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Simple renal cyst as an independent risk factor for hypertension

Yaqing Zhou MD, PhD[1] | Limei Jia MM[2] | Baojin Lu MM[2] | Long Bai MM[1] |
Wei Cui MD, PhD[1]

[1]Department of Cardiology, The Second
Hospital of Hebei Medical University and
Institute of Cardiocerebrovascular Disease of
Hebei Province, Shijiazhuang, China

[2]Department of Physical Examination Center,
The Second Hospital of Hebei Medical
University, Shijiazhuang, China

Correspondence
Wei Cui, The Second Hospital of Hebei Medical
University and Institute of
Cardiocerebrovascular Disease of Hebei
Province, No. 215, He Ping West Road
Shijiazhuang 050000, China.
Email: cuiwei21c@163.com

Abstract

A simple renal cyst (SRC) may increase the risk for hypertension. The authors examined the relationship between a SRC and hypertension in participants receiving physical examinations at Hebei Medical University. This study enrolled 66 883 participants who received physical examinations at our center from January 2012 to December 2017. Demographic data, medical history related to hypertension, hematological indexes, hypertension, and SRC subtype based on ultrasound examinations were examined. The relationship between SRC and hypertension was analyzed using univariate and multivariate logistic regression analysis in different models. Subgroup analysis and propensity score (PS) matching were also performed. Based on SRC subtype (unitary vs. multiple, small vs. large, unilateral vs. bilateral), a comprehensive scoring system was established to determine the effect of SRC load on hypertension. The results of univariate and multivariate analysis indicated that SRC was a risk factor for hypertension ($P < .01$). Subgroup and interaction analysis showed the homogeneity that SRC was an independent risk factor for hypertension in multiple subgroups ($P > .05$). A SRC remained an independent risk factor for hypertension after PS matching ($P < .01$). Based on a scoring system that considered different SRC subtypes, the risk for hypertension increased with renal cyst load ($P < .01$). In conclusions, a SRC was an independent risk factor for hypertension, and there was a positive correlation between SRC load and hypertension. The risk of hypertension increased gradually with the size, number, and location of a SRC. Careful follow-up or excision should be considered for patients with SRCs.

KEYWORDS
hypertension, propensity score matching, risk factor, scoring system, simple renal cyst, subgroup analysis

1 | INTRODUCTION

Hypertension is a significant risk factor for cardiovascular and cerebrovascular disease, and a serious public health issue worldwide. Despite the high prevalence of hypertension, there is insufficient awareness, treatment, and control of this condition in China.[1-4] To improve the prognosis of patients with hypertension, it is imperative to identify causes that may be reversible so that normal blood pressure can be restored. Numerous studies showed that the presence of a simple renal cyst (SRC) was associated with hypertension.[5-10] Many cases reports found that patients with hypertension complicated with SRCs experienced decreased or normalization of blood pressure after use of different interventions to eliminate these cysts.[11,12]

A SRC, defined as a cystic mass in or on the surface of the kidney, is the most common type of renal cyst, and is considered a nonhereditary congenital condition. However, the pathogenesis of the SRC has not been fully elucidated. It is generally believed that a SRC originates from a structural variation of a renal tubular diverticulum. A SRC can also be caused by trauma or infection. These cysts are ellipsoid or spheroid in shape, vary in size, may contain clear fluid, occur alone or with other cysts, and occur in one or both kidneys. Ultrasound is the preferred method used to diagnose a SRC. In ultrasound, a typical SRC appears as a nonechoic cystic mass with a clear and smooth boundary that has spherical or ellipsoid morphology. Most SRCs are considered benign and do not require special treatment, and this may have led to neglect of this condition. Studies have increasingly reported a relationship between a SRC and hypertension. However, whether a SRC is an independent predictor of hypertension and the underlying mechanism of this connection is not clear.

Most studies that examined the relationship between SRC and hypertension were case reports, cross-sectional studies, and small-sample studies, so evidence supporting a causal connection is uncertain. Thus, many studies reported that a SRC was positively correlated with hypertension,[5-10] but other studies reported no such relationship.[13] Moreover, some studies concluded that the number, size, and location of a SRC was related to hypertension,[5,8,14] but other research reported contrary results.[7] These many uncertainties pose a dilemma for clinicians who encounter patients with hypertension and SRCs.

It is necessary to clarify the relationship between the number, size, and location of SRCs with hypertension. We therefore examined a large sample of patients to study the relationship between SRC and hypertension, with strict control of confounding factors. Moreover, we assessed this relationship from different perspectives and also examined the influence of the number, size, and location of a SRC on hypertension.

