outcomes of stroke/vascular events, and changes in cognitive performance and

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neuroimaging after treatment in theses patients. Both aggressive medical therapy alone and combined carotid revascularization in severe asymptomatic carotid stenosis may not only prevent stroke but also preserve cognition during follow-up. Their therapeutic potential for dizziness alleviation and cognitive enhancement will also be discussed.

SY2-04

Similarity and Disparity of Its Development of Carotid Intima and Media Thickness with Aging

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It is still unclear which layer (intima or media) is mainly involved in increased carotid intima-media thickness (CIMT) by aging and also unclear regarding CIMT value suggesting high cardiovascular risk, although 75th percentile value of CIMT is known as a high risk in asymptomatic adults. We sought to find the changes of carotid intima thickness (CIT) and carotid media thickness (CMT) by aging and the 75th percentile value of CIMT in asymptomatic Korean adults. In an observational cohort study, carotid ultrasound findings (n = 2,204, 58.1 ± 13.5 years old (52% of men) from 12 hospital) were prospectively collected. The carotid images were sent to Korea Research Institute of Standards and Science for analysis using specialized software which can measure intima and media wall.

1. Pearson correlation coefficient between age and right CIMT ($r = 0.489$, $p < 0.001$) and right CMT ($r = 0.482$, $p < 0.001$) were higher than those between age and right CIT ($r = 0.284$, $p < 0.001$).

2. Mean right CIMT in male and female was 0.6960.163 mm and 0.686 ± 0.167 mm ($p = 0.180$) and the 75 percentile value was 0.778 mm and 0.771 mm, respectively.

3. Mean right CIT was 0.311 ± 0.069 mm and 0.303 ± 0.064 mm ($p = 0.009$) and mean right CMT was 0.391 ± 0.124 mm and 0.388 ± 0.131 mm ($p = 0.694$) in male and female, respectively.

4. In diabetic patients (n = 634, 42.9%) vs. nondiabetic patients showed higher carotid intima-media thickness (CIMT, 0.70 ± 0.15 mm vs. 0.66 ± 0.16 mm, $p < 0.001$) and media thickness (CMT, 0.41 ± 0.12 mm vs. 0.36 ± 0.12 mm, $p < 0.001$) than non-DM patients, whereas intima thickness (CIT) showed no significant difference (0.29 ± 0.07 mm vs. 0.30 ± 0.06 mm, $p = 0.067$) between 2 groups.

5. Old age and LDL-cholesterol were the independent factors for CIMT, CIT and CMT in total asymptomatic adults as well as DM patients.

In conclusion, an increased CIMT by aging was mainly due to increased CMT rather than CIT in asymptomatic adults. The increased CIMT in DM patients was mainly due to the increased CMT. Lipid control rather than glucose control may be the most important factor to decrease atherosclerosis progression in subclinical adults.

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SY3-01

Hemodynamic Biomarker-initiated Anticipation Medicine in the Future Management of Hypertension: Renal Protection

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There are notable differences between Asians and Westerners regarding hypertension and cardiovascular disease (Kario. Ann Glob Health. 2016;82:254–257). Asians show greater morning blood pressure (BP) surges (Hoshide, Kario, et al. Hypertension. 2015;66:750–756) and a steeper slope illustrating the link between higher BP and the risk of cardiovascular events. It is thus particularly important for Asians to achieve 24-hr BP control. There are three components of 'perfect 24-hr BP control': the 24-hr BP level, nocturnal BP dipping, and BP variability, such as the morning BP surge that can be assessed by ambulatory BP monitoring (Kario. Essential manual of 24-hr BP management. Wiley-Blackwell, London, pp. 1–138, 2015). The morning BP surge and disrupted circadian rhythm (riser and extreme-dipper patterns) are the independent risks for stroke in hypertensives (Kario.Circulation. 2003;107:1401–1406). The Ohasama study first demonstrated that home BP is superior to office BP for predicting cardiovascular prognosis (Imai, Ohkubo, et al. Blood Press Monit. 1996;1:251–254). The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH2014) recommends the home BP-guided approach (Hypertens Res. 2014;37:253–387). The recent results of the nation-wide cohort, J-HOP study indicate that morning home BP itself should be evaluated to ensure best stroke prediction (Hoshide, Kario, et al. Hypertension. 2016;68:54–61). In addition, in the largest real-world prospective HONEST study on >21,000 hypertensives, morning home BP could detect the risk of coronary artery disease similarly to stroke (Kario, et al. J Am Coll Cardiol. 2016;67:1519–1527), and when on-treatment morning systolic BP was well-controlled <125 mm Hg during 2-year-follow-up, there was no increase in cardiovascular events even in those with office BP maintained >150 mm Hg (Kario, et al. Hypertension. 2014;64:989–996). Thus, the morning BP-guided approach is the first step toward perfect 24-hr BP control, followed by the control of nocturnal hypertension (Kario. Nat Rev Cardiol. 2016;13:125–126). BP variability includes different time-phase variability from the shortest beat-by-beat, diurnal, day-by-day, visit-to-visit, seasonal, and yearly changes (Kario. Hypertension. 2015;65:1163–1169). The synergistic resonance of each type of BP variability would produce a great dynamic BP surge, which triggers a cardiovascular event (resonance hypothesis) (Kario. Am J Hypertens. 2016;29:14–16), especially in high-risk patients with systemic hemodynamic atherothrombotic syndrome (SHATS) (Kario. Hypertension. 2015;65:1163–1169). We have recently developed the hypoxia-and heart rate-trigger nocturnal BP monitoring at home (Kario, et al. J Clin Hypertens. 2014;16:459–466). In the future, the innovative management of hypertension based on the simultaneous assessment of all BP variability phenotypes using a wearable beat-by-beat 'surge' BP monitoring and an ICT-based system will produce a paradigm shift from 'dots' BP management to 'seamless' ultimate individualized 'anticipation medication' for reaching a zero cardiovascular event (Kario. Prog Cardiovas Dis. 2016;59:262–281. Kario. Am J Hypertens 2017; in press).

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SY3-02

Mechanisms of Kidney Injury and Dysfunction due to Large Artery Stiffening

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Chronic kidney disease (CKD), which is defined as the presence of (micro)albuminuria and/or a reduced glomerular filtration rate (GFR), constitutes a growing health concern. Epidemiological studies have shown that mild-to-moderate as well as end-stage CKD is a strong risk factor of all-cause and cardiovascular mortality. Since aortic stiffness can predict total mortality and cardiovascular events in CKD, it is thought to be involved in the mechanism(s) responsible for the predisposition of CKD to cardiovascular disease. Also, aortic stiffness is shown to be an independent determinant of GFR and albuminuria, as well as a strong predictor of progressive GFR decline. Central aortic pressure and flow are greatly influenced by systemic large and small artery stiffness through the Windkesssel function and wave transmission/reflection phenomena. In CKD, aortic stiffness and pulse pressure are generally increased, and aortic flow waveform is often altered because of an enhanced flow reversal. Recent studies indicate that renal hemodynamics is under strong influence of central hemodynamics. Because of the low-impedance properties, renal microvasculature is usually exposed to high pressure pulsation traveling from the central aorta, even in normal conditions. Such pulsatile tensile stress to fragile renal microvasculature is excessively increased by aortic stiffening and the resultant pulse pressure widening, thus leading to microvascular injury and albuminuria. Aortic pulse pressure also correlates closely with renal resistive index, implying that aortic pressure pulsation determines intrarenal flow pulsation. Furthermore, aortic stiffening can increase backward flow from the supra-renal aorta toward the supra-aortic arteries, and thereby reduce renal artery inflow and deteriorate GFR. In this symposium, recent evidence on the central hemodynamic mechanisms of renal damage/dysfunction will be discussed.

SY3-03

Association among Arterial Stiffness, Endothelial Dysfunction and Kidney Arteriosclerosis in Chronic Kidney Disease; Possible Role of Inflammation

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Chronic kidney disease is an important risk factor for cardiovascular diseases, where inflammation is known to be involved in such association. Small arterial changes, especially pre-glomerulus occurred with aging and presence of hypertension. We investigated association of small artery sclerosis in the kidney, endothelial dysfunction in conduit artery and arterial stiffness of large artery in 139 patients with chronic kidney disease who underwent renal biopsy. Small artery changes were semi-quantitatively evaluated by small artery intimal thickening in biopsy specimen. Endothelial function was evaluated by flow-mediated vasodilation in the brachial artery. Arterial stiffness was evaluated by pulse wave velocity (PWV). These changes in three arteries were significantly associated with each other. C-reactive protein was correlated with renal arteriopathy and PWV. Multiple logistic analysis revealed that higher hs-CRP concomitant with decreased FMD and higher PWV were further associated with the risk of severe renal arteriopathy, compared with their

individual effects. These results are compatible to our hypothesis that inflammation and endothelial dysfunction would be ones of key factors which connect alterations of small, conduit and large arteries.

SY3-04

Cardiorenal Syndrome in Acute Heart Failure Patients

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Increased pulsatile hemodynamics and the presence of cardiorenal syndrome (CRS) may increase post-discharge events in patients hospitalized for acute heart failure (AHF). The present study investigated whether the pulsatile hemodynamics is associated with CRS and modulates the impact of CRS on post-discharge outcomes in patients with AHF. We have conducted a study of a total of 240 AHF patients (69.3 ± 15.6 years, 76.7% men) and the participants were followed for up to 3 years after discharge. Measures of the renal function and the pulsatile hemodynamics, including carotid systolic blood pressure (SBPc) and pulse pressure (PPc), carotid-femoral pulse wave velocity (cf-PWV), carotid augmented pressure (cAP), and the amplitude of reflected wave (Pb) were obtained within 24 hours of admission and before discharge. CRS was defined by an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2. We found that on admission cf-PWV and Pb were significantly independently associated with the presence of on-admission and at-discharge CRS and jointly predicted the change of eGFR during hospitalization. During a mean follow-up duration of 769 ± 386 days, 140 subjects incurred their first clinical events of either re-hospitalization for AHF or mortality. Either on-admission or at-discharge CRS or measures of cf-PWV and Pb significantly predicted post-discharge events independently of age, sex, left ventricular ejection fraction, and serum N-terminal pro B-type natriuretic peptide (NT-proBNP). In the full-model, persistent CRS, in addition to age and NT-proBNP were significantly predictive of post-discharge clinical events. We believed that increased pulsatile hemodynamics, excessive wave reflections in particular, contributed to the development of CRS in patients with AHF. Both increased pulsatile hemodynamics and CRS independently predicted post-discharge outcomes.

SY4-01

The Steno-stiffness Chart Deriving from Simultaneous Measurement of Ankle Brachial Pressure Index (ABI) and Brachial-ankle Pulse Wave Velocity (baPWV) for the Wide Range Risk Stratification

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Cardiovascular disease (CVD) remains major cause of morbidity and mortality in developed countries. However, it is not fully predicted by traditional risk factors. Thus, more specific and more accurate marker of subclinical organ damage is indispensable. Arterial stenosis and stiffness, two major aspects of vascular damages, are believed to be important risk markers of CVD.

ABI is known to be an indicator of arterial stenosis or occlusion. Subjects with ABI less than 0.9 are diagnosed as Peripheral Artery Disease (PAD) and subjects with ABI between

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0.90 and 1.0 are classified PAD if their waveform of the ankle pulse is blunted, and their cardiovascular risk is very high.

Pulse Wave Velocity (PWV) is known to be an indicator of arterial stiffness. A meta-analysis of Japanese observational studies demonstrated the cut off value of baPWV of 1,800 cm/s for high and 1,400 cm/s for moderate cardiovascular risk.

In this session, I introduce a new concept of steno-stiffness chart for risk stratification algorism deriving from simultaneous measurement of ABI and baPWV. First, a patient with an ABI ≤0.9 and patient with ABI between 0.9 and 1.0 with blunted pulse wave of ankle are considered at very high risk. Second, a patient with an ABI >1.0 and a baPWV ≥1,800 cm/s is considered at high risk. Third, a patient with an ABI >1.0 and baPWV between 1,800 and 1,400 cm/s is considered at moderate risk. Finally, ABI >1.0 and baPWV <1,400 cm/s is considered at low risk. This stratification algorism is easily measured and would be applicable in the clinical or health screening setting.

SY4-02

A Novel Device for Measuring Electromechanical Coupling: Hemodynamic Principles and Potential Application

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Background: Echocardiographic examination can provide evidence of systolic and/or diastolic left ventricular dysfunction in patients being evaluated for cardiac disease. However, the echocardiogram requires highly specialized training to obtain and interpret, is expensive, not always available and not well-suited for screening. Acoustic cardiography using the AUDICOR DxPatch device involves the collection of simultaneous ECG and heart sound data and is an alternative diagnostic method. Automated algorithms produce measurements of the third (S3) and fourth (S4) heart sounds, electromechanical activation time (EMAT, Qonset to mitral valve closure) and the systolic dysfunction index (SDI, a combination of QRS duration, QR interval, EMAT and S3 strength). The AUDICOR DxPatch can be used to collect 10-second recordings or up to 48 hours of continuous data.

Objectives: The purpose was to assess the correlates of acoustic cardiography derived parameters using independent invasive and non-invasive hemodynamic measurements in heart failure patients.

Methods: Patients underwent Doppler echocardiography and/or left heart catheterization and contemporaneous acoustic cardiography recording. Hemodynamic measurements included LVEF, E/A ratio, LV end-diastolic dimension, diastolic deceleration time, patterns of LV diastolic relaxation, LV end-diastolic pressure (LVEDP) and LV maximum dP/dt, Acoustic cardiography assessed the S3 and S4 strength, EMAT and SDI as continuous parameters.

Results: The presence of an S3 is associated with significantly lower LVEF and significantly increased E deceleration, abnormal E/a and increased E/E' and LVEDP. The presence of an S4 is associated with echocardiographic markers of increased LV stiffness. Prolonged EMAT correlates with reduced LVEF and lower LV maximum dP/dt. Increased SDI is associated with reduced LVEF and increased LVEDP.

Conclusion: The S3 and S4 strength, abnormal EMAT and SDI correlate with invasive and non-invasive parameters of hemodynamic dysfunction. Acoustic cardiography allows for noninvasive, inexpensive and rapid assessment of systolic and diastolic function.

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SY4-03

Heart Rate Variability and Chronic Heart Failure

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Chronic heart failure (CHF) is related to autonomic dysfunction, which may lead to the sudden cardiac death. With high mortality, CHF has become an important clinical challenge. Heart rate variability (HRV) is a popular and reliable method to assess the autonomic activity, including sympathetic and parasympathetic activity. There have been variable indices proved to be independently associated with the prognosis of CHF. In this talk, we will review predictors based on different t surveillance intervals. Left ventricular end-systolic diameter has been reported to be correlated with sudden death from 24 hr Holter recordings, while left ventricular end-diastolic diameter was the predictor from short-term recordings. In addition, low-frequency power was the significant variable of sudden death no matter the recording duration was short or long. As to the time domain analysis, another prospective study showed that the reduction in the standard deviation of normal-to-normal RR intervals (SDNN) could predict the mortality risk related to progressive heart failure. HRV was a noninvasive measure with high specificity, but the sensitivity was too low that the traditional parameters such as left ventricular ejection fraction (LVEF) should be considered in conjunction with HRV in routine screening. Further study could pay more attention to integrate the results of HRV and ECG to improve the value of the derived information.

SY4-04

National Prevalence of Hypertension Defined by a Central BP Monitor

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Hypertension is one of the major risk factors of cerebrovascular and coronary arteries diseases. The prevalence of hypertension increases with the ageing process, and aging population is rapidly increasing in East Asian. Therefore, the importance of comprehending hypertension statistics and related public health burden cannot be overemphasized.

Hypertension is currently diagnosed and treated based on brachial blood pressure measurements. Studies had demonstrated that central blood pressure had better prognostic value for cardiovascular disease than brachial blood pressure in many previous longitudinal cohort studies. Those with high central blood pressure are not identified by measuring brachial blood pressure and may not be appropriately treated in the early stage of hypertension. Fortunately, the devices for measuring central blood pressure has been developed and readily available, which makes the estimation of central hypertension the diagnosis of hypertension based on central blood pressure measurements and criteria, an easier task. However, central blood pressure measurement hasn't been used to investigate the national prevalence of hypertension across the globe including in Taiwanese population. Therefore, in the present talk, I will present the prevalence of central hypertension, as well as conventional hypertension prevalence. The characteristics of populations classified into different central and/or conventional hypertension status will also be compared. Such statistics should be helpful for designing the future prevention and treatment strategist for hypertension and its complications.

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SY5-01

The Clinical Utility of Ambulatory Blood Pressure Monitoring

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Ambulatory blood pressure monitoring makes it possible to record blood pressure during regular daily activities, including daytime hours with mild or moderate physical activity and sleeping hours at night. Ambulatory blood pressure has several advantages over casual measurements either in the clinic, at home or in other measurement settings. First, ambulatory blood pressure monitoring may be devoid of white coat effect, and therefore by comparing with clinic blood pressure may recognize white coat hypertension in untreated people and white coal uncontrolled hypertension in patients on antihypertensive treatment. White coat hypertension is common and confers much lower risk than sustained hypertension. Second, ambulatory blood pressure monitoring may detect masked hypertension, which is also common and confers high cardiovascular risk, but is not possible to diagnose if blood pressure is only measured in the clinic. Third, ambulatory blood pressure monitoring may provide information on circadian rhythm of blood pressure to identify non-dipping pattern of nighttime blood pressure and exaggerated morning blood pressure surge. These disorders in circadian rhythm of blood pressure confer cardiovascular risk over and above the average levels of blood pressure. Fourth, ambulatory blood pressure monitoring provides the possibility to assess reading-to-reading variability, which may also has clinical relevance in cardiovascular prediction and prevention. Fifth, ambulatory blood pressure monitoring may help assess arterial properties by performing regression analysis for systolic against diastolic blood pressure. The changes in diastolic blood pressure per 1 mm Hg changes in systolic blood pressure can be calculated and to some extent may behave as a measure of arterial stiffness. This ambulatory blood pressure index, called ambulatory arterial stiffness index (AASI), is closely correlated with carotid femoral pulse wave velocity, and improves cardiovascular prediction. Ambulatory blood pressure apparently becomes indispensable in the management of hypertension and in cardiovascular prevention.

SY5-02

Effects of Antihypertensive Agents on Central Hemodynamics

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Central BP is indicative of the pressure directly exerted on target organs and often varies from peripheral BP. Differences between the various classes of antihypertensive agents regarding their effects on central hemodynamics have been reported. First evidence came from the Conduit Artery Function Evaluation (CAFE) study, which was one of the first trials to show differing clinical outcomes despite similar reductions in peripheral BP. Recent meta-analysis suggested that β-Blockers showed less effect in central blood pressure compared with peripheral blood pressure. α-Blockers, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, diuretics showed similar blood pressure reduction between central blood pressure and peripheral blood pressure. Augmentation index was significantly reduced with angiotensin converting enzyme inhibitors, angio-

tensin II receptor blockers, calcium channel blockers, diuretics, whereas beta blockers had a nonsignificant reduction. In conclusion, beta blockers are less effective than other antihypertensives at reducing both central blood pressure and augmentation index. Future antihypertensive drug trials are needed to determine the true magnitude of benefit of current and emerging pharmacological and lifestyle interventions in regards to central hemodynamic endpoints.

