

Original Paper

# Potential Blood Pressure Goals in IgA Nephropathy: Prevalence, Awareness, and Treatment Rates in Chronic Kidney Disease Among Patients with Hypertension in China (PATRIOTIC) Study

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## Key Words

Blood pressure goal • decreased renal function • hypertension • IgA nephropathy

## Abstract

**Background/Aims:** IgA nephropathy is the most prevalent form of primary glomerulonephritis worldwide. Among patients with kidney disease, hypertension is one of the most important risk factors of disease progression. Considering the limited evidence regarding the appropriate blood pressure (BP) goal for patients with IgA nephropathy, our aim was to critically appraise the potential BP goal in IgA nephropathy. **Methods:** We performed a retrospective analysis of the BP data from 1055 patients with IgA nephropathy, extracted from the database of a nationwide, multi-center, cross-sectional study, including 61 tertiary hospitals in China. Hypertension was defined by a BP  $\geq$  140/90 mmHg. Three BP cutoff levels were evaluated as control values: <140/90 mmHg, <130/80 mmHg and <125/75 mmHg. The primary outcome of our study was the prevalence of BP control among patients with a 24-h proteinuria <1 g/d or  $\geq$  1 g/d. Multivariate logistic regression analysis was used to identify demographic and clinical factors associated with a decrease in renal function for the different target levels of BP. **Results:** The overall prevalence of hypertension was 63.3%. BP was controlled under 140/90 mmHg in 49.1% of patients, with 34.3% of patients with proteinuria <1 g/d reaching the target BP <130/80 mmHg and only 12.9% of patients with proteinuria >1 g/d achieving a BP <125/75 mmHg. Among patients with proteinuria <1 g/d, the adjusted odds ratios (OR) and 95% confidence interval (95% CI) of a decrease in renal function, for the 3 target BP levels, were as follows ( $P > 0.05$ ): <140/90 mmHg, 0.9 (0.5 - 1.6); <130/80 mmHg, 1.0 (0.5 - 1.8); and

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<125/75 mmHg, 1.0 (0.5 - 2.0). With proteinuria  $\geq 1$  g/d, the adjusted ORs (95%CI) of attaining the BP targets of <140/90 mmHg, <130/80 mmHg and <125/75 mmHg were 0.4 (0.2 - 0.6), 0.2 (0.1 - 0.4) and 0.3 (0.1 - 0.5), respectively ( $P < 0.05$ ). **Conclusion:** Hypertension was common in IgA nephropathy and hypertensive control was suboptimal. Our result supports a benefit of intensive control of BP <130/80 mmHg for patients with proteinuria  $\geq 1$  g/d. However, in patients with proteinuria <1 g/d, a renoprotective effect of this BP goal was not identified.

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## Introduction

IgA nephropathy is the most prevalent form of primary glomerulonephritis worldwide [1, 2]. Given its ethnic and regional diversity, the prevalence of IgA nephropathy among causes of glomerular disease vary widely between countries, with a prevalence rate of 11.8% in the United States, 22.1% in Europe, 39.5% in Asia (data from Japan and Thailand), and 6.1% in Latin America [3]. In China, IgA nephropathy accounts for 40.5%-45% of all glomerular diseases [4, 5]. Most patients with IgA nephropathy exhibit a clinical course of slowly progressing deterioration in kidney function, leading to end-stage renal disease (ESRD) in 20%-40% of cases, within 20 years of the initial diagnosis [6]. Therefore, IgA nephropathy results in a significant disease burden and, as such, there is an important need to develop effective clinical management strategies for this disease.

A predominance of IgA deposits in the glomerular mesangium is the diagnostic hallmark of IgA nephropathy. It is widely accepted that IgA nephropathy is an autoimmune kidney disease, with critical interactions between an intrinsic antigen (galactose-deficient IgA1) and circulating anti-glycan antibodies underlying its pathophysiology [6]. However, the role of immunosuppression in IgA nephropathy treatments is controversial [7-10]. Certainly, the clinical management of IgA nephropathy aims to control blood pressure and maintain renal function [1, 6]. The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommended blood pressure (BP) goals of <130/80 mmHg for patients with a proteinuria (24-h urine protein excretion, UPE) level <1 g/d, and <125/75 mmHg for initial proteinuria >1 g/d [11]. Of note, however, the KDIGO recommendations are based on limited evidence. Therefore, given that hypertension is one of the most important factors of accelerated progression of IgA nephropathy and that hypertension is treatable, the necessity of improving BP control in the clinical management of IgA nephropathy is evident. Accordingly, our aim in this study was to critically appraise the potential BP goals for the clinical management of IgA nephropathy.