2 | MATERIALS AND METHODS

2.1 | Study population

This retrospective study examined 67 744 consecutive individuals who received routine physical examinations with renal ultrasound at the Physical Examination Center of the Second Hospital of Hebei Medical University from January 2012 to December 2017. The inclusion criterion was receipt of a renal ultrasound examination during a routine physical examination. The exclusion criteria were polycystic kidney disease, complex renal cysts, suspected malignant renal tumors, congenital kidney disease, solitary kidney, renal dysplasia, nephrectomy, organ transplantation, recent use of an oral medication known to affect kidney function, or other severe organ disease.

After the exclusion of 861 individuals, 66 883 individuals were enrolled. This study was approved by the Ethics Committee of the Second Hospital of Hebei Medical University.

2.2 | Methods

2.2.1 | General data collection

The medical staff of the examination center was responsible for collecting all data. These data included general demographic and clinical information (name, sex, age, height, weight, heart rate, and systolic and diastolic blood pressure [SBP and DBP]), medical history associated with hypertension (hyperlipidemia, diabetes, cardiovascular disease, cerebrovascular disease, smoking, and drinking), supplementary examinations related to the kidneys (kidney cyst, kidney stone, adrenal change, renal calcification, renal hamartoma), and hematological indicators (blood routine, blood lipids, liver and kidney function).

2.2.2 | Measurement methods, diagnosis and treatment of hypertension

Blood pressure measurements were performed by professional nurses using an electronic sphygmomanometer (Omron HBP-9012; OMRON Healthcare Product Development Dalian Co., Ltd.). Before measurement, the patient was asked to refrain from smoking and drinking tea or coffee for 30 min and to remain quiet and at rest for 5 min. The blood pressure was then measured three times in a row, with an interval of 1–2 min between measurements. The average blood pressure of the second and third measurements was used as the final result.

Hypertension was defined as a SBP of 140 mm Hg or more, and/or a DBP of 90 mm Hg or more, or controlled blood pressure (< 140/90 mm Hg) due to use of an antihypertensive medication, according to the 2018 ESC/ESH guidelines.[15]

The treatment of hypertension was mainly by oral antihypertensive drugs. If the physical examination indicated a history of hypertension in patients receiving antihypertensive drugs, daily blood pressure monitoring was recommended. If blood pressure control was successful (BP < 140/90 mm Hg), the current drug treatment was maintained. If blood pressure control was unsuccessful (BP > 140/90 mm Hg), the Cardiology Outpatient Department was notified. Monitoring of blood pressure and referral to the cardiology clinic were also recommended if the blood pressure was elevated in any person without a history of hypertension.

2.2.3 | Measurement methods, diagnosis and treatment of SRC

For identification of a SRC, doctors used a PhilipsIU22 color ultrasound device and a C5-11-5MHZ probe for a bilateral kidney examination.

The SRC was defined as a cystic mass in or on the surface of the kidney. A SRC was usually diagnosed when a cystic mass of the kidney had the following ultrasonic characteristics: no echo, a clear boundary, good internal sound transmission, enhanced posterior echo, a wall that is slender and hyperechoic, an inner wall that is smooth, and a spherical or ellipsoid morphology.[16] The number, location, and size of each SRC were recorded. A large SRC was one with the largest diameter of 20 mm or more, a patient with 2 or more SRCs was considered to have multiple cysts, and a patient with 1 or more SRCs in each kidney was considered to have bilateral cysts.

Most SRCs were asymptomatic and did not require special treatment. Treatment was recommended only when a SRC was complicated with infection or when a very large SRC caused compression of the surrounding tissue. Surgery was the main treatment.

2.2.4 | Description and diagnosis of other indicators

Smoking was defined as current smoking or smoking cessation fewer than 2 weeks previously. Drinking was defined as current drinking or drinking cessation fewer than 2 weeks previously. Patients were divided into four groups based on body mass index (BMI): thin (< 18.50 kg/m^2), normal (18.50–24.00 kg/m^2), overweight (24.00–28.00 kg/m^2), and obese ($\geq$28.00 kg/m^2). Patient age was classified as young (18–45 years), early-middle-age (45–65 years), late-middle age (60–74 years), or elderly ($\geq$75 years). Heart rate (HR) was classified as normal (60–100 beats per minute [bpm]), bradycardia (< 60 bpm), or tachycardia (> 100 bpm). Serum creatinine (SCr) was measured and the estimated glomerular filtration rate (eGFR, ml/min/1.73 m^2) was calculated according to the CKD-EPI (Chronic Kidney Disease-Epidemiology Collaborative Group)[17]:

$$\text{Males}: \text{ for SCr} \leq 0.9, \text{ eGFR} = 141 \times (\text{SCr}/0.9)^{-0.411} \times (0.993)^{\text{age}}$$
$$\text{for SCr} > 0.9, \text{ eGFR} = 141 \times (\text{SCr}/0.9)^{-1.209} \times (0.993)^{\text{age}}$$

$$\text{Females}: \text{ for SCr} \leq 0.7, \text{ eGFR} = 144 \times (\text{SCr}/0.7)^{-0.329} \times (0.993)^{\text{age}}$$
$$\text{for SCr} > 0.7, \text{ eGFR} = 144 \times (\text{SCr}/0.7)^{-1.209} \times (0.993)^{\text{age}}$$

where SCr is in mg/dl and age is in years.

The eGFR was used to define CKD stage[18]: CKD1 (eGFR $\geq$ 90, normal function), CKD2 ($60 \leq$ eGFR < 90, mildly decreased function), CKD3 ($30 \leq$ eGFR < 60, moderately decreased function), CKD4 ($15 \leq$ eGFR < 30, severely decreased function), or CKD5 (eGFR < 15, renal failure). The relationship of SRC and hypertension was analyzed in two eGFR subgroups (< 90 and $\geq$90).

2.3 | Statistical analysis

General demographic data and clinical characteristics were presented as continuous measurement data, count data, or grade data, as appropriate. The measurement data were tested for normality; if the data had a normal distributions, they were expressed as means ± standard deviations (SDs), and they were otherwise expressed as medians (interquartile ranges [IQRs]). Count data and grade data were expressed as numbers and percentages (%). An independent samples t-test was used for comparisons of measurement data that had normal distributions, and a nonparametric test was used for comparisons of measurement data that had non-normal distributions. The nonparametric test was also applied to infer the difference of grade level of two or more populations. The χ^2 test and Fisher's exact probability method were used to compare count data.

A univariate logistic regression was first used to analyze the relationship of a SRC with hypertension in the total population. Then, multivariate logistic regression was performed using a minimally adjusted model (adjustment for sex and age group) and using a fully adjusted model (adjustment for sex, age group, BMI group, HR group, eGFR group, smoking, drinking, history of different diseases [diabetes, hyperlipidemia, cardiovascular disease, cerebrovascular disease], family history of hypertension, renal stone, adrenal change, renal calcification, renal hamartoma, renal hydronephrosis, and nephropathy).

Multiple imputation was used to account for missing data in the BMI groups, HR groups, and hypertension family history. The relationship between SRC and hypertension was determined before and after multiple imputations.

Subgroup analysis was used to assess the relationship between SRC and hypertension with stratification of different subgroups after adjustment for confounding. Moreover, the homogeneity between SRC and hypertension within a subgroup (such as males or females) was tested by interaction analysis. The Bonferroni procedure was used to reduce the type I error rate.

In addition, propensity score (PS) matching was used to reduce bias and balance the clinical baseline data balanced prior to comparisons. For this analysis, the SRC and non-SCR groups were matched by sex, age, BMI, eGFR, HR, smoking history, history of alcohol consumption, history of diabetes, hyperlipidemia, cardiovascular, cerebrovascular, renal stone, adrenal change, renal calcification, renal hamartoma, renal hydronephrosis, and nephropathy. The SRC and non-SRC groups were matched at a ratio of 1:2 and the caliper value was .05. Multiple logistic regression models were then used to verify the association between SRC and hypertension in the PS matched data.

After the relationship between SRC and hypertension was determined, a SRC load scoring system was established based on the results of multiple logistic regression to determine the overall effect of different renal subtypes with hypertension. Based on the odds ratios (ORs) for hypertension in the different subtypes of SRCs (small vs. large, unilateral vs. bilateral, unitary vs. multiple) a score of 1 (OR = 1–1.5) or 2 (OR = 1.5–2.5) was assigned, and the total scores were then added together to determine the final score (range: 0–6). Finally, multivariate

logistic regression was used to analyze the relationship between SRC load and hypertension.

All statistical analyses were performed using R statistical software (http://www.R-project.org, The R Foundation) and EmpowerStats (http://www.empowerstats.com, X&Y Solutions, Inc.,Boston, MA, USA).

3 | RESULTS

3.1 | Demographic and clinical characteristics of study patients

This study examined 67 744 consecutive individuals. A total of 861 individuals were excluded, 265 who were younger than 18 years old, 212 who had polycystic kidney disease or complex renal cysts, 57 who had malignant renal tumors, 30 who underwent nephrectomy, 18 who had congenital kidney malformations, and 279 due to other severe organ disease. The remaining 66 883 individuals were included. The average age was 46.36 ± 13.35 years-old and there were 34 179 males (51.10%; average age: 47.20 ± 13.33 years-old) and 32 704 females (48.90%; average age: 45.49 ± 13.30 years-old).