SY5-03

Diurnal Blood Pressure Rhythmicity in Relation to Environmental and Clock Gene Variations

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Diurnal blood pressure rhythmicity were related to environmental and genetic variations. From 24-h ambulatory blood pressure recordings obtained in untreated patients (51% women; mean age, 51 years), we computed the night-to-day systolic blood pressure ratio in 897 and morning blood pressure surge in 637 patients. Environmental cues included season, mean daily outdoor temperature, atmospheric pressure, humidity and weekday and the genetic cues 14 single-nucleotide polymorphisms in 10 clock genes. Systolic blood pressure averaged (±Standard Deviation) 126.7 ± 11.9 mm Hg, night-to-day ratio 0.86 ± 0.07 and morning surge 24.8 ± 10.7 mm Hg. In adjusted analyses, night-to-day ratio was 2.4% higher in summer and 1.8% lower in winter ($P < 0.001$) compared with the annual average with a small effect of temperature ($P = 0.079$); morning surge was 1.7 mm Hg lower in summer and 1.1 mm Hg higher in winter ($P < 0.001$). The other environmental cues did not add to the night-to-day ratio or morning surge variance ($P \geq 0.37$). Among the 14 genetic variations, only CLOCK rs180260 was significantly associated with morning surge after adjustment for season, temperature and other host factors and after Bonferroni correction ($P = 0.044$). In CLOCK rs1801260 C allele carriers (n = 83), morning surge was 3.7 mm Hg higher than in TT homozygotes (n = 554). Of the night-to-day ratio and morning surge variance, season and temperature explained ~8% and ~3%, while for genetic cues these proportions were ~1% or less. In conclusion, environmental compared with clock genetic variations are substantially stronger drivers of the diurnal blood pressure rhythmicity.

SY5-04

Pulmonary Arterial Hemodynamics Analyzed with the Reservoir-wave Model

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Pulmonary arterial system, like its arterial counterpart, may be understood as a reservoir–wave system; as a wave system, compression and decompression waves generated by the right ventricle (RV) propagate along pulmonary arteries, transmitting energy downstream, while during systole, blood accumulated via pulmonary elastance, discharged during diastole continuing lung perfusion. In anaesthetized dogs, pulmonary arterial pressure and flow were measured at the root of the main pulmonary artery under control condition and during effects

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of hypoxia and nitric oxide, volume loading and positive end-expiratory pressure. The excess pressure and flow, regarded as wave-related, were calculated by subtracting reservoir effects from the measured pulmonary arterial pressure and flow. Wave intensity analysis was employed to quantify the directions of waves, originated upstream from the RV or reflected downstream from periphery. We observed that incident waves generated by the RV reflected negatively by the pulmonary arterial tree at 5.7 ± 0.2 cm from the pulmonary valve, the first bifurcation of main pulmonary artery. During 100% O_2 ventilation, the strength of reflections increased 10% with volume loading and decreased 4% with 10 cmH_2O positive end-expiratory pressure. The geometry of pulmonary arterial tree may reduce peak systolic pressure, while increasing blood flow.

Orals

OS-01

Validity and Repeatability of a New Reactive Hyperemia Index Using Calibrated Pulse-volume Recording in Evaluation of Endothelial Function

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Background: Endothelial function is clinically important for evaluation of cardiovascular risk and its prediction, but its method is impractical for use in clinic. We aimed to assess that volume changes using calibrated pulse-volume recording, MultiLab Series II LHS (Unetixs Vascular, Inc. USA) as an alternative to evaluate endothelial function and compared with flow mediated dilation (FMD) measured by ultrasound.

Method: Reactive hyperemia volume index (RHVI) was calculated as (average amplitude during reactive hyperemia/average amplitude at baseline –) × 100. Outlier, defined as <Q1–0.5 × (Q3–1) or >Q3+1.5 × (Q3–1) by Turkey's outlier rule were three from RHVI and two from FMD and excluded from analysis.

Results: Thirty seven subjects (mean age: 39.04 ± 10.10 years, male 5) recruited. Mean systolic and diastolic blood pressures were 120.40 ± 15.27 and 75.22 ± 9.57 mm Hg. Endothelial function (FMD) by ultrasound was 14.97 ± 6.13% and RHVI by plethysmography was 68.53 ± 64.77%, with the correlation coefficient of 0.3182 (p-value = 0.0229). The regression was remained significant after adjustment with age, sex and body mass index (β = 3.555 (se = 1.749), p-value = 0.0481). Short-term (15-minute interval) and longer-term (1-week interval) reproducibility was tested. Intra-class correlation coefficient was 0.620 (95% confidence interval –0.080 to 0.910) with correlation of 0.6429 for short term and 0.693 (95% confidence interval 0.156 to 0.914) with correlation of 0.5879 for longer-term.

Conclusion: This method may provide a simple and repeatable alternative for evaluating endothelial function, but need further studies in large volumes for its potential use in clinic.

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OS-02

Relation of Pulse Features between Intracranial Pressure and Carotid Blood Flow Waveforms

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Background: Measurement of intracranial pressure (ICP) is an invasive procedure prohibitive for routine measurement in all but extreme cases. ICP is pulsatile at the frequency of the cardiac cycle. The aim of this study was to investigate the relationship between elements of the ICP and cardiovascular waveforms.

Method: Sprague-Dawley rats (18–21 weeks of age, 3 male, 3 female) were anaesthetised (1.3 g/kg urethane) and instrumented to measure and record aortic blood pressure, carotid blood flow, and ICP waveforms. A pacing electrode was used to change heart rate (HR) from resting rate (approximately 300 bpm) upward to 400 and 500 bpm. Measurements were taken at baseline ICP and a raised ICP (infusion of artificial intracranial fluid into the intracranial space). Aortic mean blood pressure was controlled at 100 mm Hg. The minima (p0) and first and second peaks (p1 and p2) of the ICP and corresponding peaks in the carotid flow waveforms were detected. Peak ratios (R) were calculated as (p2-p0)/(p1-p0) for both ICP (RICP) and carotid flow (Rflow).

Results: The relationship to ICPmean, and HR was investigated using mixed effects modelling. Rflow had a significant, positive effect on RICP (β = 0.81 [0.40 1.22], mean [95% CI]; $p < 0.001$), whereas HR had a negative effect on RICP (β = –0.14 [–0.18 –0.10] $(100\ bpm)^{-1}$, $p < 0.001$). ICPmean across the range of heart rate did not influence RICP (β = –0.13 [–0.32 0.06] $(100\ mm\ Hg)^{-1}$, $p = 0.184$). An Rflow-HR interaction term did not significantly improve the model ($p = 0.857$).

Conclusion: The ratio of consecutive peaks of the ICP waveform was negatively correlated with the ratio of consecutive peaks in the blood flow waveform. Given that the carotid flow waveform can be detected non-invasively, this provides a proof-of-concept for further investigation into use of non-invasively acquired cardiovascular signals for the assessment and quantification of the ICP waveform.

OS-03

Association between Arterial Reservoir Function and Cognitive Impairment: Results from the Longitudinal Aging Study of Taipei

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Background: Vascular aging characterized by increased arterial stiffness has been associated with cardiac and cerebral damages. Excess pressure integral (XSPI), which derived from reservoir-excess pressure analysis, is proposed as a novel marker of circulatory

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dysfunction. However, the relationship between XSPI and cognitive function has never been investigated.

Method: In total, 293 community subjects (71.7% female; mean age: 65.7 ± 7.2; education 12.7 ± 3.8 years) from the Longitudinal Aging Study of Taipei (LAST) were invited to receive a comprehensive assessment of hemodynamic measurements for cardiovascular structure and function by echocardiography. Carotid pressure waveforms were obtained by applanation tonometry. XSPI was derived based on the reservoir-excess pressure theory. We used the Montreal Cognitive Assessment (MoCA) instrument Taiwan version to assess the cognitive function and cognitive impairment was defined by MoCA score less than 26. Logistic regression model were constructed to examine the relationship between hemodynamic parameters and global cognition as well as individual cognitive domains.

Results: Compared with subjects with normal cognitive function, a higher XSPI was noted in eighty-four subjects with cognitive impairment (13.0 ± 5.3 vs. 11.3 ± 4.3, p = 0.011), whereas none of the cardiovascular hemodynamic parameters significantly associated with the total MoCA score after adjusting for age, sex, education and blood pressure level. However, in the multivariable model, significant associations between XSPI and abnormal language performances were noted both in the word repetition (OR = 1.07; 95% CI. 1.005–1.138; p = 0.035) and verbal fluency (OR = 1.127; 95% C.I. 1.02–1.244; p = 0.019).

Conclusion: Our study demonstrated that subjects with worse language function had increased XSPI but similar PWV and cardiac structure and function. Excess pressure integral may be a mechanical biomarker in the complex cardiac-arterial-cerebral interactions.

OS-04

Integrated Flow-mediated Vasodilation Response Predicts Cardiovascular Events in Elderly Patients at Cardiovascular Risk Factor

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Background: The integrated flow-mediated vasodilation (FMD) response was shown to be associated with cardiovascular risk factors, but the association between the integrated FMD response and consequent cardiovascular events has been unclear.

Method: We enrolled 555 patients who had at least one cardiovascular risk factor (hypertension, dyslipidemia, diabetes, or smoking). We measured the FMD magnitude of the percentage change in peak diameter (ΔFMD), and we measured the integrated FMD response calculated as the area under the dilation curve during a 120-sec dilation period (FMD-AUC120) using a semiautomatic edge-detection algorithm. The primary outcome was defined as any cardiovascular event, which we defined as a composite of cardiovascular death, and hospitalization for myocardial infarction, stroke, or heart failure.

Results: The mean duration of follow-up was 35 ± 22 months (range: 1–74 months). During the follow-up period, 34 cardiovascular events were recorded. Among the elderly patients (age ≥65 yrs, n = 270), the patients with the lowest tertile of FMD-AUC120 (FMD-AUC120 <5.6) suffered a higher incidence of cardiovascular events compared with the patients with the higher two tertiles (FMD-AUC120 ≥5.6) (log rank 4.16, p = 0.041). The association remained significant after adjusting for age, gender and office systolic blood pressure (hazard ratio 2.51, p = 0.039). In the younger patients (age <65 yrs, n = 285), cardiovascular events were similar among the patients with the lowest tertile and those with the higher two tertiles of FMD-AUC120 (log rank 0.39, P = 0.53). Cardiovascular events were also similar in

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the patients with the lowest tertile and the higher two tertiles of ΔFMD in both the elderly and younger patients.

Conclusion: The Integrated FMD response, but not ΔFMD, predicted cardiovascular events in elderly patients with a cardiovascular risk factor.

OS-06

Blood Pressure Variability Predicted Long-term Mortality in Uremic Patients

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Background: Cardiovascular morbidity and mortality in patients with ESRD are disproportionally elevated, and the change in cardiovascular structures and functions have been recognized. Blood pressure (BP) variability has been identified as a useful prognostic factor for adverse cardiovascular outcomes, however, its utility in patients with end-stage renal disease (ESRD) has not been comprehensively investigated. We, therefore, investigated the prognostic value of blood pressure variability in patients with ESRD.

Method: A total of 155 uremic patients (52.9% male; mean age: 53.99 ± 15.02 years) receiving regular hemodialysis for more than 6 months were prospectively enrolled with 24-h ambulatory blood pressure monitoring (ABPM) data. During a median follow-up of 15.3 years, 77 deaths (55 cardiovascular deaths) were confirmed from the National Death Registry. BP variabilities including weighted standard deviation (wSD), average real variability (ARV) and coefficient of variation were calculated. ARV, the total variability of real analysis in mathematics, was derived from the average absolute difference between consecutive measurements from the ABPM.

Results: Multivariable Cox models adjusting for age, sex, diabetes, body mass index, albumin, intact parathyroid hormone, and 24 hr-averaged SBP revealed that ARV of SBP (P = 0.0073; HR = 1.792; 95% CI 1.17–2.746), daytime SBP ARV (P = 0.0201; HR = 1.745; 95% CI 1.091–2.792), and nighttime SBP ARV (P = 0.0483; HR = 1.329; 95% CI 1.002–1.762) were significantly associated with greater mortality risk, and daytime SBP ARV (P = 0.0423; HR = 1.148; 95% CI 0.807–1.632) was also significantly associated with the risk of cardiovascular mortality. The coefficient of variation and wSD failed to demonstrate independent prognostic value.

Conclusion: In ESRD patients undergoing regular hemodialysis, ARVs of SBP were independently predictive of long-term all-cause mortality, and daytime SBP ARV was also an independent predictor of cardiovascular mortality.

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Abstracts: The Pulse of Asia 2017 Taipei

Moderated Posters

MP-01

Amyloid Beta Neurotoxicity and Neuroprotective Role of 17β Estradiol in Aging Rat Brain Synaptosomes

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Background: Alzheimer's disease (AD) is the most common form of dementia in the elderly. During aging the brain experiences structural, molecular, and functional alterations. These changes increase during menopausal condition in females when the level of estradiol is decreased. The aim of the present study was to determine the effect of neuropeptide, neurokinin B (NKB) and amyloid beta fragment Aβ (25–35) on 17β estradiol (E2) treated aging female rat brain of 3 months (young), 12 months (adult) and 24 months (old) age groups.

Method: The aged rats (12 and 24 months old) (n = 8 for each group) were given subcutaneous injection of 17β estradiol (0.1 μg/g body weight) daily for one month. Synaptosomes were incubated with NKB, Aβ (25–35) and NKB+ Aβ (25–35) in a microfuge tubes at 37˚C for 60 min in a shaking water bath with 0.1, 1 and 5 μM concentration of each of the peptides in all age groups of control and estradiol treated rats.

Results: The results obtained in the present work revealed that increased activities of antioxidant enzymes, membrane bound ATPases and decrease in level of calcium levels, MAO actiivty and lipid peroxidation in presence of NKB and combined NKB and Aβ in vivo estradiol (E2) treated ageing rat brain. NKB treatment reversed the beneficial in preventing some of the age related changes in the brain. An in vitro incubation of E2 treated synaptosomes with Aβ showed toxic effects on all the parameters, while NKB showed stimulating effects and the combined NKB and Aβ showed a partial effects as compared to Aβ (25–35) and NKB alone.

Conclusion: Present study elucidates an antioxidant, neuromodulatory and neuroprotective role of tachykinin peptide NKB against the beta amyloid induced toxicity in E2 treated female rats.

MP-02

Angiotensin Receptor Blocker Reduces Cellular Senescence in Human Coronary Artery Smooth Muscle Cells by Inhibiting CYR61 and f ERK/p38 MAPK/p53 Signaling Pathway

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Background: Angiotensin II is known to a typical peptide hormone causing cardiovascular disease, and most of the well-known Angiotensin II-mediated physiological actions are reported to mediate by stimulation of AT1R. ARBs, including Fimasartan, have pleiotropic effects as well as selective AT1R blockade effect in cardiovascular system, and may be effective in Angiotensin II-induced cellular senescence. However, there is still insufficient evidence to explain the anti-senescence effect of ARBs. Also, although CYR61 is known to induce various cellular activities, including fibroblast senescence, what signaling component is more related to the acceleration of the vascular aging is not clear defined. Therefore, we focus on anti-

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senescence effect of Fimasartan, and evaluated the role of CYR61 on Angiotensin II-induced VSMC senescence.

Method: We stimulated hCSMCs with Angiotensin II to induce senescence and treated with Fimasartan.

Results: Senescent cells were quantitatively measured by SA-β-Gal staining assay, the number of SA-β-Gal positive cells increased by AngII (18.75 ± 1.75%) was significantly decreased by Fimasartan (6.5 ± 1.0%). And molecular senescence markers were measured by western blot, both p53 and p16 expressions increased by AngII (p53: 1.39 ± 0.10, p16: 1.19 ± 0.06 fold vs. control) were suppressed by Fimasartan (p53: 1.02 ± 0.07, p16: 0.97 ± 0.07 fold vs. control). In addition, it was confirmed that CYR61 was induced by AngII. As CYR61 was independently increased, the number of SA-β-Gal positive cells was increased (33.0 ± 3.1% vs. 9.5 ± 1.3% in control), and as CYR61 was inhibited, the number was decreased (11.0 ± 0.5% vs. 24.7 ± 0.9% in AngII). Also, Fimasartan inhibited the activation of ERK and p38 MAPK by Angiotensin II. As ERK was inhibited, CYR61 and p53 decreased, And as p38 MAPK was inhibited, CYR61, p53 and p16 decreased.

Conclusion: Fimasartan provides anti-senescence effect by suppressing CYR61 and ERK/p38 MAPK/p53 signaling pathway in hCSMCs. In addition, this anti-senescence effect will be a basis for identification of pleiotropic effect by ARBs.

MP-03

Aortic Stiffness and Orthostatic Changes in Blood Pressure

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Background: Orthostatic blood pressure (BP) changes are associated with cardiovascular disease. It has been suggested that central artery stiffness could affect BP responses to postural changes, but this is unclear. We aimed to investigate the relationship between aortic stiffness and orthostatic BP changes among patients with hypertension.

Method: Seated, supine and standing BP was recorded among 310 patients with uncomplicated hypertension (54% male; aged 58 ± 9). Standing BP was calculated as the average of duplicate readings after two minutes of standing. Orthostatic changes in BP were determined as the difference in systolic BP (SBP) from seated to standing (ΔSBPstanding-seated) and from supine to standing (ΔSBPstanding-supine). Aortic stiffness was measured in duplicate by carotid-to-femoral pulse wave velocity (aPWV) after three minutes of supine rest.

Results: ΔSBPstanding-seated and ΔSBPstanding-supine were on average –2.0 ± 10.1 and –4.8 ± 11.3 mm Hg, respectively. aPWV was 8.2 ± 1.7 m/s. There were no significant correlations between aPWV and ΔSBPstanding-seated ($r = -0.08$; $p = 0.17$) or ΔSBPstanding-supine ($r = 0.03$; $p = 0.61$). These associations were unchanged in multivariable analyses after adjusting for age, sex, body mass index and total daily antihypertensive dose. There were no significant differences in ΔSBPstanding-seated or ΔSBPstanding-supine between patients with aPWV below or above the median (7.9 m/s; $p = 0.43$ and $p = 0.29$, respectively).

Conclusion: Contrary to expectations, aortic stiffness is not related to orthostatic changes in BP among patients with uncomplicated hypertension.

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MP-04

Arterial Stiffness and Wave Reflections in Relation to the Genetic Polymorphisms in the Receptor of Advanced Glycation End Products

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Background: We investigated arterial stiffness and wave reflections in relation to the Gly82Ser (rs2070600) and –374T/A (rs1800624) polymorphisms in the receptor of advanced glycation end products (RAGE) in a Chinese population.