## Materials and Methods

### *Study Design and Population*

The study group was enrolled through the Prevalence, Awareness and Treatment Rates in Chronic Kidney Disease Patients with Hypertension in China (PATRIOTIC) study, which is a nationwide, multicenter, cross-sectional study designed to evaluate the epidemiology of hypertension among patients with chronic kidney disease (CKD) [12-14]. The PATRIOTIC study enrolled all patients,  $\geq 15$  years of age, who were hospitalized for CKD across 61 tertiary hospitals in the 31 provinces and municipalities of the autonomous regions of China (with the exception of Hong Kong, Macao and Taiwan), between November 2009 and March 2010. The study was approved by the Ethics Committee of the General Hospital of the Chinese People's Liberation Army and conformed to the Declaration of Helsinki. Patients under 18 years old and their guardians decided together whether they would participate in the study. Written informed consents were obtained from all patients, and from the guardians of patients under 18 years of age.

#### Data collection and blood pressure measurements

Only patients with a primary diagnosis of IgA nephropathy were included in our analysis. The details for data collection and BP measurement have previously been described [12-14], with key aspects summarized as follows. Trained physicians obtained BP measurements, using a mercury-filled sphygmomanometer. Two measurements were obtained, with a third measurement obtained in cases where the difference between two measurements was >5 mmHg [15]. The mean of the BP measurements was used in the analysis.

#### Definitions

Hypertension was defined by a systolic BP (SBP)  $\geq 140$  mmHg and / or a diastolic BP (DBP)  $\geq 90$  mmHg. To evaluate BP control, we used the following 3 thresholds, as per the recommendations in different guidelines: <140/90 mmHg, <130/80 mmHg and <125/75 mmHg [11, 16, 17].

To evaluate renal function, participants were stratified into 5 stages of CKD according to their estimated glomerular filtration rates (eGFRs), as per criteria of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines [18]. The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation for Asian populations [19]. eGFR < 60 ml/min/1.72m<sup>2</sup> was defined as reduced renal function.

The body mass index (BMI) was calculated by dividing weight (kg) by height (m<sup>2</sup>). For analysis, participants were categorized into 3 BMI groups, as per the recommendations of the cooperative meta-analysis conducted by the Working Group on Obesity in China (WGO) [20]: <23.9 kg/m<sup>2</sup>, 24–27.9 kg/m<sup>2</sup> (overweight), and  $\geq 28$  kg/m<sup>2</sup> (obese).

Cardiovascular disease (CVD) included the following (with the International Classification of Diseases, 10<sup>th</sup> Revision (ICD-10) codes): coronary artery disease (I20-25); congestive heart failure (I50); arteriosclerosis (I70); left ventricular hypertrophy, diagnosed by echocardiography; and stroke (I60-69) [21-23].

#### Statistical analyses

Continuous data were described using the mean  $\pm$  standard deviation (SD), with categorical data presented as proportions. As appropriate for data distribution, between-group differences were evaluated using *t*-tests or nonparametric tests for continuous variables and the chi-squared or Fisher's exact test for categorical variables. A logistic regression analysis was used to identify the demographic and clinical characteristics associated with hypertension and decreased renal function among patients with IgA nephropathy. Multivariate odds ratio (ORs), and their corresponding 95% confidence interval (95% CI), were calculated for significant variables identified on univariate analyses, adjusted for covariates. For all analyses, a two-tailed *P* value < 0.05 was considered significant. All analyses were performed using statistical package SPSS (version 23.0, Armonk, NY, IBM Corporation).

## Results

Of the 10786 participants enrolled in the PATRIOTIC participants, 1055 had a primary diagnosis of IgA nephropathy, with available BP and eGFR data for analysis. Hypertension was identified in 63.3% of these cases, with the characteristics of these patients summarized in Table 1. Of note, patients with hypertension were significantly older than those without hypertension:  $38.3 \pm 12.3$  years *versus*  $32.3 \pm 10.7$  years, respectively ( $P < 0.001$ ). IgA nephropathy was identified in a greater proportion of men (55.2%) than women (44.8%).

Older, male, patients with higher BMIs, elevated 24-h UPE, lower eGFRs and CVD had a higher prevalence of hypertension ( $P < 0.05$ ). After multivariate adjustment, the risk for decreasing renal function among patients with IgA nephropathy increased with age (every 1-year increase), a BMI  $\geq 24$  kg/m<sup>2</sup> (overweight), a 24-h UPE  $\geq 1$  g, hypertension, and CVD (all  $P < 0.05$ ; Table 2).