For analysis, we initially performed four pair-wise comparisons: SRC versus non SRC groups, unilateral versus bilateral SRC groups, small versus large SRC groups, and unitary versus multiple SRC groups (Table 1, Table S1). Comparison of the SRC and non-SRC groups showed that patients in the SRC group were predominantly male, older, and overweight. Moreover, SBP, DBP, and the prevalence of hypertension were significantly higher in the SRC group. The SRC group had higher prevalence of smoking, drinking, diabetes, cerebrovascular disease, hyperlipidemia, cardiovascular disease, renal stone, renal calcification, hydronephrosis, and nephropathy (all $P < .01$). However, the SRC group had a lower prevalence of family history of hypertension, a lower eGFR, and a lower HR than the non in the non-SRC group (all $P < .01$). (Table 1) The results also showed that SBP, DBP, and the prevalence of hypertension were significantly greater in the bilateral SRC group, the large SRC group, and the multiple SRC group, but the prevalence of family history of hypertension was lower in the bilateral SRC group (Table S1).

3.2 | Univariate analysis of the relationship between SRC and hypertension

Univariate logistic regression analysis showed that a SRC, as well as many other factors, was a significant risk factor for hypertension (Table S2). In particular, the OR for hypertension in a patient with a SRC was 2.60 (95% CI: 2.46, 2.76; $P < .01$).

3.3 | Multivariate analysis of the relationship between SRC and hypertension

We then performed multivariable logistic regression analysis using a minimally adjusted model (Model I) and a fully adjusted model (Model II) to further examine the relationship between SRC and hypertension (Table 2). In both models, SRC remained a significant risk factor for hypertension (Model I: OR = 1.31, 95% CI: 1.23, 1.40, $P < .01$; Model II: OR = 1.28, 95% CI: 1.19, 1.36, $P < .01$). Moreover, bilateral renal cysts, large cysts, and multiple cysts also increased the risk for hypertension in the unadjusted and adjusted models (all $P < .05$).

Multiple imputations were further used to account for missing data in the study. The positive relationship between SRC and hypertension was found after multiple imputations (OR = 1.32, 95% CI: 1.23, 1.42, $P < .01$) (Table S3).

3.4 | Subgroup analysis of the relationship between SRC and hypertension

We then analyzed the relationship between SRC and hypertension in different subgroups and examined the homogeneity between SRC and hypertension within these subgroups (Figure 1). The results showed that SRC was a significant risk factor for hypertension in most subgroups, and that none of the interactions were significant (all $P > .05$).

3.5 | Relationship of SRC and hypertension after propensity score matching

Because of the significant baseline differences between the SRC and non-SRC groups, we used PS matching to reduce this bias before comparing these groups (Table S4). The PS matching achieved a good balance of the SRC and non-SRC groups (all $P > .05$). Moreover, analysis of PS-matched data by multiple logistic regression analysis showed that SRC remained a significant risk factor for hypertension ($P < .01$, Table 3).

3.6 | Relationship of SRC load score with hypertension

We further examined the relationship of different subtypes of SRCs with hypertension (Table 4). In particular, we first identified patients with different SRC subtypes (absent vs. present, unilateral vs. bilateral, small vs. large, and unitary vs. multiple) and then assigned SRC load scores, in which a score of 0 was used for the reference group (no SRC), a score of 1 was used if the OR was between 1 and 1.5, and a score of 2 was used if the OR was between 1.5 and 2.5. The final SRC load score thus ranged from 0 (reference group) to 6 (bilateral, large, and multiple SRCs).