Method: The study participants were recruited from a residential area in the suburb of Shanghai. Genotyping was performed using the SNapShot method. Plasma advanced glycation end products (AGEs) concentration was measured by the ELISA method and logarithmically transformed for statistical analysis. We measured carotid-femoral pulse wave velocity (PWV) and peripheral and central augmentation indexes using the SphygmoCor system, as measures of arterial stiffness and wave reflections, respectively.

Results: The 968 subjects had a mean age of 55.2 ± 13.0 years, and included 607 (62.7%) women, 361 (37.3%) hypertensive patients and 85 (8.8%) diabetic or prediabetic patients. The genotype frequencies of the Gly82Ser (GlyGly 56.3%, GlySer 38.6%, and SerSer 5.1%) and –374T/A (TT 65.4%, TA 31.4%, and AA 3.2%) polymorphisms were in accordance with the Hardy-Weinberg equilibrium. Plasma AGEs concentration did not differ across the Gly82Ser or –374T/A genotypes ($P \geq 0.06$). However, after adjustment for confounders, the difference in plasma AGEs concentration between –374A allele carriers and –374TT homozygotes reached statistical significance (5.5 g/ml vs. 4.9 g/ml, $P = 0.02$). None of the genetic associations with carotid-femoral PWV or central and peripheral augmentation indexes reached statistical significance ($P \geq 0.39$), except for a borderline significant association between peripheral augmentation index and the Gly82Ser polymorphism ($P = 0.05$).

Conclusion: The genetic polymorphisms in RAGE was weakly associated with plasma AGEs concentration and peripheral augmentation index.

MP-06

Association of Circulating Osteoprotegerin (OPG) and RANKL with Intracranial Arterial Calcification in Hypertensive Patients

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Background: The axis of osteoprotegerin (OPG), the receptor activator for nuclear factor κB (RANK), and RANK ligand (RANKL) has been reported to be critical regulators of skeletal biology and calcification process. However, whether OPG and RANKL involved in intracranial arterial calcification is unknown.

Method: Hypertensive patients with at least two cardiovascular risk factors were recruited from Shanghai Xinzhuang Community. Plasma OPG (Lifespan, Seattle, WA) and serum RANKL (Biomedica, Vienna, Austria) were measured with ELISA kits and log-transformed for analysis. Brain tomographic angiography (CTA) was performed with a GE FX/I helical CT scanner (General Electric, United States). The Hounsfield density was measured using a pixel lens on the CTA images. Calcification was defined as a focal high-density lesion of at least 120 Hounsfield units at the intracranial arteries. Pearson's correlation, single and multiple logistic regressions were applied for analysis.

Results: The 831 patients (mean age, 65 years; 54% women) included 465 (56%) with intracranial arterial calcification. Circulating OPG and RANKL averaged 144.5 pg/mL and 0.052 pmol/L, respectively. Plasma OPG, but not serum RANKL, showed seasonal variation ($P < 0.001$), 15.3% higher ($P < 0.001$) in summer and 5.8% lower ($P < 0.001$) in autumn, relative to the mean level in the whole year. Plasma OPG was negatively associated with RANKL ($r = –0.25$; $P < 0.001$). The prevalence of intracranial arterial calcification increased across OPG tertiles ($P = 0.003$), but decreased across RANKL tertiles ($P = 0.005$). In multivariable-adjusted analyses, RANKL, but not OPG ($P = 0.55$), was independently associated with intracranial arterial calcification, the odds ratio was 13% lower for each double of serum RANKL ($P = 0.043$). RANKL increased by 14.3% with total/HDL cholesterol ratio ($P < 0.001$), and decreased by 7.5% with neutrophils/lymphocyte ratio ($P = 0.022$). In pathway analyses, lipid had both a direct ($P = 0.002$) and RANKL-mediate indirect ($P = 0.008$) effect on intracranial arterial calcification.

Conclusion: Circulating RANKL was inversely associated with intracranial arterial calcification. Further research is warranted to understand the precise mechanisms underpinning this association.

MP-07

Age-Specific Improvement of Cardiovascular Function Immediately after Warm Footbath in Young and Middle-Aged Health Individuals

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Background: Warm footbath (WFB), a local thermal therapy, is thought to have vascular health-promoting benefits, including acute improvement of arterial stiffness in healthy people. However, whether such an effect is age-specific is not fully understood.

Method: The study included 17 young (7 men, mean age 21.4 ± 2.5 years), and 19 middle-aged (9 men, mean age: 56.2 ± 4.7 years) healthy volunteers. All the participants had neither known cardiovascular risk nor atherosclerotic diseases, such as smoking, hypertension, diabetes, or varicose veins. Each participant fasted over 6 hours and was asked to refrain from alcohol as well as caffeine. During WFB, participants immersed their lower legs and feet in warm water (43~45°C) for 30 minutes. We, using pulse wave analyzer (SphygmoCor®), checked before and at 5, 10, 15, 30 minutes after WFB sequentially.

Results: Baseline data revealed similar BMI, SBP, DBP, heart rate, and subendocardial viability ratio (SEVR) in both groups, but augmented index (AI) was higher in the middle-aged (23.6 ± 9.7 vs. 7.9 ± 11.3, $p < 0.0001$). After footbath, heart rate of the young group decreased at 30-minute compared to rest (71.2 ± 9.2 vs. 76.9 ± 10.1, $p = 0.006$). In contrast, the middle-aged group remained stationary. The AI in the middle-aged group showed significant decreased (21.1 ± 9.6 vs. 24.3 ± 10.2, $p = 0.005$) at 30-minute, but it changed little in the young group. As for SEVR, there was significant improvement in the middle-aged group during 5 to 15 minutes, and then returned to baseline at 30-minute. SEVR also got increased in the younger group at 30-minute (170.0 ± 22.5 vs. 154.1 ± 22.5, $p = 0.001$). The ejection duration exhibited a similar trend as SEVR in both groups. The effects effaced 2 hours later after WFB.

Conclusion: Age-specific effects of WFB exists between young and middle-aged healthy people. The acute responses to WFB include improved endothelial function in middle-aged people and improved cardiovascular function in both young and middle-aged people.

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MP-08

Diagnostic Accuracy of New Algorithm to Detect Atrial Fibrillation in a Home Blood Pressure Monitor

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Background: Several reports about the detection of paroxysmal atrial fibrillation (AF) by home blood pressure (BP) monitors have been published. The sensitivity values were near or equal to 100%, but the specificity values were 80%–90%. We evaluated a new algorithm for the detection of AF by a home BP monitor.

Method: We enrolled 16 AF patients and 20 patients with sinus rhythm. Three serial BP values (UA-1020, A&D, Japan) were measured in all patients. Pulse waves were evaluated for 30 sec after each BP measurement. We defined "monitor AF in irregular pulse peak (IPP) 25" as follows: 1) IPP: |interval of pulse peak − average of interval of pulse peak| ≥ average of interval of pulse × 25%, 2) irregular heart beat (IHB): beats of IPP ≥ total pulse × 20%, 3) the "monitor AF (IPP25)": ≥2 IHB of the three BP measurements. We also confirmed the diagnostic accuracy when the cut-off IPP values were set at 20% (IPP20) and 15% (IPP15). We confirmed the concordance between the interval of pulse wave and QRS wave in electrocardiography in five AF patients (total 100 beats).

Results: The correlation between the interval of pulse wave and QRS wave was very high ($R = 0.98$, $p < 0.001$). The diagnostic accuracy of IHB was as follows: the specificity was 1.0 in IPP25 and IPP20, and the sensitivity was 0.69–0.88 in IPP25 and 0.88–0.94 in IPP20; the specificity was 0.95–1.00 and the sensitivity was 1.0 in IPP15. One sinus rhythm case was judged as IHB by the IPP15 setting. The diagnostic accuracy of the monitor AF was as follows: specificity was 1.0 in IPP25, IPP20 and IPP15, and the sensitivity was 0.88 in IPP25, 0.94 in IPP20, and 1.0 in IPP15.

Conclusion: The new algorithm had high diagnostic accuracy to detect AF, and had a low false-positive rate.

MP-09

The Recovery of Pulsatile Hemodynamics during Hospitalization in Patients with Heart Failure with Reduced, Mid-Range and Preserved Ejection Fraction

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Background: Heart failure with mid-range ejection fraction (HFmrEF) is referred to patients with heart failure and a left ventricular ejection fraction (LVEF) of 40% to 49%. However, the hemodynamic characteristics of HFmrEF, comparing to those with reduced or preserved LVEF (HFrEF or HFpEF) remained elucidated. We investigated the hemodynamic perturbations and the clinical outcomes across various phenotypes of HF.

Method: The study population was composed of 2 cohorts of AHF. Cohort A has undergone echocardiogram and hemodynamic measures of cardiac index, stroke volume, and systemic vascular resistance index (SVRI), carotid–femoral pulse wave velocity (cf-PWV), carotid augmented index (cAI), and backward (Pb) and forward (Pf) pressure wave on admission and before discharge. Major adverse cardiovascular events of re-hospitalization for heart failure, non-fatal myocardial infarction, non-fatal stroke and death within a year were recorded. Cohort B was drawn from intramural AHF registry from October 2003 to December 2012, when echocardiographic studies have been conducted before discharge. National Death Registry was linked for the identifications of mortality.

Results: Among a total of 230 patients (age 69.9 ± 15.4 years, 77% men) in cohort A, 105 patients incurred MACEs during a mean follow-up duration of 10.2 ± 3.5 months. Both Pb and Pf on admission and before discharge were higher in HFmrEF and HFpEF than in HFrEF. All of the phenotypes of HF had similar recovery of pulsatile hemodynamics during hospitalization. Cf-PWV was predictive of MACEs in patients with HFpEF (HR and 95% CI: 1.136, 1.037–1.246). In contrast, carotid PP, Pf and Pb were associated with outcomes of HFrEF. In cohort B of 3-year follow-up, the Kaplan-Meier survival curve analyses showed a better survival in HFpEF that the others. However, HFrEF and HFmrEF shared similar risks of mortality.

Conclusion: When the hemodynamic characteristics of HFmrEF were similar to HFpEF, HFmrEF shared similar risks of mortality with HFrEF. The results may imply an unmet need of tailored therapies for HFmrEF.

MP-10

Association of the High-Normal Ankle-Brachial Index with Incident Hypertension: The Okinawa Peripheral Arterial Disease Study

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Background: We hypothesized that the increase in ankle-brachial index (ABI) with age occurs as a result of increasing arterial stiffness and wave reflection. The aim of this study is to investigate the relationship between ABI and incident hypertension in a screened cohort.

Method: We recruited 1,583 participants without hypertension at baseline who underwent ABI measurement by an automatic oscillometric method at least twice with an interval of 3 to 5 years. Participants with ABI ≤0.9 and ≥1.4 were excluded. Hypertension was defined as systolic pressure ≥140 mm Hg and/or diastolic pressure ≥90 mm Hg in the supine position and/or use of antihypertensive medications.

Results: The mean age of participants was 51.8 ± 9.8 yeas, with a range of 19 to 80 years (54% women). The ABI was lowest at <40 years, and increased with age. At the second visit (median 47 months follow-up period), hypertension developed in 264 (16.7%). The initial ABI was higher in participants with incident hypertension (1.09 ± 0.06 vs. 1.11 ± 0.06, P < 0.001). The ABI was positively correlated with change of SBP. Compared with first quartile of initial ABI, the adjusted odds ratio for incident hypertension was higher in participants with fourth quartile of initial ABI before and after multivariate adjustment for age, sex, initial systolic pressure, heart rate, brachial-ankle pulse wave velocity, body mass index, prevalence of diabetes, dyslipidemia, and low eGFR (<60 ml/min/1.73 m^2) (odds ratio 1.92, 95% confidence interval 1.23 to 3.25). Participants with high normal ABI (1.20 to 1.39) compared with

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normal ABI (1.00 to 1.19) had an adjusted odds ratio for incident hypertension of 1.89 (95% confidence interval: 1.08 to 3.27, P = 0.026).

Conclusion: This study provides the first evidence that a high-normal ABI was significantly and independently associated with the incident hypertension.

MP-11

Prognosis of Masked Hypertension Relative to Normotension and Sustained Hypertension: A Meta-analysis of Prospective Studies

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Background: Masked hypertension (MHT) has been demonstrated to be associated with increased risk of cardiovascular events and all-cause mortality. However, previous meta-analysis neither addressed the mortality risk nor compared the risk between MHT and sustained hypertension (SHT). We therefore preformed an updated systematic review and quantitative meta-analysis to synthesize evidence for the prognostic values of masked hypertension in general populations.

Method: We searched Pubmed, Embase and the Cochrane Library to identify literature published until Dec 17, 2016. We restricted our research to articles written in English. In addition, a manual search was performed including searches of all review articles on this topic, reference lists of papers and journals were not indexed in the electronic database. Fatal and nonfatal cardiovascular events were primary endpoint, and all-cause mortality was secondary endpoint.

Results: Of the 5776 initially identified papers, 15 prospective observational studies (14 studies with 38571 patients were included to compare between MHT and normotension, and 11 studies with 35210 patients to compare between MHT and SHT) were finally included in this meta-analysis. Compared with normotension, MHT was associated with a 68% and 37% increased risk of cardiovascular events and all-cause mortality after multi-variable adjustment, respectively. Moreover, the results were consistent when stratified by the methods of blood pressure measurements, treatment status at baseline and follow-up length. However, when compared with SHT without multi-variable adjustment, MHT was associated with a 29% less risk of cardiovascular events but 26% more risk of all-cause mortality.

Conclusion: MHT was associated with higher cardiovascular and mortality risks regardless of the out-of-office BP measurements, treatment status and follow-up duration. Nonetheless, the prognosis of MHT was likely better than SHT, but needs further investigation.

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MP-12

Arterial Reservoir Functions Are Associated with Clinical Outcomes in Patients with Acute Heart Failure Syndrome

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Background: Excessive arterial wave reflections play an important role in the pathogenesis of acute heart failure (AHF). Alternatively, the pulsatile hemodynamics can be analyzed by a reservoir wave model incorporating elements from both reservoir functions and wave analysis. The present study investigated the prognostic values of the arterial reservoir functions in AHF.

Method: A total of 220 AHF patients (70 ± 15 years, 76.8% men, 66.8% HFrEF) were enrolled and followed for one year after discharge. Measures of the pulsatile hemodynamics, including carotid-femoral pulse wave velocity (cf-PWV), carotid pulse pressure (PPc), carotid augmentation index (cAI), carotid augmentation pressure (cAP), the amplitude of reflected wave (Pb), and those based on the reservoir wave model: excess pressure integral (XSPI), reservoir pressure integral (PRI), amplitude of reservoir pressure (Pres), and systolic and diastolic rate constant, were obtained by arterial tonometry before discharge.

Results: During a mean follow-up of 305 ± 108 days, a total of 91 subjects incurred either AHF re-admission or mortality. Patients with post-discharge events were older, had lower estimated glomerular filtration rate (eGFR), higher cf-PWV, PPc, cAI, cAP and Pb, and higher XSPI, Pres, and diastolic rate constant. PPc, Pb, XSPI and diastolic rate constant remained significantly independently associated with the post-discharge events (1.36, 1.10–1.68; 1.14, 1.04–1.24; 1.29, 1.04–1.59; 1.37, 1.03–1.82, respectively) in a multi-variable Cox model accounting for age, sex, eGFR and NTproBNP. Using a backward stepwise model, both XSPI and diastolic rate constant but not PPc or Pb, persistently stayed in the prediction model (1.37, 1.11–1.70 and 1.56, 1.16–2.09, respectively). Combining PPc and diastolic rate constant further stratified the risks of the patients.

Conclusion: Arterial reservoir functions measured by the reservoir wave model are independent prognostic indicators in patients with AHF. Combining parameters of wave reflections arterial reservoir functions may further improve the prediction of post-discharge adverse events.

MP-13

The Association of Chronic Renal Disease with Clinical Outcomes in Patients Undergoing Endovascular Revascularization for Peripheral Arterial Disease

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Background: Chronic kidney disease (CKD) is associated with an increased risk of cardiovascular disease. The aim of this study is to evaluate the association of CKD with clinical outcomes in patients with peripheral artery disease (PAD) who underwent percutaneous transluminal angioplasty (PTA).

Method: The outcomes of 559 consecutive patients with symptomatic PAD who underwent PTA from November 2004 to October 2012 at Korea University Guro Hospital

were enrolled for analysis. Patients were divided into two groups: PAD patients with CKD (n = 158) and PAD patients without CKD (n = 401).

Results: PAD patients with CKD were elderly and had suffered from more hypertension (86.1% vs. 63.3%, p < 0.001), diabetes mellitus (DM, 90.5% vs. 67.6%; p < 0.004), treated with percutaneous coronary intervention (PCI, 34.2% vs.25.2%; p = 0.036), and the use of beta blocker (41.1% vs. 24.4%; p < 0.001). The incidence of DM foot (81.0% vs. 45.6%, p < 0.001), wound (87.3% vs. 55.6%, p < 0.001) were higher in PAD patients with CKD. At 1-year follow up, the incidence of total death (TD, 11.0% vs. 3.2%, p = 0.001) and major adverse cardiovascular event (MACE, 12.3% vs. 6.5%, p = 0.003) were higher in PAD patients with CKD. Adjusted multiple logistic regression showed that CKD was an independent predictor of TD (hazard ratio (HR) 3.6, confidence interval (CI) 1.7–7.9, P = 0.001) and MACE (HR 2.018, CI 1.059–3.844, P = 0.033).

Conclusion: In this study, PTA patients with CKD had more traditional cardiovascular risks and significantly associated with mortality and MACE. Therefore, more intensive therapies will be needed for this particular subset of risky patients.

MP-14

Central Pulsatile Hemodynamics Are Associated with Brain Structure and Cognitive Functions in Hospitalized Patients with Left Ventricular Systolic Dysfunction

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Background: Cognitive function impairment is common in patients with heart failure and is associated with increased disability and mortality. Reduced cerebral blood flow secondary to impaired cardiac pumping is expected in acute heart failure (AHF), but how heart failure affects cerebral structure and functions remains unclear.

Method: Subjects with a reduced left ventricular ejection fraction of <45% hospitalized for AHF were eligible. Measures of the central pulsatile hemodynamics including brachial and central systolic blood pressure (SBP) and pulse (PP) pressure, carotid-femoral pulse wave velocity (cf-PWV), carotid augmentation index (cAI), carotid augmented pressure (cAP) and characteristic impedance were obtained before discharge. Echocardiography and brain MRI and evaluation were also performed. In addition, a neuropsychological test battery (NTB) was tested including Wechsler Memory Scale visual immediate, Wechsler Memory Scale verbal immediate, Rey Auditory Verbal Learning Test (RAVLT), Wechsler Memory Digit Span, Controlled Word Association Test (COWAT) and Category Fluency Test (CFT).