Based on current guidelines for BP control among patients with IgA nephropathy [11, 16, 17], we assessed differences in the proteinuria levels for the 3 BP control targets (Table 3). BP was maintained under 140/90 mmHg in 49.1% of patients with IgA nephropathy and hypertension, under 130/80 mmHg in 25.7% and under 125/75 mmHg in 17.0%. BP was controlled at a significantly lower level among patients with a 24-h UPE  $\geq 1$  g/d than among patients with a 24-h UPE  $< 1$  g/d ( $P < 0.05$ ).

We also evaluated BP control, as a function of proteinuria, relative to the KDIGO guidelines, namely a target BP  $< 130/80$  mmHg for patients with IgA nephropathy and proteinuria  $< 1$  g/d and  $< 125/75$  mmHg for patients with proteinuria  $> 1$  g/d [11]. In our study group, 34.3% of patients with proteinuria  $< 1$  g/d achieving the BP goal of  $< 130/80$  mmHg, with only 12.9% of patients with proteinuria  $> 1$  g/d achieving the BP goal of  $< 125/75$  mmHg.

The OR of a decrease in renal function (eGFR  $< 60$  mL/min/1.73 m<sup>2</sup>) was determined for the 3 different BP targets (Table 4). Among patients with IgA nephropathy and proteinuria  $< 1$  g/d, the ORs (95% CI) of decreased renal function were non-significant ( $P > 0.05$ ):  $< 140/90$  mmHg, 0.9 (0.5 - 1.6);  $< 130/80$  mmHg, 1.0 (0.5 - 1.8); and  $< 125/75$  mmHg, 1.0 (0.5 - 2.0). In contrast, among patients with IgA nephropathy and proteinuria  $\geq 1$  g/d, the ORs (95% CI) were significant ( $P < 0.05$ ):  $< 140/90$  mmHg, 0.4 (0.2 - 0.6);  $< 130/80$  mmHg, 0.2 (0.1 - 0.4); and  $< 125/75$  mmHg, 0.3 (0.1 - 0.5). To

further elucidate the relationship between BP and a decrease in renal function, we analyzed the relationships between the different BP ranges and decreased renal function, controlling for age (1-year increment increase), sex, BMI classification, and CVD (Table 5). For patients with proteinuria  $< 1$  g/d, the OR (95% CI) of decreasing renal function was non-significant for SBP values  $< 130$  mmHg and increased for SBP values  $> 140$  mmHg. Specifically, the adjusted

**Table 1.** Characteristics of patients with IgA nephropathy. Note: Values for categorical variables are given as percentages and values for continuous variables as the mean  $\pm$  standard deviation. Because of missing data, the numbers of patients were not equal in some characteristics (including insurance, education, BMI, and 24-h UPE). 24-h UPE, 24-hour urinary protein excretion; BP, blood pressure; BMI, body mass index; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HBP, high blood pressure/hypertension

Characteristic	Total	HBP	non-HBP	P
Total, %	1055 (100.0)	668 (63.3)	387 (36.7)	
Age, years	36.1 $\pm$ 12.1	38.3 $\pm$ 12.3	32.3 $\pm$ 10.7	<0.001
Sex, %				<0.001
Men	582 (55.2)	400 (59.9)	182 (47.0)	
Women	473 (44.8)	268 (40.1)	205 (53.0)	
Ethnic group, %				0.016
Han	1004 (95.4)	645 (96.8)	359 (93.0)	
Other	48 (4.6)	21 (3.2)	27 (7.0)	
Insurance, %				0.537
Yes	728 (71.9)	459 (71.9)	269 (71.7)	
No	285 (28.1)	179 (28.1)	106 (28.3)	
Education, %				0.146
< High school	121 (11.7)	84 (12.7)	37 (9.8)	
High school	509 (49.1)	328 (49.8)	181 (48.0)	
College or more	406 (39.2)	247 (37.5)	159 (42.2)	
BMI, kg/m <sup>2</sup>	23.6 $\pm$ 4.0	24.0 $\pm$ 4.1	22.8 $\pm$ 3.6	<0.001
BMI, kg/m <sup>2</sup> , %				<0.001
< 24	586 (58.4)	338 (53.3)	248 (67.2)	
24-27.9	309 (30.8)	214 (33.8)	95 (25.7)	
$\geq 28$	108 (10.8)	82 (12.9)	26 (7.0)	
eGFR, mL/min/1.73 m <sup>2</sup>	82.1 $\pm$ 40.4	70.5 $\pm$ 40.5	102.1 $\pm$ 31.4	<0.001
eGFR $< 60$ mL/min/1.73 m <sup>2</sup>	313 (29.7)	270 (40.4)	43 (11.1)	<0.001
CKD stages, %				
Stage 1	518 (49.1)	244 (36.5)	274 (70.8)	
Stage 2	224 (21.2)	154 (23.1)	70 (18.1)	
Stage 3				
3a	89 (8.4)	67 (10.0)	22 (5.7)	
3b	74 (7.0)	65 (9.7)	9 (2.3)	
Stage 4	56 (5.3)	51 (7.6)	5 (1.3)	
Stage 5	94 (8.9)	87 (13.0)	7 (1.8)	
24-h UPE, g	2.0 $\pm$ 2.5	2.1 $\pm$ 2.4	1.8 $\pm$ 2.6	0.005
24-h UPE, g, %				0.065
< 1	442 (46.5)	265 (44.2)	177 (50.4)	
$\geq 1$	508 (53.5)	334 (55.8)	174 (49.6)	
CVD, %	44 (4.2)	42 (6.3)	2 (0.5)	<0.001