We then analyzed the relationship of SRC load score with hypertension using multivariate logistic analysis (Table 5). The results showed that the prevalence of hypertension increased significantly with SRC load score. Moreover, patients with SRC load score of 6 had a 1.64-fold increased OR for hypertension relative to the reference group (OR = 1.64, 95% CI: 1.38, 1.94, $P < .01$).
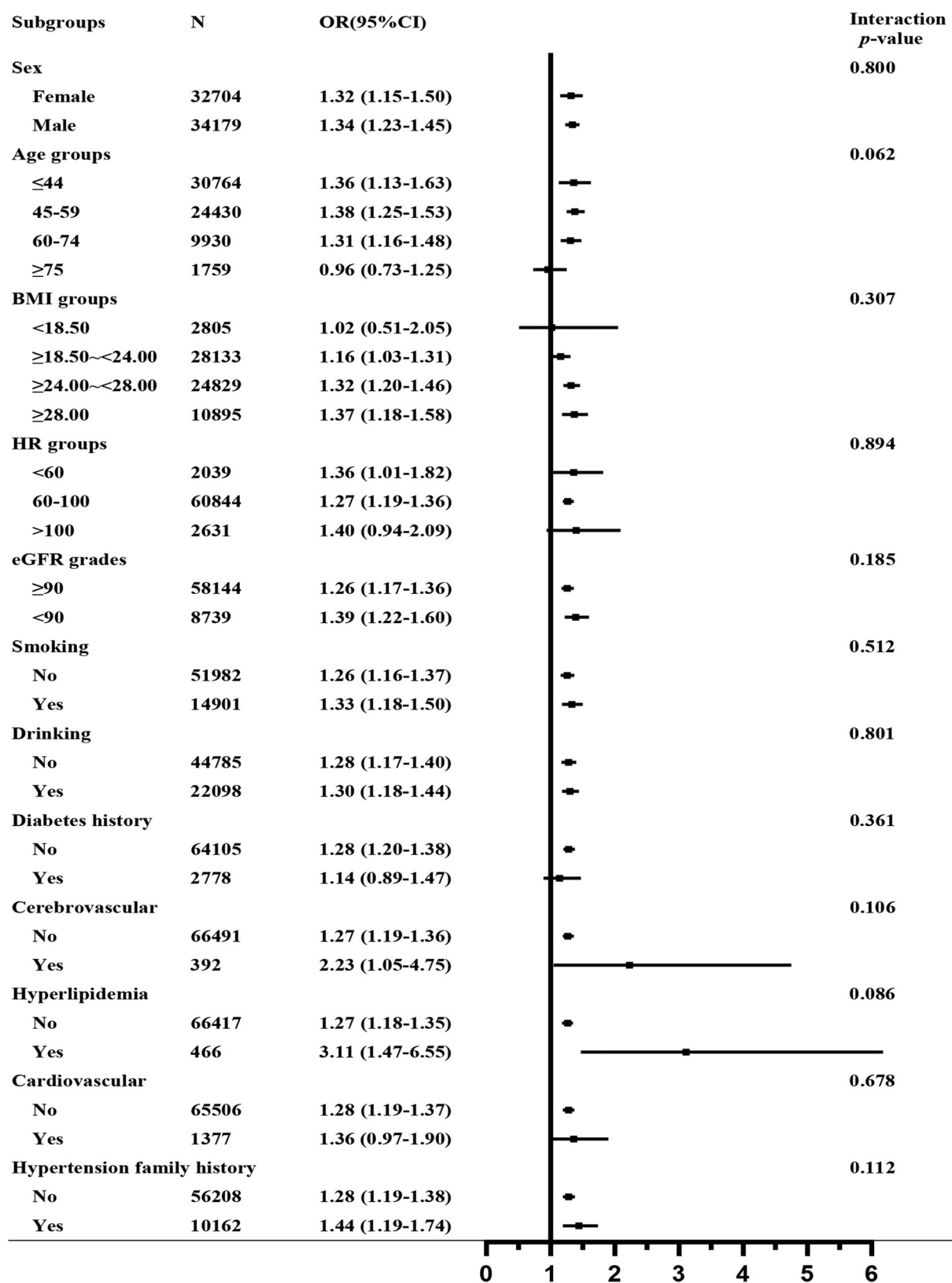
Subgroups	N	OR(95%CI)		Interaction p-value
Sex				0.800
Female	32704	1.32 (1.15-1.50)		
Male	34179	1.34 (1.23-1.45)		
Age groups				0.062
≤44	30764	1.36 (1.13-1.63)		
45-59	24430	1.38 (1.25-1.53)		
60-74	9930	1.31 (1.16-1.48)		
≥75	1759	0.96 (0.73-1.25)		
BMI groups				0.307
<18.50	2805	1.02 (0.51-2.05)		
≥18.50~<24.00	28133	1.16 (1.03-1.31)		
≥24.00~<28.00	24829	1.32 (1.20-1.46)		
≥28.00	10895	1.37 (1.18-1.58)		
HR groups				0.894
<60	2039	1.36 (1.01-1.82)		
60-100	60844	1.27 (1.19-1.36)		
>100	2631	1.40 (0.94-2.09)		
eGFR grades				0.185
≥90	58144	1.26 (1.17-1.36)		
<90	8739	1.39 (1.22-1.60)		
Smoking				0.512
No	51982	1.26 (1.16-1.37)		
Yes	14901	1.33 (1.18-1.50)		
Drinking				0.801
No	44785	1.28 (1.17-1.40)		
Yes	22098	1.30 (1.18-1.44)		
Diabetes history				0.361
No	64105	1.28 (1.20-1.38)		
Yes	2778	1.14 (0.89-1.47)		
Cerebrovascular				0.106
No	66491	1.27 (1.19-1.36)		
Yes	392	2.23 (1.05-4.75)		
Hyperlipidemia				0.086
No	66417	1.27 (1.18-1.35)		
Yes	466	3.11 (1.47-6.55)		
Cardiovascular				0.678
No	65506	1.28 (1.19-1.37)		
Yes	1377	1.36 (0.97-1.90)		
Hypertension family history				0.112
No	56208	1.28 (1.19-1.38)		
Yes	10162	1.44 (1.19-1.74)		