Results: A total of 45 subjects (49.7 ± 11.9, 86.7% men) were enrolled. MMSE, NTB memory score, and executive function were 27.5 ± 2.3, 122.8 ± 29.7, and 53.0 ± 11.7, respectively. Brain MRI demonstrated grey matter, white matter, and white matter hyperintensity were 37 ± 3.1%, 29 ± 2.2%, and 0.2 ± 0.1% of the intra-cranial volume, respectively. While cAI and Pf were highly correlated with grey matter volume, both brachia and carotid DBP were significantly related to the volume of white matter hyperintensity. In addition, brachial SBP and DBP, cf-PWV, right carotid vascular resistance, and right carotid characteristic impedance positively correlated with MMSE.

Conclusion: Central pulsatile hemodynamics were significantly correlated with brain structures and cerebral high-cortical functions in patients with AHF. The results may support that the perturbation of pulsatile hemodynamics in AHF is related to brain perfusion and the subsequent structural remodeling and functional impairments, indicating a close cardiac-cerebral interaction.

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MP-15

The Mechanical Cause of Age-related Dementia: The Brain Is Destroyed by the Pulse

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Background: Recent hypotheses of the cause of age-related dementia (Alzheimer's disease) include that the dementia is caused by molecular pathology of the Ab peptide or of the intracellular skeletal protein tau, or by breakdown of the cerebral capillary bed. External trauma to the head in boxing and football is known to induce dementia (dementia pugilistica, chronic traumatic encephalopathy), usually showing onset some years after the individual's retirement from active sport. In dementia pugilistica, haemorrhage from cerebral vessels is prominent.

Method: We will review evidence that age-related dementia (ARD) is caused by internal trauma to vascular bed of the brain, by the pulse. Between the ages of 50 and 80 years, the heart will beat ~1b times and, because of the low impedance of the cerebral circulation, each pulse penetrates to the cerebral veins. Further, the elasticity of the walls of the aorta and great arteries falls with age; vessel walls stiffen and the pulsatility index of cerebral vessels (a measure of the sharpness of the cerebral pulse) increases several fold with age.

Results: This pounding of cerebral vessels by the pulse induces haemorrhages from cerebral vessels. When the vessel that haemorrhages is large, the patient may display symptoms of stroke and any resulting dementia is designated 'vascular'. When the vessels that haemorrhage are small (capillaries), the patient may experience no acute symptoms; but the cumulative effect of many such haemorrhages becomes evident as loss of memory and of cognition.

Conclusion: The pathologies which Alzheimer described in the demented brain (senile plaques, neurofibrillary tangles and inflammation) occur, we argue, as a result of haemorrhage. The age at which dementia becomes evident is determined by the fragility of cerebral vessels, which may vary between individuals with genetic and lifestyle factors. The hypothesis accounts better than previous proposals for the greatest risk factor for dementia – age.

MP-16

Habitual Endurance Exercise and Vascular Mechanical Biomarkers Derived from Arterial Reservoir Pressure Analyses

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Background: A number of vascular mechanical biomarkers have been developed and proposed to predict cardiovascular outcomes. Among them, systolic (SC) and diastolic rate constants (DC) of reservoir pressure waveform have recently been shown to predict future cardiovascular events in large cohort studies. Impairments in arterial reservoir functions can result in a larger reservoir pressure wave with accelerated reservoir filling rate (higher SC) and faster reservoir emptying rate (higher DC). Currently, the effects of regular exercise training on these vascular biomarkers are unknown. Purpose: We determined the role of

habitual aerobic exercise on well-established vascular function measures and novel arterial reservoir pressure parameters by using both cross-sectional and interventional approaches.

Method: First, we studied 60 apparently healthy, normotensive adults who were either sedentary (SED) or endurance-exercise trained (ET). Second, we studied 16 sedentary healthy subjects before and after a 3-month endurance training, and their data were compared with a sedentary time control group (N = 10).

Results: The cross-sectional analyses showed that ET had higher aerobic fitness, carotid artery distensibility, and lower pulse wave velocity compared with SED. Of the reservoir pressure waveform analysis, ET demonstrated a lower DC, the rate of reservoir pressure decay during diastole phase, than SED. DC was negatively associated with aerobic fitness and positively associated with central systolic blood pressure (cSBP) and pulse wave velocity. In the intervention approach, regular aerobic exercise reduced cSBP and DC. Changes in cSBP were positively associated with SC.

Conclusion: Both cross-sectional and interventional approaches consistently demonstrate that regular aerobic exercise modulates diastolic constant of reservoir pressure waveform that represents reservoir emptying. This may be one mechanism by which habitual endurance exercise lowers the risk of vascular diseases.

MP-17

Single Bout Hiking Improves Endothelial Function, Arterial Stiffness and Endothelial Progenitor Cells in Young Healthy Volunteers

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Background: We investigated even single bout hiking can improve endothelial function, arterial stiffness and endothelial progenitor cells (EPCs) or not. We measured the number of circulating EPCs, flow mediated dilation (FMD), brachial ankle pulse wave velocity (ba PWV), and Augmentation index (AIx) before and after hiking in young healthy volunteers.

Method: 24 young healthy volunteers were enrolled. They hiked the Seorak mountain (1708 m height, 16 km long, 11 hours 20 minutes distance by walk) together once summer time. We tested FMD, baPWV, AIx and measured EPCs (CD34/KDR, CD34/CD117, CD34/CD133) at baselines and immediate after hiking. We checked exercise intensity by Polar monitoring. All volunteers completed hiking within 13 hours.

Results: 16 were male (67%) and mean age was 27.3 (±5.7). mean BMI (body mass index) was 21.4 (±3.4) and they did not have medical history including hypertension and diabetes mellitus. After moderate degree hiking, FMD and AIx improved significantly compared with baseline. (P = 0.001, 0.003, respectively). Absolute numbers of all EPCs improved significantly after hiking (all EPCs, P < 0.001). There is no significant difference of blood pressure and baPWV (Table 1).

Conclusion: Even single bout hiking improved vascular endothelial function and arterial stiffness and augmented the number of circulating EPCs in young healthy volunteers.

Table 1. (for Abstract MP-17)

	Pre-hiking	Post-hiking	p value
FMD (%)	8.7±5.5	15.2±6.1	0.001
AIx (%)	62.2±14.4	54.1±13.6	0.003

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MP-18

Determinants of Pulmonary Hypertension: Role of Vascular Aging

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Background: Pulmonary artery hypertension (PAH) is a progressive disease mainly involving the pathologic remodeling of distal small pulmonary arteries and the subsequent elevations of pulmonary arterial pressure (PAP), leading to right ventricular (RV) failure. How the vasculr aging of pulmonary arteries contributes to pulmonary hypertension remained elucidated. We therefore investigated the associaitons of pulmonary arterial functions and pulmonary artery pressure.

Method: Patients who were referred for right heart catheterization (RHC) under the impression of PAH were enrolled. Pulmonary artery pressure waves were recorded by Millar catheter at a left segmental pulmonary artery (A9 or A10) and main pulmonary artery. By using a customized software, systolic and mean pulmonary artery pressure (sPAP and mPAP), pulse wave velocity (PWV), augmentation index (AI), the amplitude of the decomposed forward (Pf) and backward (Pb) pressure, and pulmonary input impedance (Zc) wave were acquired. Patients with pulmonary hypertension would undergo a vasoreactivity test by inhaling 5 ug prostacyclin. The measures would therefore be repeated in 30 minutes.

Results: A total of 20 patients (age 47.4 ± 10.5 years, 80% women) constituted this study. Seventeen patients were diagnosed as PAH, while they have significantly higher mPAP (52 ± 24 mm Hg), sPAP (77 ± 29 mm Hg), PWV (8.8 ± 4.3 m/sec), AI (27.9 ± 24.7%), Pb (12.7 ± 4.5 mm Hg), and Zc (86 ± 42 dyne/s.cm-5) than the others. However, the pulmonary pressure amplification was similar. When PWV, Pb, and Zc positively correlated with sPAP, only Pb and Zc were significantly related to mPAP. In forward stepwise multivariate linear regression analysis, Pb is the major determinants of mPAP and sPAP (Standardized Coefficients $\beta = 0.709$ and 0.807, respectively) The vasoreactivity test showed a substantial reduction of Pf rather than Pb.

Conclusion: Pb is the maor determinant of pulmonary artery hypertension. The results may support distal pulmonary arterioles was the pathological involvement in PAH.

MP-19

Rosuvastatin Dose-dependently Improves Flow-mediated Dilation, But Reduces Adiponectin Levels and Insulin Sensitivity in Hypercholesterolemic Patients

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Background: Increased risk of type 2 diabetes noted with statins is at least partially explained by HMG-coenzyme A reductase inhibition. We investigated vascular and metabolic phenotypes of different dosages of rosuvastatin in hypercholesterolemic patients.

Method: This was a randomized, single-blind, placebo-controlled, parallel study. Age, sex, and BMI were matched among groups. Forty-eight patients were given placebo, and 47, 48, and 47 patients given rosuvastatin 5,10, and 20 mg, respectively daily during a 2 month treatment period.

Results: Rosuvastatin 5, 10, and 20 mg dose-dependently and significantly improved flow-mediated dilation (34, 40, and 46%) after 2 months therapy when compared with

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baseline (P < 0.001 by paired t-test) or when compared with placebo (P < 0.001 by ANOVA), and increased insulin (median% changes; 16, 20, and 20%, respectively) and glycated hemoglobin levels (mean% changes; 2, 2, and 3%, respectively), and decreased adiponectin levels (mean% changes; 3, 9, and 14%, respectively) and insulin sensitivity (mean% changes; 2, 3, and 4%, respectively) after 2 months therapy when compared with either baseline (all P < 0.05 by paired t-test), or when compared with placebo (P = 0.006 for insulin, P = 0.012 for glycated hemoglobin, P = 0.007 for adiponectin, and P = 0.002 for insulin sensitivity by ANOVA).

Conclusion: Rosuvastatin treatment dose-dependently and significantly resulted in decreasing insulin sensitivity and increasing ambient glycemia by reducing adiponectin levels and increasing insulin levels in hypercholesterolemic patients.

MP-20

The Impact of Angiotensin Converting Enzyme Inhibitor versus Angiotensin Receptor Blocker on Clinical Outcomes in Patients Undergoing Endovascular Intervention for Peripheral Artery Disease

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Background: Angiotensin-converting enzyme inhibitors (ACEI) have a well-established role in the treatment of patients with high risks of cardiovascular disease. The aim of this study is to evaluate the impact of ACEI versus angiotensin receptor blocker (ARB) of the on clinical outcomes in patients with peripheral artery disease (PAD) who underwent percutaneous transluminal angioplasty (PTA).

Method: The outcomes of 518 consecutive pts with symptomatic PAD who underwent PTA from November 2004 to October 2012 at Korea University Guro Hospital were enrolled for analysis. Patients were divided into the three groups; PAD without ACEI or ARB (n = 253), PAD with ACEI (n = 61), and PAD with ARB (n = 204).

Results: Left ventricular ejection fraction (LVEF) were the lowest in PAD patients with ACEI (P = 0.004) and the prevalence of hypertension (p < 0.001) and diabetes mellitus (p = 0.005) were the highest in PAD patients with ARB, and the use of beta blocker was the highest in PAD patients with ACEI (p < 0.001). The incidence of claudication and resting pain as the initial diagnosis for PAD were similar between the two groups. At 1-year follow up, repeated revascularization of coronary artery disease (CAD) was the lowest in PAD patients with ACEI (p = 0.025) and adjusted multiple regression showed that ACEI was an independent predictor for preventing repeated revascularization of CAD (Hazard ratio 0.345, confidence interval 0.776–1.87, p = 0.009).

Conclusion: In this study, although PTA patients with ACEI had more cardiovascular risks, the use of ACEI was useful to preventing repeated revascularization of CAD.

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MP-21

Rolipram, A PDE-IV Inhibitor Protects against Experimental Parkinsonism in Mice

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Background: Rolipram, a specific inhibitor of the phosphodiesterase IV (PDE IV), has recently been shown to exert neuroprotective effects in an Alzheimer transgenic mouse model and in hypoxic-ischemic damage in the rat brain. In the present study, we tested neuroprotective effects, if any, of rolipram drug, a specific inhibitor of the phosphodiesterase IV in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced parkinsonism in mice.

Method: Experimental animal is muscular weighing 25–30 g of 4–5-month-old. The drug was given four times at 12 h intervals by gavation (25–100 mg/kg) in animals made parkinsonian following two doses of MPTP (30 mg/kg, i.p.). Control mice were injected with the same volume of pure DMSO. MPTP-induced striatal dopamine depletion was significantly attenuated by higher dose of rolipram. MPTP-induced catalepsy and akinesia, as well as loss in swim ability, were blocked dose-dependently by rolipram. Brain was used for biochemical and histopathological study.

Results: Present study further shows that rolipram can dose-dependently attenuate both in vitro hydroxyl radical production in a Fenton-like reaction, and also ex vivo 1-methyl-4-phenylpyridinium (MPP+)-induced hydroxyl radical generation in isolated mitochondria. These results indicate that the observed neuroprotective effects of rolipram stem from its significant antioxidant action.

Conclusion: The preliminary results suggest that rolipram is a neuroprotector, and mechanism other than lipid lowering action could be the basis of this effect. Present data show a neuroprotective effect of the PDE IV specific inhibitor rolipram against dopaminergic neuron degeneration, suggesting that PDE IV inhibitors might be a potential treatment for Parkinson's disease.

MP-22

One-year Cardiovascular Prognosis of the Randomized, Controlled, Short-term Heart Rate Variability Biofeedback among Patients with Coronary Artery Disease

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Background: Heart rate variability biofeedback (HRV-BF) is an effective psychophysiological intervention, which shows short-term effects on increasing cardiac autonomic and decreasing hostility among patients with coronary artery disease (CAD). The study aims to examine the long-term effect of HRV-BF on the cardiovascular prognosis among patients with CAD.

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Method: We randomly assigned 209 patients with CAD to the HRV-BF or control group, and then received psychophysiological measurement and psychological questionnaires at pre-intervention, post-intervention, and 1-year follow-up. Cardiovascular prognosis regarding hospital readmission, emergency revisits, and mortality were obtained from the medical records at 1-year follow-up.

Results: Long-term effects were found on lower recurrence of all-cause readmission (12.00% vs. 25.42%) and all-cause emergency visits (13.33% vs. 35.59%) in the HRV-BF group compared with the control group. Low frequency of HRV in the HRV-BF group increased at post-intervention and 1-year follow-up compared with that at pre-intervention, and the depression and hostility scores decreased significantly at post-intervention and 1-year follow-up compared with those at pre-intervention. However, improvement was not found in the control group.

Conclusion: This study confirmed the long-term effects of HRV-BF, including improving patients' cardiovascular prognosis, increasing cardiac autonomic activations, and decreasing depression and hostility. HRV-BF is an effective clinical psychophysiological intervention with short and long-term effects in the cardiac rehabilitation program.

MP-23

Age-dependent Different Action of Curcumin in Thyroid of Rat

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Background: The aging is associated with alterations in the hypothalamic-pituitary-thyroidal axis which can lead to hypothyreosis. Our previous investigations has shown that polyphenol curcumin can enhance the manifestation of hypothyreosis in rats simultaneous treated with propylthiouracil.

Method: The aim of the study was to investigate the relationship between age-related changes and curcumin action in the thyroid of old rats. To this end, morphometric and radio-immunological methods were used. The study was conducted on 3- and 18-month-old male Wistar rats. The experimental rats were treated daily for 30 days by gavage with 100 mg/kg b.w. of curcumin.

Results: There were observed age-related changes in morphology and endocrine function of the thyroid. It was increase in the percentages of large follicles and significant decrease in FT3 level in 18-month-old rats in comparison to 3-month ones. Curcumin treatment lead to significant increase in FT3 and FT4 levels in 3-month-old experimental rats, but the level of FT3 significantly decreased in 18-month-old rats after curcumin administration.

Conclusion: Our results show that curcumin activity depends on the functional condition of the rat thyroid which changes with age. This compound exerts stimulatory influence on the secretory function of the thyroid gland in young rats, but has rather weak antithyroid activity in old animals.

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MP-24

Renal Sodium Handling in Relation to Environmental and Genetic Cues in Untreated Chinese

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Background: Renal tubular sodium handling plays a key role in blood pressure regulation. Several studies reported association between higher proximal tubule fractional reabsorption of sodium and genetic variations response to blood pressure, but no previous study evaluated the contributions of environmental and genetic cues to renal sodium handling in population-based study. Thus, the goal of the present study was to assess the effect of environmental and genetic cues on renal sodium handling.

Method: The participants were suspected hypertensive patients being off antihypertensive medication for at least 2 weeks and referred to our hypertension clinic for 24-hour ambulatory blood pressure. We collected serum and 24-hour urine for measurements sodium, creatinine and lithium concentration. Environmental information was obtained from online website. Fractional excretion of lithium (FELi) and fractional distal reabsorption rate of sodium (FDRNa) were calculated as markers of proximal and distal sodium handling, respectively.

Results: Our study included 1409 untreated patients and 664 men (mean age, 51.0 years). In adjusted analysis, FELi was positively associated with age but negatively with the ratio of the total cholesterol and high density lipid ($P \leq 0.003$). FDRNa was negatively with current smoking and waist circumference. After adjusting the host and environmental factors and after Bonferroni correction, among the 18 genetic variations, only AGTR1 rs2131127 was significantly associated with FELi ($P = 0.032$). In AGTR1 rs2131127 CC homozygotes (n = 162) had lower daytime systolic blood pressure than T allele carriers (131.4 vs. 133.6 mm Hg, $P = 0.04$). Of the fractional excretion of lithium and distal reabsorption of sodium, season and humidity explained ~1.3% and ~3.5%, while genetic cues just 0.98% or less.

Conclusion: In conclusion, environmental compared with genetic cues are critical drivers of renal sodium handling.

MP-25

White Matter Hyperintensities in Migraine: Clinical Significance and Central Pulsatile Hemodynamic Correlates

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Background: To explore the role of central pulsatile hemodynamics in the pathogenesis of cerebral white matter hyperintensities (WMHs) in young migraine patients.

Method: Sixty patients with migraine, 20 to 50 years old, without overt vascular risk factors and 30 demographically-matched healthy controls were recruited in this prospective study. Cerebral WMHs volume was determined by T1-weighted magnetic resonance imaging with CUBE-fluid-attenuated-inversion-recovery sequences. Central systolic blood pressure (cSBP), carotid-femoral pulse wave velocity (cf-PWV), and carotid augmentation index (AI) were measured by applanation tonometry. Carotid pulsatility index (CPI) was derived by Doppler ultrasound carotid artery flow analysis.