**Table 2.** Factors associated with decreased renal function in patients with IgA nephropathy. 24-h UPE, 24-hour urinary protein excretion; BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; OR, odds ratio

Factors	eGFR $< 60$ mL/min/1.73 m <sup>2</sup>			
	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
Age, years	1.0 (1.0 - 1.0)	<0.001	1.0 (1.0 - 1.0)	<0.001
Women	0.8 (0.6 - 1.1)	0.125	0.9 (0.7 - 1.3)	0.672
BMI, kg/m <sup>2</sup>				
< 24	1.0		1.0	
24-27.9	0.8 (0.6 - 1.1)	0.247	0.5 (0.3 - 0.8)	0.001
$\geq 28$	0.6 (0.4 - 1.0)	0.046	0.4 (0.2 - 0.7)	0.001
24-h UPE $\geq 1$ g	3.1 (2.2 - 4.2)	<0.001	3.4 (2.4 - 4.8)	<0.001
Hypertension	5.4 (3.8 - 7.7)	<0.001	5.1 (3.3 - 7.7)	<0.001
CVD	6.9 (3.5 - 13.6)	<0.001	3.1 (1.3 - 7.1)	0.009

ORs and *P*-values were similar for SBP ranges <130 mmHg, as follows: SBP 90-109 mmHg, OR 1.5 (0.5 - 4.6), *P* =0.490; SBP 110-119 mmHg, OR 1.5 (0.6 - 4.0), *P* =0.411; and 120-129 mmHg, OR 1.7 (0.7 - 4.4), *P* =0.263. In contrast, for SBP >140 mmHg, the OR increased, approaching significance, as follows: SBP 140-149 mmHg, OR 2.8 (0.9 - 8.7), *P* =0.072; and SBP ≥150 mmHg, OR 3.1 (1.0 - 10.2), *P* =0.058. Therefore, the risk of decreasing renal function was markedly different for SBP value <130 mmHg and >140 mmHg. For patients with proteinuria ≥1 g/d, the risk of a decrease in renal function increased significantly for SBP values >130 mmHg and DBP >80 mmHg (*P* < 0.05).

## Discussion

In our large data set, obtained from 61 tertiary care centers across China, we identified a high prevalence of hypertension among patients with IgA nephropathy, with hypertensive management being suboptimal, overall, in this clinical population. For patients with a 24-h UPE ≥1 g/d, achieving a BP goal of <130/80 mmHg is appropriate to lower the risk of progressive decline in renal function. However, for patients with an initial proteinuria <1 g/d, intensive hypertensive control to achieve the target levels did not provide a statistical renoprotective effect.