FIGURE 1 Relationship of simple renal cyst with hypertension in different subgroups and interaction *P* values after adjustment for confounding. Adjusted for sex, age group, BMI group, HR group, eGFR group, smoking, drinking, history of diabetes, hyperlipidemia, cardiovascular disease, cerebrovascular disease, hypertension family history, renal stone, adrenal change, renal calcification, renal hamartoma, renal hydronephrosis, and nephropathy (except for the subgroup variable)

TABLE 1 Pair-wise comparisons of the demographic and clinical characteristics of enrolled study patients

Parameter	Total (n = 66883)		
	Non-SRC	SRC	P
N	61576	5307	
SBP (mm Hg)	**126.24 ± 18.39**	**135.34 ± 20.52**	**<.01**
DBP (mm Hg)	**77.16 ± 12.41**	**81.59 ± 12.82**	**<.01**
Hypertension	**17671 (28.70%)**	**2716 (51.18%)**	**<.01**
Age (years)	45.54 ± 13.01	55.95 ± 13.45	<.01
BMI (kg/m²)	24.35 ± 3.70	25.35 ± 3.44	<.01
HR (bpm)	78.64 ± 11.52	76.58 ± 11.57	<.01
eGFR (ml/min/1.73m²)	104.14 ± 14.06	95.90 ± 16.59	<.01
Sex			<.01
Female	31150 (50.59%)	1554 (29.28%)	
Male	30426 (49.41%)	3753 (70.72%)	
Age group (years)			<.01
≤44	29756 (48.32%)	1008 (18.99%)	
45–59	22224 (36.09%)	2206 (41.57%)	
60–74	8351 (13.56%)	1579 (29.75%)	
≥75	1245 (2.02%)	514 (9.69%)	
BMI group (kg/m²)			<.01
< 18.50	2718 (4.43%)	87 (1.65%)	
≥18.50~ < 24.00	26382 (42.98%)	1751 (33.16%)	
≥24.00~ < 28.00	22502 (36.66%)	2327 (44.07%)	
≥28.00	9780 (15.93%)	1115 (21.12%)	
Medical history			
Smoking	13407 (21.77%)	1494 (28.15%)	<.01
Drinking	19932 (32.37%)	2166 (40.81%)	<.01
Diabetes history	2381 (3.87%)	397 (7.48%)	<.01
Cerebrovascular disease	320 (.52%)	72 (1.36%)	<.01
Hyperlipidemia	399 (.65%)	67 (1.26%)	<.01
Cardiovascular disease	1064 (1.73%)	313 (5.90%)	<.01
Hypertension family history	9545 (15.62%)	617 (11.73%)	<.01
Renal diseases			
Renal stone	1058 (1.72%)	213 (4.01%)	<.01
Adrenal change	145 (.24%)	3 (.06%)	.008
Renal calcification	359 (.58%)	124 (2.34%)	<.01
Renal hamartoma	383 (.62%)	37 (.70%)	.506
Renal hydronephrosis	220 (.36%)	47 (.89%)	<.01
Nephropathy	45 (.07%)	23 (.43%)	<.01

Abbreviations: BMI, body mass index; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated of glomerular filtration rate.
Values are presented as mean ± SD, median (IQR), or number (%).