Results: Compared to controls, migraine patients had a higher WMHs frequency (OR, 2.75; P = 0.04) and greater WMHs volume (mean volume, 0.174 vs. 0.049, cm^3, P = 0.04). Multivariable regression analysis showed that WMHs volume in migraine patients was positively associated with cSBP (P = 0.04) and cf-PWV (P < 0.001), but negatively associated with CPI (P = 0.04) after controlling for potential confounding factors. The interaction effects observed indicated that the influence of cf-PWV (P < 0.001) and cSBP (P = 0.03) on WMHs formation was greater for the lower-CPI subgroup of migraine patients. WMHs volume in migraine patients increased with decreasing CPI and with increasing cSBP or cf-PWV levels.

Conclusion: WMHs are more common in patients with migraine than in healthy controls. Central pulsatile insults in the presence of low intracranial artery resistance may predispose patients with migraine to WMHs formation.

Posters

P-01

Age-associated Imbalance of MFG-E8 and SIRT1 in VSMC Proinflammation and Stiffening

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Background: Milk fat globule EGF-VIII (MFG-E8) expression is increased; in contrast, silent mating type information regulation 2 homolog (SIRT1) abundance is decreased in the arterial wall which stiffens with advancing age. Proinflammation with aging is known to contribute to vascular smooth muscle cells (VSMC) stiffening. How the effects of an age-associated imbalance of MFG-E8 and SIRT1 signaling on VSMC proinflammation and how this imbalance relates to arterial wall stiffening, however, remains unknown.

Method: Early passage VSMC in cultures were isolated from young (8 mo) and old (30 mo) FXBN rat aorta; expression and location of MFG-E8 and SIRT1 were determined by

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immunoblotting and immunostaining; and matrix metalloproteinase type II (MMP-2) activity was analyzed by zymography.

Results: With advancing age, there was a significant increase in the abundance of MFG-E8 protein and a marked decrease in the amount of activated nuclear SIRT1 protein in VSMC. Exposure of young VSMC to recombinant human MFG-E8 (rhMFG-E8) significantly decreased the amount of nuclear SIRT1 protein and this was accompanied by a substantial upregulation of p-SMAD2/3 and MMP-2 activation, to the levels that occurred in old untreated VSMC. In contrast, an inhibition of p-SMAD2/3 by SB431542 significantly retarded this effect of rhMFG-E8 induction in young VSMC. Furthermore, exclusively in old VSMC, resveratrol, an activator of SIRT1, substantially increased nuclear SIRT1, and this was accompanied by a reduction in MFG-E8 expression and MMP-2 activation.

Conclusion: These findings suggest that an age-associated imbalance of MFG-E8 and SIRT1, contributes to VSMC proinflammation and therefore to arterial wall stiffening (E.G.L. and M. W.: equally contributed).

P-02

Impact of Very Old Age on Long Term Prognosis in Elderly Patients with ST Segment

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Background: Age was reported as a significant risk factor in coronary artery disease. Worldwidely, age of 65 years was accepted as a definition of 'elderly' or older person. However, there was no guideline about the very elderly patients (≥80 years) with ST segment elevated myocardial infarction (STEMI) treated with PCI. Therefore, we investigated the impact of very old age (≥80 years) on long term prognosis in elderly patients who were treated with PCI for STEMI.

Method: A total of 337 elderlypatients who were treated with PCI due to STEMI were analyzed. Patients were divided into the two groups according to the age: 65–79 years patients (n = 269) vs. over 80 years patients (n = 68).

Results: Baseline clinical characteristics showed that past history of PCI (14.9% vs. 4.4%, p = 0.024), diabetes mellitus (39.0%, vs. 13.2%, p < 0.001), and smoking (38.7% vs. 20.6%, p = 0.007) were higher in elderly patients as compared with very elderly patients. Angiographic characteristics were similar between the two groups. Clinical outcomes showed that mortality up to 30 days were higher in very elderly patients, but total mortality up to 3 years were similar between the two groups. Multivariate regression showed that very old age (≥80 years, HR 3.5, CI 1.16–10.7, p = 0.026), past history of cerebrovascular events (HR 4.7, CI 1.4–15.4, p = 0.011), and past history of coronary bypass graft (HR 1.8, CI 1.0–3.2, p = 0.044) were independent risk factors of mortality up to 3 years.

Conclusion: Very old age was associated with short term mortality, and was an independent risk factor of mortality up to 3 years. Therefore, more intensive and careful therapies will be needed for very elderly patients with STEMI treated with PCI.

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P-03

Limits to Longevity: The Still-changing Face of Death

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Background: Longevity has been increasing in societies throughout the world since the late 19th Century, when sanitation and vaccination began the control of infectious diseases. Lifespan is increasing because death rates are falling in all age groups, from <1 year to >85 years. Also falling are the rates of death from all causes except two: dementia and kidney failure. Deaths from these two causes are on the rise; they seem to be emerging as default causes of death, the way we die if we survive the infections of childhood, the recklessness of adolescence and the killers of mid-life – malignancies and cardiovascular disease. So commonly do dementia and kidney failure co-occur that investigators propose a link between the two.

Method: We propose that dementia and kidney failure are fatal sequelae of vascular ageing, the hardening of the aorta and great arteries. The brain and kidney are the two most vascular organs of the body; vascular resistance is kept low in these circulations, to allow the high blood flow needed for neural function and renal filtration. As a consequence, the pulse penetrates the smallest vessels of both organs.

Results: As the great arteries harden with age, the pulse pressure increases until the pulse damages the small vessels of the two circulations; that in the brain, microhaemorrhages cause the pathology that Alzheimer described in the brains of dementia cases; that damage to the small blood vessels of the kidney disrupts the diffusion and resorption functions of the glomerulus and tubules; and that the risk factors for both dementia and kidney failure are predominantly cardiovascular.

Conclusion: We give a new perspective to William Osler's quote –"longevity is a vascular question–a man is as old as his arteries" by opining that in the healthy aged, lifespan is limited by pulse-induces damage to brain and/or kidney.

P-04

Metabolic Function in Ageing Red Blood Cells of Diabetic Animals

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Background: The life-span of red blood cells is approximately 120 days, the cells die thereafter in which some of the metabolites are reused. Therefore, RBC is a good model to study the ageing process. The reticulocytes which come out from the bone marrow have a packet of high efficiency of metabolic activities. As the reticulocytes come in the blood circulation, go through young red blood cells, middle aged cells and old red cells due to their decreased metabolic activities due to enormous stress they face during their circulation in the blood.

Method: The young cells have a higher activities of most of the glycolytic enzymes and decreases in senescent cells in which the enzymes are hexokinase, glucose-6 phosphate dehydrogenase, lactate dehydrogenase, pyruvatekinase. Diabetics further shows a decrease in metabolic function in ageing of red blood cells as most of the glycolytic enzymes further decrease with the age of cells.

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Results: The first enzyme of PPP also decreases with the age of cells resulting in a decrease of redox potential of NADP/NADPH ratio, thereby decreases the activity of glutathione peroxidase. With the age of cells the levels of GSH decreases and an increase in GSSG was observed in old cells. The GR activity has been observed to be increased in old cells trying to maintain GSH levels and lowering GSSG levels but it fails in the process. The percentage increase in GR is less than percentage decrease in GSH-Px in old cells. In diabetes there is a further decline in GSH-Px lowering further NADP/NADPH ratio and shows a lower defense system.

Conclusion: The diabetes further led to decrease in enzymes and metabolites of the red blood cells, showing a fast ageing process in old cells of diabetics.

P-06

Protective Effects of Sodium Orthovanadate in Diabetic Reticulocytes and Ageing Red Blood Cells of Wistar Rats

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Background: Ageing is a slow, continuous and irreversible process involving genetic, metabolic, physiological and structural changes once the reproductivephase of life is over. Therefore, most of the metabolic changes have been shown to be biphasic, the beginning is the growth and development till the attainment of adolescence, thereafter, a decline in the metabolic rate finally rewarding the cells a death.

Method: The reticulocytes and the ageing red blood cells (RBCs) namely young (Y), middle-aged (M) and old RBCs (O) of female Wistar rats from different groups such as control animals (C), controls treated with vanadate (C + V), alloxan-induced diabetic (D), diabetic-treated with insulin (D + I) and vanadate (D + V), were fractionated on a percoll/BSA gradient. The following enzymes were measured – hexokinase (HK), glutathione peroxidase (GSH-Px), glutathione reductase (GSSG-R), glutathione-s-transferase (GST), alanine aminotransferase (AlaAT), aspartate aminotransferase (AsAT) and arginase in the hemolysates of all the RBCs fractions.

Results: Decreases in the activity of HK and AsAT by about 70%, arginase and GSH-Px by 30% in old RBCs were observed in comparison to reticulocytes of control animals. Increases in the activity of GSSG-R by 86%, AlaAT by more than 400% and GST by 70% were observed in old RBCs in comparison to reticulocytes of control animals. Alloxan diabetic animals showed a further decrease in the activities of HK in Y RBCs by 37%, M RBCs by 39% and O RBCs by 32%, GSH-Px activity in Y RBCs by 13%, M RBCs by 20% and O RBCs by 33% and GST activity in Y RBCs by 14%, M RBCs by 42% and O RBCs by 60% in comparison to their corresponding cells of control animals.

Conclusion: Insulin administration to diabetic animals reversed the altered enzyme activity to control values. Vanadate treatment also reversed the enzyme levels except for that of GST in old cells.

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P-07

Role of Vanadium, Trigonella and Vitamin C on Defensive Enzymes of Red Blood Cells of Diabetic Animals

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Background: The treatment to diabetic animals was grouped into (a) vanadium with trigonella and (b) vanadium with vitamin C. To know the efficacy and lowering the toxic effects of vanadium it was proposed to use the ageing animals so that young and old diabetic animals were affected severely or not.

Method: The diabetic animals which were mostly used of 190–200 gms weight and 3–4 months old. The amount of trogonella was designed to be most effective and widely used was 5% in the solid feeds of animals. The amount of Vitamin C used was 0.2 mg/ml in drinking water. nimals were divided into a) Controls (C) injected with vehicle only b) Diabetics (D) c) Diabetics treated with insulin – D+I d) Diabetics treated with vanadate – D+V e) Diabetics treated with vanadate and trigonella D+V+T, and f) Diabetics treated with vanadate and vitamin C – D+V+C.

Results: In diabetic animals catalase activity did not change but SOD and GPx decreased whereas GR and GST increased. Insulin though normalized these enzymes activities, but trigonella also normalized the enzymes activities except SOD. Vanadate in combination with Vitamin C normalized all the defensive enzymes studied. Vanadate with NaCl also could not recover CAT recovered SOD, GPx, GR and GST that shows vanadate with NaCl is more in comparison to vanadate in water. Ghb% and GSSG levels increased in diabetics whereas GSH level went down in this condition. Vanadate normalized GHb%, GSH and GSSG to some extent. Trigonella and Vitamin C in combination with vanadate normalized these metabolites levels.

Conclusion: Vanadate prepared in combination with Vitamin C was found to be more effective as diabetic animals survived for a longer time and found to be healthy and may be a good formulation for humans use.

P-09

Brain-derived Neurotrophic Factor and Central Pulse Pressure after an Oral Glucose Tolerance Test

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Background: Central pulse pressure is a surrogate marker for arterial stiffening that is associated with endothelial dysfunction and may blunt postprandial vasodilatation. Brain-derived neurotrophic factor (BDNF) may modulate the postprandial vascular response by protecting endothelial function. Therefore, we investigated the relationship between central pulse pressure and serum BDNF levels after oral glucose intake.

Method: The subjects, aged between 50 and 80 years, received a 75-gram oral glucose tolerance test (OGTT) after overnight fasting. The serum BDNF levels were determined at 0, 30 and 120 min to calculate the area under the curve (AUC). Brachial and central blood pres-

sures were measured using a noninvasive central blood pressure monitor before blood withdrawals at 0 and 120 min.

Results: A total of 82 subjects (aged of 62 ± 8 years and 79.3% male) without diabetes were enrolled in the study. With the median AUC of BDNF of 45 (ng/mL)*hr as the cutoff value, the central pulse pressure after glucose intake was significantly higher in the subjects with a low BDNF than in those with a high BDNF (63 ± 16 vs. 53 ± 11 mm Hg, P = 0.003), while the brachial pulse pressure was not significantly different between the two groups (P = 0.099). In a multivariate linear regression model, a lower AUC of BDNF was an independent predictor of a higher central pulse pressure after oral glucose intake (linear regression coefficient –0.202, 95% confidence interval –0.340 to –0.065, P = 0.004).

Conclusion: After oral glucose challenge, a lower serum BDNF response is significantly associated with a higher central pulse pressure.

P-10

Central Aortic Pressures and Outcomes of Percutaneous Coronary Intervention in End-stage Renal Disease Patients

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Background: Increased central aortic pulse pressure is associated with higher restenosis rate, mortality, and major adverse cardiac events following percutaneous coronary intervention (PCI). We aim to investigate the relationship between central aortic pressure and cardiovascular outcomes in patients with end-stage renal disease who received percutaneous coronary interventions.

Method: We retrospectively reviewed charts and procedures of patients with end-stage renal disease (ESRD) who received percutaneous coronary intervention in our center. The central aortic pressure and pulse pressure were collected. The outcome was coronary restenosis after the index procedure.

Results: Total 95 ESRD patients were identified in our database. The median age was 74 (63–80) years old. Among them, 32 (34%) were male, 79 (83%) had hypertension, 59 (62%) had diabetes mellitus, 35 (37%) had dyslipidemia, 87 (92%) had coronary artery disease, 21 (22%) had history of myocardial infarction, and 8 (8%) had ischemic stroke. In the central aortic pressure measurements, the median and IQR of central aortic pressure were 158 (137–187)/72 (63–82) mm Hg. The pulse pressures were 90 (70–112) mm Hg. Comparing cohorts of patients with coronary restenosis versus without coronary restenosis, there are significant differences in the central diastolic blood pressure. The central diastolic pressures were 75 (70–88) in patients with restenosis, while the central diastolic pressures were 70 (61–78) mm Hg (p-value = 0.005) in patients without restenosis. This finding remained significant in multivariate analysis. Diabetes mellitus is an already established predictor of coronary restenosis (DM: OR 5.43, 95% CI 1.40–21.04, p-value = 0.01). Central diastolic blood pressure is another possible predictor (central diastolic BP: OR 1.04, 95% CI 1.00 to 1.08, p-value = 0.05).

Conclusion: In patients with ESRD, central diastolic blood pressure and diabetes mellitus were associated with post-PCI coronary restenosis.

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P-11

Chronic Insulin Infusion Induces Reversible Glucose Intolerance in Lean Rats yet Ameliorates Glucose Intolerance in Obese Rats

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Background: Although insulin resistance (IR) is a key factor in the pathogenesis of type 2 diabetes (T2D), the precise role of insulin in the development of IR remains unclear. Therefore, we investigated whether chronic basal insulin infusion is causative in the development of glucose intolerance.

Method: Normoglycemic lean rats surgically instrumented with i.v. catheters were infused with insulin (3 mU/kg/min) or physiological saline for 6 weeks. At infusion-end, plasma insulin levels along with glucose tolerance were assessed.

Results: 6 weeks of insulin infusion induced glucose intolerance and impaired insulin response in healthy rats. Interestingly, the effects of chronic insulin infusion were completely normalized following 24 h withdrawal of exogenous insulin and plasma insulinresponse to glucose challenge was enhanced, suggesting improved insulin secretory capacity. As a result of this finding, we assessed whether the effects of insulin therapy followed by a washout could ameliorate established glucose intolerance in obese rats. Rats were similarly instrumented and infused with insulin or physiological saline for 7 days followed by 24 h washout. Seven day-insulin therapy in obese rats significantly improved glucose tolerance, attributed to improved insulin secretory capacity and improved insulin signaling in liver and skeletal muscle.

Conclusion: Moderate infusion of insulin alone is sufficient to cause glucose intolerance and impair endogenous insulin secretory capacity, whereas short-term, intensive insulin therapy followed by insulin removal effectively improves glucose tolerance, insulin response and peripheral insulin sensitivity in obese rats.

P-14

Secondary Polycythemia in Obstructive Sleep Apnea: The Prevalence and Cadiovascular Damages

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Background: It is widely believed that obstructive sleep apnea (OSA) leads to polycythemia, but the evidence is largely anecdotal. In order to further explore this finding in a larger sample, we used the discharge data from the Japanese high-volume center inpatient sample. Furthermore, we investigated the relationship between polycythemia and cardiovascular function.

Method: This study included 1877 male patients (mean age 54 ± 15 yr) with OSA (apnea-hypopnea index: AHI >5/h), all of whom underwent polysomnography. Polycythemia was defined when haemoglobin is above 18 g/dL in a man. All patients were performed echocardiography and ankle-brachial pulse wave velocity (baPWV).

Results: There were significant relation between haemoglobin and AHI ($r = 0.13$, $P < 0.0001$), but this relation was not significant in multiple regression analysis. Of the 1877 patients, only 27 patients (1.4%) had clinically significant polycythemia. In the overlap group

of OSA and polycythemia, left ventricular mass index and baPWV were higher than those in non-overlap group.

Conclusion: OSA alone is therefore not sufficient to explain secondary polycythemia, but the overlap of OSA and polycythemia may be high risk group for cardiovascular disease.

P-15

Self-measured Home Pulse Pressure Is an Independent Predictor of Arterial Stiffness in Hypertensive Patients: Results from the Taiwan Clinical Trial Consortium of Cardiovascular Diseases (TCTC-12 Registry)

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Background: Arterial stiffness measured by pulse wave velocity (PWV) is increasingly recognized as an important prognostic predictor and a potential therapeutic target in patients with hypertension. Pulse pressure has been considered as a surrogate measure of arterial stiffness. The present study aimed to investigate whether self-measured home pulse pressure (HPP) is associated with PWV.

Method: The registry of hypertension-associated cardiovascular diseases from the Taiwan Clinical Trial Consortium of Cardiovascular Diseases (TCTC-CVD) enrolled hypertensive patients at 11 medical sites across Taiwan and collected blood pressure variables from office, home, and ambulatory blood pressure monitoring, echocardiographic variables, arterial stiffness variables, and blood and urine biochemistry variables. The mean HPP was calculated from self-measurement of home brachial blood pressure twice daily for consecutive 7 days. PWVs were measured between heart and common carotid artery (hcPWV), heart and femoral artery (hfPWV), and brachium and ankle (baPWV) using an oscillometric device. The association between HPP and PWVs was evaluated using linear regression with multivariate adjustment for age, sex, body mass index, history of diabetes mellitus, history of dyslipidemia, serum creatinine level, and mean home systolic pressure.

Results: Of totally 1814 patients enrolled in the registry, 469 patients with complete data of PWV measurement were included in the final analysis. HPP had a significant correlation with hfPWV ($R = 0.262$; $P < 0.001$). In the multivariate model, HPP was found to be independently associated with hfPWV ($\beta = 0.401$; $P < 0.001$), hcPWV ($\beta = 0.212$; $P = 0.005$), and baPWV ($\beta = 0.374$; $P < 0.001$). An HPP ≥54 mm Hg predicted an hfPWV ≥10 m/s (with sensitivity 0.64, specificity 0.63, and C-statistics 0.676; $P < 0.001$).