In the largest cohort study of patients with IgA nephropathy worldwide, Diciolla et al. reported a prevalence rate of hypertension of 41.83% [24]. In their case series of 1, 134 patients in the Norwegian Kidney Biopsy Registry, Knoop et al. reported a

**Table 3.** The BP control rate in patients with IgA nephropathy using different BP targets. 24-h UPE, 24-hour urinary protein excretion; BP, blood pressure

BP target, mmHg	Total, %	24-h UPE, g		P
		<1	≥1	
< 140/90	294 (49.1)	159 (60.0)	135 (40.4)	<0.001
< 130/80	154 (25.7)	91 (34.3)	63 (18.9)	<0.001
< 125/75	102 (17.0)	59 (22.3)	43 (12.9)	0.002

**Table 4.** Relationships between different BP targets and decreased renal function in patients with IgA nephropathy. Abbreviations: 24-h UPE: 24-hour urinary protein excretion; BMI: body mass index; CI: confidence interval; CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate; OR: odds ratio. <sup>a</sup> adjusted by age (every year), sex, BMI classification, CVD

BP targets	eGFR < 60 mL/min/1.73 m <sup>2</sup>	
	Adjusted OR (95% CI) <sup>a</sup>	P
24-h UPE < 1 g		
< 140/90 mmHg	0.9 (0.5 - 1.6)	0.640
< 130/80 mmHg	1.0 (0.5 - 1.8)	0.957
< 125/75 mmHg	1.0 (0.5 - 2.0)	0.998
24-h UPE ≥ 1 g		
< 140/90 mmHg	0.4 (0.2 - 0.6)	<0.001
< 130/80 mmHg	0.2 (0.1 - 0.4)	<0.001
< 125/75 mmHg	0.3 (0.1 - 0.5)	0.001

**Table 5.** The association among BP range frequencies and decreased renal function in patients with IgA nephropathy. Note: Because of missing 24-h UPE data, and exclusion of cases with SBP < 90 mmHg or DBP < 60 mmHg, the numbers of patients were not equal to the total population. Values for categorical variables are given as percentages; decreased renal function was defined as eGFR < 60 mL/min/1.73 m<sup>2</sup>. Abbreviations: 24-h UPE: 24-hour urinary protein excretion; DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate; OR: odd ratio; SBP: systolic blood pressure. <sup>a</sup> adjusted by age (every year), sex, BMI classification, 24-h UPE (<1 g or ≥1 g) and CVD. <sup>b</sup> adjusted by age (every year), sex, BMI classification, and CVD

BP, mmHg	Total	24-h UPE < 1 g		24-h UPE ≥ 1 g			
		Adjusted OR (95% CI) <sup>a</sup>	P	Adjusted OR (95% CI) <sup>b</sup>	P		
SBP	90-109	0.7 (0.3 - 1.4)	0.254	1.5 (0.5 - 4.6)	0.490	0.4 (0.1 - 1.4)	0.166
	110-119	1.1 (0.7 - 1.9)	0.720	1.5 (0.6 - 4.0)	0.411	1.3 (0.7 - 2.8)	0.418
	120-129	1.0		1.7 (0.7 - 4.4)	0.263	1.0	
	130-139	1.6 (1.0 - 2.6)	0.073	1.0		2.9 (1.5 - 5.7)	0.001
	140-149	3.6 (2.1 - 6.1)	< 0.001	2.8 (0.9 - 8.7)	0.072	6.1 (3.0 - 12.4)	<0.001
	≥ 150	5.7 (3.4 - 9.7)	<0.001	3.1 (1.0 - 10.2)	0.058	11.3 (5.6 - 22.7)	<0.001
DBP	60-69	0.7 (0.3 - 1.4)	0.271	0.9 (0.3 - 2.3)	0.762	0.4 (0.1 - 1.4)	0.166
	70-79	1.0		0.8 (0.4 - 1.5)	0.460	1.0	
	80-89	1.7 (1.1 - 2.6)	0.012	1.0		2.0 (1.2 - 3.3)	0.011
	90-99	2.7 (1.7 - 4.3)	< 0.001	2.1 (0.9 - 4.7)	0.077	2.7 (1.4 - 4.8)	0.002
	≥ 100	4.1 (2.4 - 7.1)	< 0.001	1.2 (0.4 - 3.8)	0.698	6.1 (3.1 - 12.1)	<0.001

prevalence rate of hypertension of 36% among patients with IgA nephropathy [25]. Other studies regarding the prevalence rate of hypertension associated with IgA nephropathy reported similar values, as follows: 56% in a single-center study in the Czech Republic [26]; 58% among a study cohort of 478 Indian patients [27]; and 31% among 1155 Chinese patients [28]. The Therapeutic Evaluation of Steroids in IgA Nephropathy Global (TESTING) study [8] reported a prevalence rate of 46.9%. Our prevalence rate of 63.3% was higher than all previous studies. This may reflect differences with regard to inclusion criteria across different studies. For example, Knoop et al. and Le et al. used the BP obtained at the time of IgA nephropathy diagnosis, resulting in a relatively lower prevalence rate of hypertension as the measures were obtained early in the course of the disease [25, 28]. In contrast, we obtained our BP measures during a period of hospitalization due to deteriorating course of IgA nephropathy, which might account for the higher prevalence of hypertension.