4 | DISCUSSION

The study investigated the relationship between SRC and hypertension using a large population of individuals who received routine physical examinations. We controlled for confounding factors using univariate and multivariate stepwise models, and also examined the relationship between SRC and hypertension using subgroup analysis and propensity score matching. In addition, we used a comprehensive scoring

TABLE 2 Multivariate analysis of the relationship between simple renal cyst and hypertension

Variable	Crude model OR (95%CI)	P	Model I OR (95%CI)	P	Model II OR (95%CI)	P
Total (n = 66883)						
Renal cyst [a]						
No	Reference		Reference		Reference	
Yes	2.60 (2.46–2.76)	<.01	1.31 (1.23–1.40)	<.01	1.28 (1.19–1.36)	<.01
Renal cyst (n = 5307)						
Bilateral renal cyst [b]						
No	Reference		Reference		Reference	
Yes	1.83 (1.57–2.15)	<.01	1.39 (1.17–1.64)	.010	1.37 (1.15–1.64)	<.01
Large renal cyst [b]						
No	Reference		Reference		Reference	
Yes	1.42 (1.26–1.59)	<.01	1.19 (1.05–1.35)	.008	1.15 (1.01–1.32)	<.05
Multiple renal cyst [b]						
No	Reference		Reference		Reference	
Yes	1.89 (1.65–2.16)	<.01	1.44 (1.24–1.66)	<.01	1.39 (1.19–1.63)	<.01

[a] Total population.
[b] Population with SRC.
The crude model had no adjustments. Model I adjusted for sex and age group. Model II adjusted for sex, age group, BMI group, HR group, eGFR group, smoking, drinking, history of diabetes, hyperlipidemia, cardiovascular disease, cerebrovascular disease, hypertension family history, renal stone, adrenal change, renal calcification, renal hamartoma, renal hydronephrosis, and nephropathy.

TABLE 3 Multivariate analysis of the relationship between simple renal cyst and hypertension before and after propensity score matching

Variable	Crude model OR (95%CI)	P	Model I OR (95%CI)	P	Model II OR (95%CI)	P
Unmatched (n = 66883)						
Renal cyst [a]						
No	Reference		Reference		Reference	
Yes	2.60 (2.46– 2.76)	<.01	1.31 (1.23–1.40)	<.01	1.28 (1.19– 1.36)	<.01
Propensity-matched (n = 14226)						
Renal cyst [b]						
No	Reference		Reference		Reference	
Yes	1.18 (1.10–1.27)	<.01	1.20 (1.12–1.30)	<.01	1.22 (1.13–1.32)	<.01

[a] Unmatched population.
[b] Propensity score-matched population.
Model adjustments were as described in Table 2.

system that examined the effect of different SRC subtypes on hypertension. Our major finding was that a SRC was an independent risk factor for hypertension, and that there was a positive correlation between SRC load and hypertension. In other words, the risk of hypertension was greater in individuals who had larger cysts, more cysts, and bilateral cysts.

Our main finding was that a SRC was an independent risk factor for hypertension. Multiple logistic regression analysis showed that the risk of hypertension in the SRC group was 1.28 times higher than in non-SRC group. Although the OR values were different in univariate analysis, multivariate analysis, subgroup analysis, and propensity score matching, SRC remained associated with an increased the risk of hypertension. Our study results are consistent with the study of Hong and coworkers[8] They examined 29 666 people who received physical examinations at the Health Promotion Center of the Asan Medical Center (Seoul, South Korea) in 2006. Their results showed a significant association between a SRC and hypertension. This study was similar to our study, in that both examined individuals receiving routine physical examinations. However, our research examined more patients over a longer time. Moreover, Hong and coworkers only used

TABLE 4 Scoring system used to calculate the load of simple renal cyst

Variable	Crude model		Model I		Model II		Score (points)
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	
Renal cyst							
No	Reference		Reference		Reference		0
Yes	2.60 (2.46– 2.76)	<.01	1.31 (1.23–1.40)	<.01	1.28 (1.19– 1.36)	<.01	1
Location of renal cyst							
No-renal cyst	Reference		Reference		Reference		0
Unilateral	2.39 (2.25–2.54)	<.01	1.27 (1.19–1.36)	<.01	1.23 (1.15–1.32)	<.01	1
Bilateral	4.38 (3.78–5.08)	<.01	1.64 (1.39–1.93)	<.01	1.64 (1.38–1.94)	<.01	2
Size of renal cyst							
No-renal cyst	Reference		Reference		Reference		0
Small renal cyst	2.35 (2.20–2.52)	<.01	1.26 (1.17–1.36)	<.01	1.24 (1.14–1.34)	<.01	1
Large renal cyst	3.33 (3.01–3.69)	<.01	1.45 (1.29–1.62)	<.01	1.40 (1.24–1.58)	<.01	1
Number of renal cysts							
No-renal cyst	Reference		Reference		Reference		0
Unitary renal cyst	2.29 (2.15–2.44)	<.01	1.24 (1.16–1.33)	<.01	1.21 (1.12–1.30)	<.01	1
Multiple renal cyst	4.32 (3.82–4.89)	<.01	1.66 (1.45–1.91)	<.01	1.63 (1.41–1.89)	<.01	2

Model adjustments were as described in Table 2.