Conclusion: HPP is an independent predictor of arterial stiffness and can be a useful clinical tool guiding further vascular examinations for patients with hypertension.

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P-19

Can Cerebral and Systemic Pulse Wave Analysis Explain Pulsatile Cerebral Haemodynamics in Raised Intracranial Pressure?

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Background: Raised intracranial pressure (ICP) from closed head trauma or haemorrhage can reduce cerebral blood flow, predisposing to secondary stroke. Direct invasive ICP measurement carries risks of haemorrhage and infection, while proposed indirect methods have not proven sufficiently reliable for clinical use. In investigating a new method of ICP monitoring using cerebral and systemic arterial pulse wave analysis, a study in Cambridge (Kim et. al, J Hyp 2015 (33)) showed that raised ICP from closed head trauma is associated with changes in transcranial Doppler flow waves and aortic pressure waves. We reviewed 5 relevant studies (Kim et. al in Circulation 2014;130:A12309-A and Springer Nature 2016; Kim, 2014 Macquarie University thesis, and Hirata et. al, Stroke 2006 (27)) including the Cambridge study to determine if characteristic changes of cerebral flow waves and systemic pressure waves can be identified in raised ICP.

Method: Study cohorts were normal subjects (n = 1090), and patients with normal pressure hydrocephalus (n = 10) and raised ICP from head trauma (n = 8). Doppler flow waves were recorded in the carotid, middle or anterior cerebral arteries. Pressure waves from the carotid and aorta (surrogate for carotid), derived using SphygmoCor from radial artery pressure measured with intra-arterial line and/or tonometry. Pulse waves were analysed in the time domain, where the relationship between cerebral flow augmentation (FAIx) and central pressure augmentation (PAIx) were compared between normal and abnormal cohorts.

Results: In normal subjects, when FAIx rises, PAIx rises – indicating a linear FAIx/PAIx relationship. In patients with raised ICP, FAIx decreased while PAIx increased. Deviations from the normal linear relationship in raised ICP may be explained by mechanisms of increased wave reflection from the cranium.

Conclusion: Pulse wave analysis of cerebral and systemic arteries shows promise in explaining pulsatile cerebral haemodynamics in raised ICP, opening the possibility of using available non-invasive indices for ICP estimation.

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P-20

Brachial Cuff Reservoir Characteristics and End-organ Markers of Cardiovascular Risk in Australian Adults: A Cross-sectional Study

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Background: Reservoir-excess pressure measured using tonometry methods predicts cardiovascular events, but the operator-dependency of tonometry is an impediment to widespread use. A cuff-based blood pressure device has been developed to derive reservoir-excess pressure from measured brachial pressure waveforms, but whether this method is independently associated with cardiovascular risk has never been investigated and this was the aim of this study.

Method: 1874 adult participants (age 43.7 ± 5.2 years, 11% male) from the Longitudinal Study of Australian Children's Child Health CheckPoint study had reservoir pressure (RP) and excess pressure (XSP) derived from the brachial pressure waveform measured using cuff oscillometry (SphygmoCor XCEL, AtCor Medical, Sydney). Central hemodynamics (augmentation index and central blood pressure) were estimated from the central pressure waveform. Carotid intima-media thickness (cIMT, n = 1467) and carotid-to-femoral pulse wave velocity (cf-PWV, n = 1674) were measured as end-organ markers of cardiovascular risk.

Results: XSP and RP were associated with cIMT after adjusting for age, sex, waist-to-hip ratio, heart rate (HR) and central hemodynamic indices ($\beta = 0.070$, $p = 0.027$ and $\beta = 0.052$, $p = 0.047$). XSP was also significantly associated with cf-PWV after adjusting for the same variables as above ($\beta = 0.128$, $p < 0.001$). The addition of reservoir-excess pressure variables in a model that included the Framingham risk score and HR strengthened the evidence for associations with cIMT and cf-PWV ($p < 0.001$ for all R2 changes).

Conclusion: Cuff-based measures of reservoir-excess pressure are significantly associated with end-organ markers of cardiovascular risk independent of traditional risk factors. This cuff method may provide additional information to improve cardiovascular risk stratification.

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Estimation of Central Aortic Systolic Pressure from Cuff-based Brachial Arterial Pressure by Statistical Learning Methods

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Background: Central aortic systolic blood pressure (cSBP) has been shown to be a better marker of physiological and pathological changes associated with central hemodynamics as compared to brachial systolic pressure (bSBP). However, the noninvasive estimation of cSBP requires the registration of the radial or brachial blood pressure waveform. This study assessed methods of estimating cSBP without the peripheral pulse waveform.

Method: Three statistical learning methods: (i) multiple linear regression (LR), (ii) artificial neural network (ANN) and (iii) support vector regression (SVR) were investigated for the estimation of cSBP directly from cuff-based oscillometric brachial systolic, diastolic and

mean pressure without the peripheral pressure waveform. These models were established using a development group of normal subjects (n = 77) and validated by a noninvasive validation group (n = 312) and by an invasive validation group (n = 62, subjects undergoing catheterization and nitroglycerin infusion).

Results: Noninvasive validation showed that the cSBP estimated by these three models agreed well with the cSBP measured by the SphygmoCor (AtCor, Australia) using a peripheral waveform (LR: r2=0.95, ANN: 0.95, SVR: 0.95, all $p < 0.001$; mean difference = 0.4 ± 3.7, 0.5 ± 3.6 and 0.6 ± 3.7 mm Hg respectively; all $p < 0.001$). Invasive validation showed the cSBP estimated by the SVR model achieved the smallest mean difference (1.3 ± 5.5 mm Hg, $p < 0.05$) relative to invasive cSBP as compared with the LR model (3.3 ± 4.7 mm Hg, $p < 0.001$) and ANN model (6.8 ± 5.3 mm Hg, $p < 0.001$), respectively.

Conclusion: The study demonstrated that statistical learning methods, especially the SVR, have a potential application for the simplification of noninvasive measurement of central blood pressure measurement in clinical practice when the peripheral pulse waveform is not available.

P-22

New Methods for Arterial Analysis in Patients with Primary Aldosteronism

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Background: Primary aldosteronism (PA) is one of the leading causes for secondary hypertension. Beyond the high blood pressure, excessive aldosterone would directly impact the cardiovascular system. Compared with essential hypertension (EH) patients, PA patients have more severe myocardial hypertrophy, myocardial fibrosis, and stiffer arterial wall. New methods regarding arterial pressure waveform analysis provide better predictive values of cardiovascular outcomes than traditional methods. The influence of aldosterone on arterial waveform is still unclear. This study investigated the effect of aldosterone on arterial waveform.

Method: This is a prospective case-control study, which enrolled PA and EH patients, and registered in the Taiwan Primary Aldosteronism Investigation (TAIPAI) data bank. We obtained their baseline medical history, biochemistry data, pulse wave velocity (PWV) and carotid pressure wave form. We compared the between-group direct measurements and the parameters derived from the pressure wave form. We further analyzed them with correlation study and multi-variable linear regression analysis.

Results: A total of 78 patients were enrolled in our study with 39 patients in each group. The systolic blood pressure (SBP), diastolic blood pressure (DBP) were comparable between these groups and the PA patients had significantly higher PWV, forward pulse pressure (Pf) (PA vs. EH, 36.2 ± 12.4 mm Hg vs. 29.9 ± 8.1 mm Hg, $p = 0.003$) and backward pulse pressure (Pb) (PA vs. EH, 28.4 ± 4.5 mm Hg vs. 24.5 ± 5.2 mm Hg, $p = 0.001$) than EH patients. The presence of PA was strongly correlated with Pf, Pb, and carotid pulse pressure. After multiple linear regression analysis, the presence of PA was a strong independent predictor for both Pf (beta = 0.065, 95% C.I. 0.22~0.108, P = 0.004), and Pb (beta = 2.389, 95% C.I. 0.507~4.272, P = 0.014).

Conclusion: From the wave form analysis, we solidify the impacts of primary aldosteronism on cardiovascular system. The new derivatives may provide additional values to predict long-term outcome.

P-23

Non-invasive Estimation of Intracranial Pressure Based on Increased Wave Reflection in Arteries Which Enter the Cranium to Supply the Brain

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Background: Reduction of high IntraCranial Pressure (ICP) by any method, even Craniectomy, can improve the outcome of Traumatic Brain Injury (TBI) by decreasing Secondary Stroke. Raised ICP narrows arteries, increases resistance and decreases cerebral flow. Aim was to develop a non-invasive method, based on pressure and flow contour of arteries entering the cranium, to measure ICP.

Method: Transcranial Middle Cerebral Artery or Internal Carotid Artery flow waves were recorded in 8 patients with TBI at baseline and when ICP was further increased during "Plateau Waves". Data were combined with other data on pressure/flow from the literature under normal conditions and with rise in ICP. Attention was directed at evidence of increased wave reflection, caused by increased cerebral vascular resistance.

Results: Intensity of wave reflection was based on the normal close relationship of Pressure Augmentation Index (PAIx) and Flow Augmentation Index (FAIx) in persons with normal <10 mm Hg ICP. Increased ICP, by increasing wave reflection, increases PAIx, but decreases FAIx, so that the normal relationship is breached. Extent of breach depends on severity of ICP rise.

Conclusion: Changes in wave reflection caused by raised ICP can be used to estimate ICP and its increase with cerebral disease, and decrease with therapy. Our study will help enable cardiovascular team members to estimate ICP and predict risk of secondary stroke.

P-24

The Impact of Endovascular Aneurysmal Repair on Left Ventricular Function in Patients with Abdominal Aortic Aneurysm

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Background: Endovascular aneursymal repair (EVAR) is an emerging predominant treatment for patients with abdominal aortic aneurysm (AAA). Given pulse wave velocity increased significantly after EVAR, the subsequent impacts on left ventricular performance remained elucidated.

Method: Patients undergoing EVAR for AAA in Taipei Veteran General Hospital was prospectively enrolled. All patients have undergone non-invasive hemodynamic measures of carotid femoral-pulse wave velocity (cf-PWV), augmentation index (AI) and backward pressure amplitude (Pb), and transthoracic echocardiography before and 6 months after EVAR. Cardiac function was evaluated with two-dimensional speckle tracking by using Tomtec software.

Results: A total of 30 patients (age 74 ± 11, 100% men) underwent successful EVAR without any complications. None of the patients incurred adverse event during the follow-up. cf-PWV significantly increased 6 months after EVAR compared with baseline (1207 ± 476 vs. 1742 ± 170, P = 0.008) while there was no significant change in systolic blood pressure (136 ± 18 vs. 137 ± 15, P = 0.795). In addition, Pb also decreased significantly after EVAR (20.68 + 7.44 vs. 12.89 + 7.91, P = 0.001), but AI remained unchanged (0.28 + 0.13 vs. 0.25 + 0.13, P = 0.177). However, both the global circumferential strain (GCS) (–21.29 ± 4.84 vs. –21.08 ± 5.93, P = 0.838) and the global longitudinal strain (GLS) (–15.78 ± 3.1 vs. –14.67 ± 4.1, P = 0.16) did not change after EVAR.

Conclusion: The study demonstrated that EAVR did not impair left ventricular function which may further support our previous findings that the measures of cf-PWV were not reliable at the presence of AAA. In contrast, AI may be a better surrogate to evaluate the impact of EVAR on the arterial function. Further clinical follow-up is warranted.

P-25

Usefulness of Arterial Velocity Pulse Index (AVI) as a Non-invasive Assessment for Severe Aortic Stenosis Screening

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Background: Severe aortic stenosis (AS) generally predicts poor prognosis. The gold standard non-invasive method to evaluate the severity is echocardiogram. The echocardiogram cannot perform as a routine examination although screening of severe AS is very important. The pulsus tardus is a well-recognized clinical finding of severe AS, however, the objectively assessment is difficult. The arterial velocity pulse index (AVI) is a parameter of arterial stiffness measurable by pulse wave analysis with the cuff oscillometric method (AVE-1500, PASESA, Japan). The AVI indicates rising slope of the arterial pulse wave. We consider that high AVI value will indicate in the slow rising slope such as pulsus tardus. This method is easy and cost-effectiveness for AS screening. Purpose The purpose of this study was to evaluate the AVI values between the patients with severe AS and those with non-severe AS or without AS.

Method: We enrolled 145 patients (80 males, 75.6 ± 11.2 years) who underwent echocardiographm and measurement AVI. We defined as severe AS when aortic peak velocity was greater than 4.0 m/s in echocardiogram. We assessed about the association between the values of AVI and various parameters of severe AS.

Results: The AVI provided a positive significant correlation with aortic peak velocity ($r = 0.43$, $p < 0.001$) and was significantly higher in patients of severe AS than other subjects (38.2 ± 7.2 vs. 31.0 ± 9.6, $p < 0.001$). In multivariate analysis demonstrated that AVI was one of the independent determinants of severe AS adjusted with age, sex, and systolic blood pressure (OR per 1, 1.10; 95% CI, 1.04–1.17; $p < 0.001$).

Conclusion: The AVI values of severe AS patients were significantly higher than other subjects. The AVI value might help to perform the severe AS screening in easily.

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Vascular Elastovisicous Biomarkers Derived from Oscillometric Pulse Waveform Analysis Was Useful to Improve Risk Stratification for Cardiovascular Mortality

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Background: Risk stratification is fundamental to prevention for cardiovascular disease. However, it remains unclear whether physiological biomarkers of vascular elastovisicous properties could strengthen risk prediction of developing cardiovascular events.

Method: We enrolled a subpopulation of 525 women and 437 men in a prospective community-based cohort. The vascular elastovisicous properties were derived from the analysis of oscillometric waveforms of brachial arterial pressure non-invasively obtained at baseline using a DynaPulse device (DynaPulse 200 M, Pulse Metric, San Diego, CA). Cardiovascular mortality was defined as death caused by atherosclerotic heart and vascular diseases, sudden death, non-valvular heart failure, or stroke.

Results: Among the 962 participants (mean age, 62.2 ± 10.8 years), there were 57 cardiovascular deaths during a median follow-up period of 13.3 years. As compared with absence of cardiovascular mortality, occurrence of cardiovascular mortality was associated with higher the maximal first derivative of estimated left ventricular pressure (LV dP/dtmax) and cardiac index; and lower brachial arterial compliance and distensibility, and systemic vascular compliance. The association of cardiovascular mortality remained significant with LV dP/dTmax and systemic vascular compliance (hazard ratio [95% confidence interval] for each increase in 1 standard deviation, 1.51 [1.06–2.14] and 0.62 [0.41–0.95], respectively), after adjusting for age; sex; status of hypertension, diabetes mellitus, and smoking; lipid profiles; and fasting glucose. Incorporating the biomarkers of LV dP/dTmax or systemic vascular compliance conferred significant, albeit modest, improvements on the conventional risk model regarding risk prediction for cardiovascular mortality (integrated discriminatory improvement, 1.4%, p = 0.011 and 0.7%, p = 0.009, respectively). Moreover, cardiovascular risk stratification based on the established algorithm could be enhanced after LV dP/dTmax or systemic vascular compliance was taken into consideration.

Conclusion: We have demonstrated that vascular elastovisicous measures could be independent biomarkers for predicting the risk for cardiovascular mortality. Integrating vascular elastovisicous biomarkers into the established risk assessment algorithm might be beneficial to refine cardiovascular risk stratification.

P-27

Cyclic Stretch Frequency-modulated Response of Protein Expression Related to Nitric Oxide Release in Human Umbilical Vein Endothelial Cells

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Background: Pulsatile blood flow mediates shear stress and cyclic strain on endothelial cells, activating endothelial nitric oxide synthase (eNOS). Phosphorylation of eNOS (peNOS) at serine 1177 (S1177) is known to be regulated by phosphorylated-Akt (pAKT) at S473 and

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activated intercellular cell adhesion molecule-1 (ICAM-1), a key regulatory event in endothelial nitric oxide (NO) production leading to cyclic guanosine monophosphate (cGMP)-mediated-vasorelaxation. Although the effect of cyclic stretch on peNOS is documented, the effect of frequency (simulating changes in heart rate) with the stretch intensity has not been established in endothelial cells. This study aimed to investigate the frequency effect of pulsatile stretch on endothelial protein expression.

Method: ICAM-1, eNOS, protein kinase B (Akt) expression and phosphorylation and downstream products of Akt signalling such as NO and cGMP levels were measured in human umbilical vein endothelial cells (HUVECs) exposed to 5–20% cyclic stretch at 0.5 or 1 Hz for 18 hours. Protein and mRNA expression were quantified using western blot and qPCR respectively. NO and cGMP were quantified using commercial assay kits. Results are represented as mean ± SEM of % control.

Results: Protein levels of eNOS increased at 1 Hz compared to 0.5 Hz (66 ± 11% vs. 211 ± 37%, $p = 0.0006$) and as did ICAM-1 (69 ± 5% vs. 210 ± 47%, $p = 0.0079$). Phosphorylated eNOS at S1177 increased with cyclic stretch in contrast to decreased phosphoralated Akt at both 0.5 Hz (55 ± 8%, $p < 0.001$) and 1 Hz (36 ± 5%, $p < 0.0001$). Similarly, at 1 Hz eNOS mRNA (204 ± 27%, $p = 0.0027$) and NO (167 ± 10%, $p < 0.0060$) increased while cGMP was not different in unstretched cells.

Conclusion: These results demonstrate that pulsatile stretch at 0.5 and 1 Hz mediate differential expression of proteins related to NO production in HUVECs. In addition, activation of eNOS might not be entirely Akt dependent as pAkT is down regulated with cyclic stretch.

P-30

Hypertension, Obesity, Diabetes, and Heart Failure-free Survival: The Cardiovascular Disease Lifetime Risk Pooling Project in New Delhi, India

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Background: This study was designed to quantify the relationship between the absence of heart failure risk factors in middle age and incident heart failure, heart failure-free survival, and overall survival.

Method: We conducted a pooled, individual-level analysis sampling from communities across the New Delhi, India as part of 4 cohort studies: the Framingham Heart, Framingham Offspring, Delhi Heart Association Detection Project in Industry, and ARIC (Atherosclerosis Risk In Communities) studies. Participants with and without hypertension (blood pressure ≥140/90 mm Hg or treatment), obesity (body mass index ≥30 kg/m^2), or diabetes (fasting glucose ≥126 mg/dl or treatment), and combinations of these factors, at index ages of 44 years and 56 years through 96 years. Competing risk-adjusted Cox models, a modified Kaplan-Meier estimator, and Irwin's restricted mean were used to estimate the association between the absence of risk factors at mid-life and incident heart failure, heart failure-free survival, and overall survival.