Our multivariate analysis identified age (every 1-year increase), sex (male), BMI classification (over-weight and obese), and CVD as predictive factors of hypertension and IgA nephropathy progression. In their study of 2, 283 patients with biopsy-proven IgA nephropathy, Goto et al. identified male sex, advanced age, earlier renal biopsy, higher SBP and DBP, more severe proteinuria, lower serum total protein and albumin, lower eGFR, and higher histological grade as being significantly associated with the risk of disease progression to ESRD [29]. Le et al. identified an eGFR <60 mL/min/1.73 m<sup>2</sup>, proteinuria >1 g/day, hypertension at presentation, and hyperuricemia as independent predictors of renal outcome among patients with IgA nephropathy [28]. Both Berthoux et al. and Shimamoto et al. reported an elevated BMI as a risk factor for IgA nephropathy progression [30, 31].

As far as we know, our study is the first to have reported on the rate of hypertension control among patients with IgA nephropathy using evidence-informed BP goals. In our study group, control of BP under the target goal of 140/90 mmHg was achieved in 49.1% of patients, with 25.7% meeting the BP target of 130/80 mmHg. When we considered the BP target recommendations in the KDIGO Clinical Practice Guideline for Glomerulonephritis [11], the target goal of <130/80 mmHg was achieved in 34.3% of patients with a proteinuria <1 g/d, but with only 12.9% of patients with a proteinuria >1 g/d achieving the recommended BP target <125/75 mmHg. It is important to note that the KDIGO guideline were “Not Graded” and, therefore, lack substantial supporting evidence.

In the absence of randomized clinical trials assessing BP goals for patients with IgA nephropathy, we selected to assess the relationship between different BP targets and a decrease in renal function. For patients with proteinuria ≥1 g/d, maintaining a BP target <130/80 mmHg was associated with the lowest risk of IgA nephropathy progression. However, a strict control of BP did not confer a renoprotective effect among patients with proteinuria <1 g/d. In a sub-analysis, we confirmed our findings using a reversed analysis strategy, that is to detect the relationship between different the BP ranges and a decrease renal function. As expected, a SBP ≥130 mmHg and DBP ≥80 mmHg were significantly associated with an increased risk of decreased renal function among patients with proteinuria ≥1 g/d. When considering the SBP specifically, we noted the SBP range of 130-139 mmHg as being critical among patients with proteinuria <1 g/d, with a marked increase in the risk of deteriorating renal function when the SBP exceeded 140 mmHg, with the OR approaching significance for BP levels >150 mmHg. Based on these results, we propose that there might be a clinical benefit in controlling BP <140/90 mmHg for patients with IgA nephropathy and proteinuria <1 g/d. There might be some other clinical characteristics that could influence the renal outcome but were not analyzed in our multi-variable logistic regression analysis limited by the observational design of our study.

The limitations of ours study need to be considered in the interpretation of findings for practice. Foremost is the observation design of our study, which allowed us to evaluate the association between variables but not causality. In addition, we did not evaluate the association between the pathological classification of IgA nephropathy and BP goals. It is well known that histological features are independent predictors of the progression of IgA nephropathy

[32, 33]. We also did not evaluate the effects of different types of antihypertensive drugs such as angiotensin converting enzyme inhibitors, ACEI, and angiotensin receptor blockers, ARB on BP control and renal function, due to the high variation in management of hypertension in patients with IgA nephropathy and the lack of alignment with recommended standards [14].

Despite these limitations, we provide a critically appraised overview of the prevalence of hypertension associated with IgA nephropathy and of the effects of controlling BP to different target levels on the progression in renal disease in a large study group. As such, we believe that our results will add knowledge to our understanding and clinical management of hypertension among patients with IgA nephropathy, as well as provide baseline evidence and direction for future studies.

## Conclusion

IgA nephropathy is associated with a high prevalence of hypertension, for which current antihypertensive strategies provide suboptimal results. Based on our findings, we suggest that a target BP <140/90 mmHg would be desirable for patients with proteinuria <1 g/d, with a target BP <130/80 mmHg for those with proteinuria ≥1 g/d. In the future, adequately powered and randomized clinical trials, with sufficient follow-up, are needed to confirm whether the BP targets we identified will be appropriate for delaying the progression of IgA nephropathy.

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