Results: For participants at age 44 years, over 516,537 person-years of follow-up, 1,677 incident heart failure events occurred. Men and women with no risk factors, compared to those with all 3, had 73% to 85% lower risks of incident heart failure. Men and women without hypertension, obesity, or diabetes at age 44 years lived on average 34.7 years and 38.0 years without incident heart failure, and they lived on average an additional 3 years to 15 years

longer free of heart failure than those with 1, 2, or 3 risk factors. Similar trends were seen when stratified by race and at index age 56 years.

Conclusion: Prevention of hypertension, obesity, and diabetes by ages 45 years and 55 years may substantially prolong heart failure-free survival, decrease heart failure-related morbidity, and reduce the public health impact of heart failure.

P-31

Target of Blood Pressure Treatment for the General Elderly Population: A Systematic Review and Meta-analysis

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Background: Recommendations on blood pressure (BP) targets for the elderly hypertensive patients are still controversial. We aimed to assess the effectiveness resulting from different BP targets for preventing adverse events in the general population older than 60 years.

Method: We conducted a systematic review by including randomized controlled trials (RCTs) of BP-lowering management for the elderly hypertensives without specified comorbidity to evaluate the effects of intensive versus standard BP reduction on coronary heart disease, stroke, heart failure, all-cause death, major adverse cardiovascular and cerebrovascular event (MACCE), renal failure, cardiovascular disease, and cardiovascular death.

Results: Eleven RCTs enrolling 37,874 participants were included in this study. Treatment with final achieved systolic BP (SBP) <150 mm Hg, compared with achieved SBP <160 mm Hg, resulted in risk reductions in all outcomes (relative risk [RR] of 0.59 to 0.83, $P \leq 0.002$), except for coronary heart disease and renal failure. Compared with treatment to <150 mm Hg, a lower achieved SBP (<140 mm Hg) was still significantly associated with a decreased risk of stroke (RR: 0.69, 95% confidence interval [CI]: 0.57–0.84), heart failure (RR: 0.72, 95% CI: 0.54–0.94), all-cause death (RR:0.79, 95% CI: 0.63–0.98), MACCE (RR: 0.67, 95% CI: 0.58–0.78), cardiovascular disease (RR: 0.79, 95% CI: 0.68–0.93), and cardiovascular death (RR: 0.68, 95% CI: 0.54–0.84). Furthermore, meta-regression showed a dose-response trend between achieved SBP and event rate for MACCE ($P < 0.001$) and stroke ($P = 0.076$). These effects of BP-lowering on vascular events were comparable between the subgroups.

Conclusion: Intensive SBP control to <140 mm Hg was associated with a significant reduction in most cardiovascular outcomes in the general elderly population as compared with the BP target <150 mm Hg recommended by the US guideline. The present evidence supports a lower SBP target for elderly hypertensive patients.

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The Associations with Target Organ Damage of Morning Hypertension by Various Definitions

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Background: Morning Hypertension (MHT) can be defined based on ambulatory blood pressure (BP) monitoring (ABPM) or home BP monitoring (HBPM). In which definition MHT is more associated with cardiovascular outcome remains unknown. In the present study, we therefore compared the associations with target organ damage of MHT by various definitions.

Method: From November 2010 to June 2015, we consecutively recruited untreated outpatients from our Hypertension Clinic. MHT was an average BP of at least 135/85 mm Hg in the morning defined either based on HBPM, or the diary (the first 2 h after awakening) or short-clock time interval (6–10 AM) on the day of ABPM, irrespective of the BP levels at other time windows. We assessed carotid-femoral pulse wave velocity (cfPWV) by SphygmoCor system, left ventricular mass index (LVMI) and carotid intima-media thickness (IMT) by ultrasonography, and the urinary albumin/creatinine ratio (ACR) as measures of target organ damage.

Results: In the 1085 untreated patients (mean age, 51.2 years), the prevalence of MHT were 63.7%, 65.1% and 48.7% based on the ABPM diary, short-clock time interval and HBPM, respectively. After adjustment for age, sex, and other cardiovascular risk factors, patients with MHT compared to normotensive subjects had significantly ($P < 0.001$) increased cfPWV, urinary ACR and carotid IMT, irrespective of the definitions. In multivariate-adjusted continuous analyses, target organ measures were all positively associated with morning systolic BP recorded by ABPM and HBPM ($P < 0.002$), except for that of LVMI with home BP. After further including the systolic BP at other time windows in the multivariate-adjusted models, morning systolic BP during 6–10 AM remained significantly associated with cfPWV ($\beta = 0.019$, $P < 0.001$), and home morning systolic BP was associated with cfPWV ($\beta = 0.024$, $P < 0.001$) and urinary ACR ($\beta = 0.012$, $P = 0.003$).

Conclusion: Irrespective of the definitions based on ABPM or HBPM, morning hypertension was associated with target organ measures.

P-33

The Contribution of Inflammation to the Development of Hypertension Mediated by Increased Arterial Stiffness

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Background: The mechanisms underlying the possible contribution of chronic inflammation to the development of hypertension remain unclear. We examined the longitudinal association of inflammation with the progression of vascular and/or renal abnormalities in the development of hypertension.

Method: In 3274 middle-aged Japanese men without hypertension at the study baseline, the brachial-ankle pulse wave velocity (baPWV), blood pressure, estimated glomerular

filtration rate (eGFR) and serum C-reactive protein (CRP) levels were measured annually over a 9-year period.

Results: During this study period, 474 subjects (14.5%) developed hypertension. Analysis of the repeated-measures data revealed that sustained elevation of the serum CRP levels was associated with an accelerated increase of the baPWV. A linear mixed model analysis revealed that higher log-transformed serum CRP values (log CRP) at each measurement were associated with a higher annual increase of the baPWV (estimate = 32.553 ± 11.635 cm/sec per log CRP, p = 0.018) and higher values of the baPWV were associated with a higher annual elevation of the blood pressure (estimate = 0.025 ± 0.002 mm Hg per log CRP, p < 0.001).

Conclusion: In middle-aged Japanese men without hypertension at the study baseline, long-term active inflammation appears to be associated with an accelerated longitudinal increase of the arterial stiffness. In turn, this accelerated longitudinal increase of the arterial stiffness appears to be associated with longitudinal elevation of the blood pressure to the hypertensive range. Thus, systemic inflammation may play a role in the pathogenesis of hypertension by accelerating the progression of arterial stiffness.

P-34

The Effect of Ambulatory Blood Pressure Monitoring on the Target Organ Damage among the Patients with Metabolic Syndrome

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Background: Ambulatory Blood pressure (BP) monitoring (ABPM) is crucial in hypertension treatment and BP variability (BPV) is known to cause target organ damage (TOD) in hypertensive patients. However, the effects of BPABPM and BPV may vary in subjects with metabolic syndrome. We aimed to explore the association of BPABPM and BPV with cardiac TOD in treated hypertensive patients with metabolic syndrome.

Method: Eligible study subjects were retrospectively identified from 1814 treated hypertensive patients registered from 11 medical centres of the Taiwan Clinical Trial Consortium of Cardiovascular Diseases (TCTC-CVD). Patients with metabolic syndrome were identified according to the definition of ATP III. BPABPM values included the 24-hour mean systolic BP (SBPABPM), diastolic BP (DBPABPM), and average real variable of SBPABPM (SBPARV), and DBPABPM (DBPARV). Cardiac TOD indices included reduced left ventricular ejection fraction (LVEF), left ventricular hypertrophy (LVH) and reduced diastolic peak velocity of the mitral annulus (E'). Multivariable logistic regression models were constructed by adjusting age, gender, body mass index (BMI), waist circumference, smoking, socioeconomic status, exercise, low-density lipoprotein cholesterol (LDL), and medication.

Results: A total of 474 patients with metabolic syndrome were identified. Their mean age was 61.7 ± 15.5 years, mean BMI was 27.2 ± 4.1 kg/m^2, and waist circumference was 92.2 ± 10.8 cm. Their BPABPM was 135.2/79.0 mm Hg (±15.1/10.1 mm Hg). SBPABPM was significantly associated with LVH and E' value <8 cm/s (adjusted p = 0.02 and p = 0.03, respec-

tively). In contrast, neither DBPABPM nor BPV was significantly associated with cardiac TOC. None of the BPABPM or BPV variables were associated with reduced LVEF.

Conclusion: Patients with metabolic syndrome and a higher SBPABPM may have a higher risk to develop cardiac TOD, including LVH and left ventricular diastolic dysfunction. No significant association was found between cardiac TOC and DBPABPM or BPV.

P-35

Albuminuria Is Independently Associated with Myocardial Diastolic Dysfunction in Patients with Early-stage Hypertension: Results from Taiwan Clinical Trial Consortium of Cardiovascular Diseases (TCTC-12 Registry)

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Background: Albuminuria is linked to the arterial stiffness in hypertension. Studies also suggested that albuminuria is related to the prognosis of heart failure preserved ejection fraction. Whether it is associated with myocardial diastolic dysfunction in patients with hypertension has not been investigated.

Method: The Taiwan Clinical Trial Consortium of Cardiovascular Diseases hypertension-associated cardiovascular diseases registry enrolled patients from 11 medical centers around Taiwan. Variables from office, home, ambulatory blood pressure monitoring, echocardiography, arterial stiffness, and biochemistry were collected. The association between urine albumin-creatinine ratio (UACR) and ratio of mitral peak velocity of early filling to early diastolic mitral annular velocity (E/e') was analyzed. Adjustments were made for age, gender, body mass index, smoking, plus variables of hypertension control (home systolic/diastolic pressure, left ventricular hypertrophy), arterial stiffness [home central pulse pressure, brachial-ankle pulse wave velocity (PWV), ambulatory arterial stiffness index (AASI)], or components of metabolic syndrome (fasting glucose, triglyceride, high/low-density lipoprotein cholesterol (HDL/LDL-C), waist circumflex).

Results: From the database, 191 patients with complete UACR and E/e' measurements were analyzed. The mean age was 62.3 years old, body mass index 26.1 kg/m^2, waist circumflex 94.1 cm, 52.9% male, 13.1% smoker, 15.7% diabetes mellitus, 30.4% dyslipidemia, 14.9% left ventricular hypertrophy, 1.6% chronic kidney disease (≥stage 3), 1.6% heart failure (ejection fraction ≤45%). The mean home blood pressure was 142.1/81.7 mm Hg, central pulse pressure 64.5 mm Hg, PWV 1.7 m/s, AASI 0.5, fasting glucose 108.3 mg/dl, triglyceride 138.9 mg/dl, HDL-C 47.3 mg/dl, LDL-C 111.5 mg/dl, UACR 77.9 mg/g, and E/e' 11.7. Log UACR was significantly correlated with E/e' ($r = 0.327$, $p = 0.00004$); the association remained robust after adjusting for demographic confounders ($\beta = 0.31$, $p < 0.001$), hypertension control ($\beta = 0.27$, $p < 0.001$), arterial stiffness ($\beta = 0.21$, $p = 0.012$), or metabolic syndrome ($\beta = 0.41$, $p < 0.001$).

Conclusion: Albuminuria, a marker of endothelium damage, was independently associated with myocardial diastolic dysfunction in patients with early-stage hypertension.

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P-36

Sag Mediated Therapy Leads to a Predominant TH1 during Visceral Leishmaniasis on Triggering CD2 Epitope Thereby Leading to Reduction in Vascular Aging and Organ Damage

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Background: Visceral Leishmaniasis is a macrophage associated disorder for the treatment of which antimony based drugs like SAG and SSG were the first choice in the recent past. The clinical value of antimony therapy is now declined against VL because increasing cases of Sodium Antimony Gluconate (SAG) resistance.

Method: We have evaluated the effect of combining CD2 with conventional antimonial (sb) therapy in protection in BALB/c mice infected with either drug sensitive or resistant strain of Leishmania donovani. Mice were treated with anti CD2 adjunct SAG subcutaneously twice a week for 4 weeks. Assessment for measurement of weight, spleen size, anti-Leishmania antibody titer, T cell and anti-leishmanial macrophage function was carried out day 0, 10, 22 and 34 post treatments.

Results: The combination therapy was shown boosting significant proportion of T cells to express CD25 compared to SAG monotherapy. Although, the level of IFN-γ was not statistically different between combination vs. monotherapy ($p = 0.298$) but CD2 treatment even alone significantly influenced IFN-γ production than either SAG treatment ($p = 0.045$) or with CD2 adjunct SAG treatment ($p = 0.005$) in Ld-S strain as well as in Ld-R strain. As shown, the super-oxide generation began enhancing very early on day 10 after SAGtreatment with CD2 during which SAG action was at minimum. Interestingly, the super-oxide generation ability remained intact in macrophage after treatment with immuno-chemotherapy even in mice infected with Leishmania resistant strain. Unlike SAG treatment, treatment of SAG with CD2 also led to production of nitric oxide and TNF-α, resulting in resulting in most effective clearance of L. donovani from infected macrophages.

Conclusion: Our results indicate that CD2, which can boost up a protective Th1 response and hence control the infection in clinical situation leading to reduction of vascular aging.

P-37

The Association of Nighttime Thoracic Fluid Content and Outcomes in Patients with Acute Heart Failure

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Background: The role of the nighttime fluid shift in the pathogenesis of acute heart failure (AHF) remains poorly defined. We aimed to investigate the clinical significance of nighttime thoracic fluid content in patients with AHF.

Method: A total of 44 patients (61 ± 19 years, 80% men, left ventricular ejection fraction 32 ± 12%) hospitalized due to AHF were studied. Before discharge, transthoracic impedance cardiography (PhysioflowTM) was performed from 6 pm to 6 am the following morning to generate data of thoracic fluid content index (TFCi) every 30 seconds. TFCi was the average of all data points. Average TFCi during each 4 fixed time intervals, namely, 6 PM

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to 9 PM (T1), 9 PM to 0 AM (T2), 0 AM to 3 AM (T3), and 3 AM to 6 AM (T4), were also calculated.

Results: A total of 44 patients (61 ± 19 years, 80% men) were studied. During a mean follow-up duration of 292 ± 156 days, 5 (11%) patients died. Patients with higher TFCi (>12.17/kOhm/m^2) were older, had higher prevalence of coronary artery disease (CAD), higher N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, lower body mass index (BMI), and serum albumin levels. Univariate Cox regression analysis suggested that a high overall nighttime TFCi might be associated with a greater mortality (HR 5.37, 95% CI, 0.60–48.10, P = 0.133). Moreover, TFCi during T2 (HR 7.88, 95% CI, 0.88–70.61, P = 0.065) appeared to be more predictive of mortality than other periods.

Conclusion: A higher nighttime TFCi, during 9 PM to 0 AM (T2) in particular, might be associated with a poorer short-term prognosis. The results might support that nighttime fluid shift may have a prognostic role in patients with AHF.

P-38

Central Aortic Pressure Is Closely Positively Associated with Vascular Calcification Especially in Hemodialysis Patient Compared with Peritoneal Dialysis

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Background: Central aortic BP is known as an independent factor of CV disease. End stage renal disease have many risk factors like as hypertension, diabetes, calcium homeostasis imbalance and LV remodeling due to chronic volume and pressure overload. We investigated the two dialysis method – hemodialysis (HD) or peritoneal dialysis (PD) effect on central aortic BP (cABP) and vascular calcification (VC).

Method: This is single center prospective observation study for 1 year. Total 75 patients (51 HD, 24 PD, mean age 54.8 ± 12.4, male 38.2%) were evaluated cABP, echocardiography, arterial stiffness with PWV and vascular calcification. The cABP was checked by non-invasive HEM-9000AI and VC was evaluated by semiquantitative abdominal aorta calcification score.

Results: Total 75 patients (HD 51, PD 24) were enrolled. PD group patients were younger (56.8 ± 11.7 vs, 50.8 ± 12.9 year), lower diabetes prevalcence (51.0% vs. 37.5%), dialysis duration (4.4 ± 4.4 vs. 3.2 ± 1.7 year), than HD groups. Baseline brachial and central SBP were higher in HD group (bSBP 157.3 ± 22.0 vs. 133.9 ± 20.4, cSBP 163.0 ± 27.5 vs. 134.2 ± 22.6 mm Hg). But DBP was not different. And brachial and central pulse pressure, augmentation index, PWV are also higher in HD group (bPP 78.4 ± 19.6 vs. 53.8 ± 15.1, cPP 83.2 ± 23.0 vs. 54.1 ± 17.5, AI 85.6 ± 15.6 vs. 71.5 ± 14.5, PWV 17.7 ± 4.0 vs. 15.2 ± 3.0). Finally Aorta vascular score is much higher in HD group than PD group (4.3 ± 5.1 vs. 1.5 ± 2.5).

Conclusion: Although there are many factors associated with vascular calcification in ESRD patients, chronic high hemodynamic pressure and volume burden by hemodialysis may increase the central aortic blood pressure and be also associated with large vascular remodeling like PWV and vascular calcification compared with peritoneal dialysis. In conclusion, PD may have vascular protective effect comparing HD in field of vascular health in ESRD patients.

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P-39

Pulse Wave Analysis in Patients with Intradialytic Hypotension

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Background: Intradialytic hypotension (IDH) is a common complication during hemodialysis in patients with chronic kidney disease and may increase the mortality. Our study aimed to investigate the hemodynamic condition of IDH.

Method: In this study, 70 ESRD patients was visited at Taoyuan Chang Gung memorial hospital during September to December in 2014. Patients under regular HD (3 times per week) for at least 3 months were enrolled as the study subjects after complete inform consent. Subjects with arrhythmia, artery–vein anastomoses on both arms were excluded. Pulse wave analysis and heart rate variability were evaluated before hemodialysis. IDH was defined as intradialytic nadir systolic blood pressure (SBP) <90 mm Hg which presented in ≥30% of 12 hemodialysis treatments in previous 4 weeks.

Results: In the results, there were there were 22 subjects in IDH group and 48 subjects in the controls. Compared to the controls, IDH group had longer dialysis vintage ($P = 0.001$), lower SBP ($p < 0.001$), lower diastolic blood pressure ($p = 0.041$), lower mean arterial pressure ($p < 0.001$), lower central SBP ($p < 0.001$), lower augmentation pressure ($p = 0.001$), lower Pb ($p < 0.001$) and lower Pf ($p < 0.001$). After adjustment of age, sex and SBP, 22 subjects in the controls were matched with 22 subjects in the IDH group, and blood pressure was similar in the two group. IDH group had higher augmentation index ($p = 0.043$), higher augmentation magnitude ($p = 0.045$), lower Pb ($p = 0.001$) and lower Pf ($p < 0.001$) compared to the controls.

Conclusion: Higher mortality in the patients with IDH was noted in the previous study. In this study, we found that the IDH group had increased central arterial stiffness and decreased central systolic blood pressure. The correlation between this hemodynamic change and the prognosis of patients with IDH is worthy of further investigation in the future.

P-42

The Risk of Major Bleeding in Patients with Atrial Fibrillation and Vascular Diseases

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Background: Atrial fibrillation (AF) is an independent cause of ischemic stroke (IS) and warfarin has been used widely for the prevention of IS. This study aimed to investigate whether patients with both AF and vascular diseases (VD) have a higher risk of haemorrhagic events after using warfarin.

Method: This retrospective study is based on the data from the claim system of a tertiary hospital in southern Taiwan from 1st January, 2010 to 31st December, 2014. The patients with ICD-9-CM code of 427.31 and CHADS-VASc score ≥1 were recruited. Only those who were prescribed with warfarin were included. VD is defined as any of the followings: myocardial infarction, coronary artery diseases and peripheral artery diseases. Those who aged <18 years, pregnant, diagnosed as AF or used oral anticoagulants before the index date, have mechanical valves, pulmonary embolism or deep vein thrombosis, were excluded. The patient was followed until the first occurrence of IS or major bleeding. The period since the inclusion to the endpoint was compared by the Cox proportional hazards model.

Results: We analyzed 486 patients with AF and 134 (27.6%) of them had VD. After adjusted with age, gender, BMI, hypertension and diabetes mellitus, patients with VD had a higher tendency to develop IS comparing to those without VD (hazard ratio 2.01; 95% CI 0.95–4.27; p = 0.07). Moreover, a trend of more major bleeding events has also been noticed in this patient group (hazard ratio 2.05; 95% CI 0.91–4.64, p = 0.08), although the statistical significance is weak because of the small sample size.

Conclusion: Despite the use of warfarin as stroke prevention in AF, those who have VD might have higher risk of IS comparing to the patients without VD. Besides, they might also suffered from more major bleeding events and frequent monitoring of PT might be necessary.

P-43

Acute Bout of Exergaming Attenuates Endothelial Dysfunction Following Postprandial Lipemia in Persons with Spinal Cord Injury

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Background: Cardiovascular disease (CVD) is a leading cause of mortality in persons with spinal cord injury (SCI). Postprandial lipemia after a high-fat meal is a predictor of CVD risk and may be exaggerated in the setting of SCI. High-fat meal has been shown to induce endothelial dysfunction, while an exergaming attenuates endothelial function following postprandial lipemia in abled body. We tested the hypothesis that postprandial lipemia following a high-fat meal may decreases in endothelial functionin and an acute bout of exergaming attenuates postprandial lipemia and endothelial dysfunction in persons with SCI.

Method: Forty persons with SCI (aged 41 ± 8 years, male 24) were randomly assigned to either an exergame group n = 20) or seated rest as a control group (n = 20) after a high-fat meal. Blood parameters and endothelial function were measured at baseline, 2 and 4 hours after a high-fat meal. Brachial artery flow mediated vasodiation FMD) was measured as an index of endothelial function. After an hour following a high-fat meal, the exergame group performed 50 minutes of moderate intensity active video games at 40–60% of heart rate reserve.

Results: A high-fat meal significantly increased triglyceride, insulin, and glucose levels, but decreased mean blood pressure in both groups in a similar manner ($p < 0.05$), no significant group-by-time interaction was found in these variables ($p > 0.05$). However, FMD significantly decreased in the control group (base 7.2 ± 3.3, post 2 hr 5.2 ± 3.2, post 4 hr 5.3 ± 2.4%) but attenuated at post 2 hr and increased at post 4 hr in the exergame group (base 7.8 ± 3.1, post 2 hr 7.1 ± 3.1 post 4 hr 9.2 ± 3.3%), with a significant interaction ($p < 0.001$).

Conclusion: These results show that a high-fat meal causes endothelial dysfunction in persons with SCI, but endothelial dysfunction following postprandial lipemia was atten-

uated by a acute bout of exergaming. These findings suggest that exergaming may have a cardioprotective effect on endothelial function in persons with SCI when exposed to a high-fat meal.

P-44

Association between Serum Uric Acid and Exaggerated Blood Pressure Response to Exercise in Normotensive Men

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Background: Exaggerated blood pressure (BP) response to maximal exercise is a predictor of cardiovascular disease, but the mechanisms for this hypertensive response are not fully understood. Increased serum uric acid levels have been associated with incident hypertension, but the relationship between serum uric acid levels and the exaggerated BP response to maximal exercise has not been established. The aim of this study was to examine the hypothesis that increasing levels of serum uric acid would be related to the exaggerated BP response to exercise, independently of confounding factors, in healthy normotensive men.

Method: We evaluated 4,640 (mean age 49.1 ± 7.4 years, range 21~80 years) healthy normotensive men who underwent maximal exercise treadmill testing and fasting blood analysis. The exaggerated systolic BP response was defined as a systolic BP of 210 mm Hg or greater during maximal exercise.

Results: The exaggerated systolic BP response was present in 152 men (3.3%). Serum uric acid was positively correlated with the maximal systolic BP response ($r = 0.15$, $p < 0.001$). Men in the highest quartile of serum uric acid (>6.6 mg/dl) had a 2.24 times [95% confidence interval (CI) 1.29–3.90] increased risk of prevalence of exaggerated systolic BP to maximal exercise than men in the lowest quartile of serum uric acid (<5.1 mg/dl) after adjusting for confounding variables. Each unit increment in serum uric acid levels was associated with a 16% increased risk of prevalence of exaggerated systolic BP to maximal exercise in the adjusted model (1.16, 95% CI 1.01–1.34).

Conclusion: These results suggest that serum uric acid levels are associated with an exaggerated systolic BP response to maximal exercise, independently of established risk factors in normotensive men.

P-45

Comparison of the Effects of Short-term Stair Climbing vs. Treadmill Walking Exercise on Endothelial Function and Arterial Stiffness in Healthy Young Adults

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Background: Stair climbing is an accessible physical activity pattern in worksites and public settings. It is well known that walking exercise improves vascular health, but limited evidence suggests similar or greater vascular health benefits may result from stair climbing exercise. The aim of this study was to compare the effects of short-term stair climbing and

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treadmill walking exercise at the same exercise intensity on endothelial function and arterial stiffness in healthy young adults.

Method: Eighteen healthy adults were randomly assigned to either the stair climbing exercise (n = 10) or the walking exercise (n = 8). The stair climbing exercise group received a stair climbing exercise in a building, while the walking exercise group received a brisk walking exercise on the treadmill at the same exercise intensity (50~60% of heart rate reserve) for 2 weeks, 30 min/day, and 3 times/week. Peak oxygen uptake was measured using a maximal treadmill exercise test. Carotid-femoral pulse wave velocity as an index of aortic stiffness and flow-mediated dilation of brachial artery were measured using applanation tonometry and ultrasound. These variables were measured at baselined and after 2 weeks of supervised exercise in both groups.

Results: The study results showed that FMD was improved in both groups with a similar manner (stair climbing: 11.49 ± 2.19 to 14.31 ± 2.35%, walking: 10.83 ± 1.28 to 12.09 ± 2.90%, $p < 0.05$), but no significant interaction effect (group X time) was found. There was a trend for time effect on carotid-femoral pulse wave velocity in both groups after interventions (stair climbing: 6.83 ± 0.8 to 6.40 ± 0.88 m/s, walking: 6.61 ± 0.8 to 6.46 ± 0.85 m/s, $p = 0.051$). No significant improvement in peak oxygen uptake was observed in any group (stair climbing: 35.47 ± 7.83 to 37.03 ± 8.26 mL/kg/min, walking: 37.46 ± 5.21 to 38.33 ± 6.73 mL/kg/min, $p = 0.726$).

Conclusion: These findings suggest both short-term stair climbing and treadmill walking exercise were comparatively effective in improving vascular function in healthy young adults. Further studies are needed to clarify the effects of long-term stair climbing exercise on the vascular function.

P-48

Parkinson's Disease Risk Score (PDRS) for Parkinson's Disease Screening in Aging Population: Effect of Yoga and Meditation

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Background: India is the country with the top most people with diabetes, and with time life style is changing among pediatric and adolescent populations well as aged peoples. Current research based on the prevalence and management of Parkinson's disease in Delhi metro population by Yoga and Meditation. There are several study are going on the patients about their social and mental problem in Parkinson's disease patients as well as their family.

Method: Total 32 aged patients (age group 60–70 years) and 35 aged patients (age 70–80 years) are scored using Parkinson'sdisease risk score (PDRS) which includes age, family history of diabetes, exercise status and Waist circumference. After scoring them they are categorised into mild, moderate and high risk group. All group were treated with Yoga and Meditation for daily one month with balance diet at Shri Mahamaya vaishnav devi mandir research institute, New Delhi, India.

Results: We get 8%, 79% and 13% aged patients in high risk, moderate and low risk group respectively for developing Parkinson's disease. After one month their blood glucose and insulin levels were closer to normal levels with increase in work efficiency in both aged group patients. Present study highlight that the successful treatment of Parkinson's disease patients of both age groups, not only requires anti-aging drugs; but also family care, life style education, harmonised mind-body-soul, awareness, psychological support, preventive approach toward activity of daily living.

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Conclusion: Through counselling with meditation and yoga, we can help people to acknowledge and share the emotional challenges raised by Parkinson's disease complications. Therefore preventive Parkinson's disease education programme & promotion of yoga and meditation will be future plan of action which can be suggested in the form of regular exercise and diet planning for the aging population as part of an integrated approach.

P-49

Blood Pressure Variability and Target Organ Indices: Results from the Taiwan Clinical Trial Consortium of Cardiovascular Diseases (TCTC-12 Registry)

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Background: A high short-term blood pressure variability (BPV) can predict long-term cardiovascular mortality independently of 24-hour systolic blood pressure (SBP). However, the relationships between various BPV parameters and target organ indices have not been systematically evaluated.

Method: The registry data of hypertension-associated cardiovascular diseases from the Taiwan Clinical Trial Consortium of Cardiovascular Diseases (TCTC-CVD) collected ambulatory blood pressure monitoring (ABPM) readings, echocardiographic variables, arterial stiffness variables, and blood and urine biochemistry variables. BPV parameters were derived from the ABPM SBP, diastolic blood pressure (DBP) and the calculated pulse pressure (PP), and included standard deviations (SBPSD, DBPSD, PPSD), read-to-read average real variability (SBPARV, DBPARV, PPARV), nighttime dipping (SBPDIP, DBPDIP, PPDIP), morning BP surge, lowest nighttime SBP, DBP and PP, and highest morning SBP, DBP and PP. Target organ indices included left ventricular mass index (LVMI), left atrium volume index (LAVI), brachial-ankle pulse wave velocity (baPWV), and urinary albumin-creatinine ratio (UACR).

Results: Complete data were available in 679 hypertensive subjects (mean age 61.0 ± 15.1 years; men 58.0%). In multivariable linear regression analyses adjusting for sex, age, body mass index, and 24-hour SBP, SBPARV (p-value 0.017) was significantly associated with UACR, DBPSD (p-value 0.041) was significantly associated with LV mass, SBPDIP (p-value 0.0002) and daytime BP surge (p-value 0.0006) were significantly associated with LAVI, daytime BP surge (p-value 0.038) was significantly associated with LVMI.

Conclusion: Among a multitude of short-term BPV parameters, only daytime BP surge was significantly associated with more than one target organ indices, after adjusting for confounding effects.

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P-52

Behavioural and Psychological Symptoms in Poststroke Vascular Cognitive Impairment

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Background: Behavioural and psychological symptoms of dementia (BPSD) cause significant patient and caregiver morbidity in vascular cognitive impairment (VCI). Objectives. To study and compare the occurrence and severity of BPSD between multi-infarct dementia (MID), subcortical ischaemic vascular disease (SIVD), and strategic infarct subtypes of poststroke VCI and to evaluate the relationship of these symptoms with the severity of cognitive impairment.

Method: Sixty patients with poststroke VCI were classified into MID, SIVD, and strategic infarct subtypes. BPSD were studied by the neuropsychiatric inventory (NPI). The severity of cognitive impairment was evaluated by the clinical dementia rating scale (CDR).

Results: 95% of cases had at least one neuropsychiatric symptom, with depression being the commonest, irrespective of subtype or severity of VCI. Strategic infarct patients had the lowest frequency of all symptoms. SIVD showed a higher frequency and severity of apathy and higher total NPI scores, compared to MID. Apathy and appetite disturbances occurred more commonly with increasing CDR scores. The total NPI score correlated positively with the CDR score.

Conclusion: Depression was the commonest neuropsychiatric symptom in VCI. The neuropsychiatric profiles of MID and SIVD were similar. The frequency and severity of apathy and the net burden of BPSD increased with increasing cognitive impairment.

P-53

Biofortified Food with Vitamin B-6, B-12 and Folic Acid Increases Concentrations of Vitamin and Shorten Concentrations of Homocysteine: Study in North Indian District

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Background: Concentrations of high homocysteine and low vitamin-B have been linked to the risk of vascular disease, stroke, and dementia and are relatively common in older adults. Concentrations of high homocysteine and low vitamin-B have been linked to the risk of vascular disease, stroke, and dementia and are relatively common in older adults.

Method: A trial was conducted in the year 2014, randomized in 120 person aged 55–85 years. The subjects had no history of hypertension, anemia, asthma, cancer, or cardiovascular or digestive disease and did not regularly consume multiple or B vitamin supplements or highly fortified breakfast cereal. Subjects were randomly assigned to consume 1 cup (0.26 L) breakfast cereal fortified with 390 microg folic acid, 1.9 mg vitamin B-6, and 4.5 microg vitamin B-12 or placebo cereal for 12 week. Blood was drawn at 0, 2, 12, and 14 week. Methionine-loading tests were conducted at baseline and week 14.

Results: The result of this study, plasma homocysteine concentrations were significantly lower and vitamin-B concentrations were significantly higher in the treatment group than in the placebo group. The percentage of subjects with plasma folate concentrations <10 nmol/L decreased from 2% to 0%, with vitamin B-12 concentrations <175 pmol/L from 8% to 3%,

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with vitamin B-6 concentrations <18 nmol/L from 5% to 2%, and with homocysteine concentrations >10.4 micromol/L (women) or >11.4 micromol/L (men) from 6.4% to 1.6%. The percentage of control subjects with values beyond these cutoff points remained nearly constant or increased.

Conclusion: Who consumption of one cup biofortified cereal food daily significantly increased vitamin-B this relatively healthy group of person and decreased homocysteine concentrations, including post-methionine-load homocysteine concentrations.

P-58

The Profile of Behavioral and Psychological Symptoms in Vascular Cognitive Impairment with and without Dementia

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Background: The objective of this study was to compare the occurrence and severity of behavioral and psychological symptoms of dementia (BPSD) between vascular dementia (VaD) and vascular cognitive impairment-no dementia (VCI-ND).

Method: Consecutive patients presenting with cognitive impairment at least 3 months after an ischemic stroke and with a Hachinski Ischemic Score ≥4 were included. VaD was diagnosed as per National Institute of Neurological Disorders and Stroke – Association Internationale pour la Recherche et l'Enseignement en Neurosciences criteria for probable VaD and VCI-ND on the lines of the Canadian study of health and aging. The severity of cognitive impairment and the behavioral/psychological symptoms were studied by means of the clinical dementia rating scale and the neuropsychiatric inventory (NPI) respectively.

Results: All patients with VaD and 89% of those with VCI-ND had at least one BPSD. The mean no. of symptoms per patient and the total NPI scores were higher in VaD than in VCI-ND. Apathy and night-time behavior disturbances were significantly more common and severe in VaD.

Conclusion: BPSD are very common both in VCI-ND and in VaD. The profile of BPSD is similar in both groups, albeit more severe in VaD. The net burden of BPSD is higher in VaD as compared to VCI-ND.

P-59

Clues of Transthoracic Echocardiography into Rapid Diagnosis of Type A Aortic Dissection in Hypertensive Patients

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Background: Aortic dissection is one of serious acute complication of hypertension. Especially, quick diagnosis of type A aortic dissection (AD) is important for early surgical intervention. Transthoracic echocardiography (TTE) is an easy and available tool before definite diagnosis with chest CT angiogram in the emergency setting. We investigated simple clues of TTE to suspect type A AD, thus, shortening time of confirming type A AD.

Method: Twenty one patients were enrolled in this retrospective study. Fifty patients were diagnosed as acute AD from January 2004 to April 2013 in Kangdong Sacred Heart

hospital. Among them, 21 patients were confirmed with type A. AD by chest CT angiogram and TTE. We evaluated baseline characteristics, general parameters and aortic distensibility (D) of ascending aorta (AscA) using TTE: D = (AscA diameter in systole – AscA diameter in diastole)/(AscA diameter in diastole X pulse pressure).

Results: In our study, patients with type A AD showed various TTE features such as pericardial effusion (76%), tamponade sign (38%), aortic regurgitation (67%), intimal flap (23.8%). Ascending aortic diameter was increased (50.1 ± 7.7 mm in systole; 48.5 ± 7.4 in diastole). Aortic distensibility of type A AD was $1.46 \pm 1.1\times10^{-3}$ mm Hg^{-1} that is smaller than aortic distensibility of dilated AscA in patients with Marfan syndrome ($3.0 \pm 2.6\times10^{-3}$ mm Hg^{-1}) and that of normal AscA ($4.4 \pm 2.2\times10^{-3}$ mm Hg^{-1}) in previous studies. There was no significant difference between aortic distensibility with and without intimal flap in type A AD patients ($1.91 \pm 0.99\times 10^{-3}$ mm Hg-1 and $1.21 \pm 1.06 \times10^{-3}$ mm Hg^{-1}).

Conclusion: In emergency setting, ascending aortic distensibility by transthoracic echocardiography might be a putative indicator for rapid diagnosis of type A. aortic dissection.

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Association of Sodium Intake with Albuminuria in Obese Patients

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Background: High sodium intake has been associated with cardiovascular events. This relation is stronger in obese population. Albuminuria was also well known marker of not only renal disease also widespread vascular damage. However, there were few data on sodium intake and albuminuria. Therefore, we examined the relation between high sodium intake and albuminuria.

Method: From 2011 to 2012, data from 315 patients hospitalizing tertiary referral center in Korea were analyzed. These patients underwent ambulatory blood pressure monitoring (ABPM) and 24 hour urine collection. Albuminuira was grade as follows: Nornoalbuminuria, Urine albumin creatinine ratio (UACR) <30 mg/g; Microalbuminuria, 30 mg/g ≤ UACR <300 mg/g; Overt albuminuira; UACR ≥300 mg/g.

Results: The mean ages for normal-weight and obese patients were 60.5 and 58.7 years, respectively. The prevalence of microalbuminuria and overt albuminuria in obese patients were 7.8% and 3.6%. The mean 24 hour blood pressure (BP) of normal weight and obese patients were 122.2/73.4 mm Hg and 125.6/76.1 mm Hg, respectively. After adjustment for age, gender and creatinine clearance, and 24 hour systolic BP in obese patients, odd ratio of sodium to potassium ratio for overt albuminuria was 1.67 (95% CI: 1.05–2.67, p = 0.03) for overt albuminuria. However, in normal-weight group, sodium to potassium ratio was not associated with albuminuria. Only 24 hour systolic blood pressure showed a significant association with albuminuria.

Conclusion: In conclusion, high sodium intake was associated with overt albuminuria in obese patients.