TABLE 5 Multivariable analysis of the relationship of the load score of simple renal cyst with hypertension

Variable	Crude Model		Model I		Model II		Hypertension prevalence
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	
Score							
0	Reference		Reference		Reference		28.70%
4	2.29 (2.15–2.44)	<.01	1.24 (1.16–1.33)	<.01	1.21 (1.12–1.30)	<.01	47.97%
5	4.18 (3.33–5.25)	<.01	1.72 (1.34–2.20)	<.01	1.62 (1.25–2.11)	<.01	62.73%
6	4.38 (3.78–5.08)	<.01	1.64 (1.39–1.93)	<.01	1.64 (1.38–1.94)	<.01	63.82%
P for trend	<.01		<.01		<.01		

Model adjustments were as described in Table 2.

multivariate logistic regression analysis, but we used multivariate logistic regression, subgroup analysis, and propensity score matching to confirm the relationship of SRC with hypertension. Our results thus provide stronger support for a relationship between SRC and hypertension. In contrast, Al-Said and coworkers found no increase in the prevalence of hypertension among patients with SRCs and suggested the reported association between hypertension and SRC might be coincidental.[13] However, the study of Al-Said was conducted nearly 20 years ago. More recent studies supported our finding of a correlation between a SRC and hypertension.[5–10,14,19–21] For example, Kim and coworkers[5] examined physical examination data over a period of 8 years and concluded there was a significant positive correlation between SRC and hypertension. Lee and coworkers[7] verified that a SRC can predict the occurrence of hypertension independent of common risk factors. A study in Taiwan by Lee and coworkers[6] found that a SRC also independently predicted the risk for pre-hypertension. Yuanyi and coworkers[20] concluded that a SRC was positively correlated with SBP and predicted the risk of systolic hypertension. Afsar and coworkers[10] found that SRC was related to an increased ambulatory blood pressure and "nondipper" nocturnal blood pressure in patients with essential hypertension. Some case reports have also documented the effect of cyst removal on reduction of hypertension. In particular, for patients who have SRCs with hypertension, their blood pressure decreased or normalized after removal of a SRC by surgical resection, puncture, and drainage.[11,12,22] The above studies suggested a relationship between a SRC and hypertension. Similarly, our study found that a SRC significantly increased the risk of hypertension. We suggest that patients with

a SRC and hypertension should be treated for the SRC when it is considered a cause of the elevated blood pressure. However, this conclusions needs further verification before adoption into clinical practice.

Another contribution of our study is that we established a SRC load scoring system to determine the overall effect of different SRC subtypes on hypertension. The results showed a positive correlation between SRC load and hypertension. Compared with the non-SRC group, even a small unitary SRC (score of 4) increased the risk of hypertension by 21%. The presence of multiple SRCs or of bilateral SRCs (score of 5) increased the risk by 62%. However, when more than two complicated subtypes (multiple cysts and bilateral cysts or large cysts; score of 6) were present, the risk only increased by 64%. Although our scoring system only had a control group (0 points) and 3 scores for patients with SRCs (4, 5, or 6 points), it still considered all subtypes, rather than a single subtype. Recent studies focused on the role of individual SRC subtypes in predicting hypertension. Some studies indicated that bilateral SRCs, large SRCs, and multiple SRCs each increased the risk for hypertension, similar to our study.[5,8,14] In agreement, Lee and coworkers[6] showed that multiple renal cysts and large cysts were positively correlated with hypertension, Afshar and coworkers[9,10] found that the total number of cysts was related to increased ambulatory blood pressure, and Yuanyi and coworkers[20] found that the risk of hypertension was significantly greater in individuals with bilateral rather than unilateral SRCs. Some case studies also reported that blood pressure levels decreased or normalized after spontaneous resolution of SRCs.[11,12,22] However, some studies reported discrepant results. For example, Lee and coworkers[7] found no association between hypertension and the number, location, and size of SRCs. This may be because they only studied healthy middle-aged men, who mostly had single small SRCs. The population deviations might obscure the effect of the number, size, and bilaterally of cysts in predicting hypertension.

The mechanism by which a SRC leads to hypertension is still unclear. The possible mechanisms include decrease of renal function, activation of the renin-angiotensin-aldosterone system (RAAS), cyst expansion, nephron loss, and decreased renal enzyme secretion. Several studies showed that a SRC is closely related to the deterioration of overall renal function.[23,24] Thus, patients with SRCs may experience decreased renal function, which leads to activation of the RAAS, renal vasoconstriction, increased reabsorption of sodium, retention of water and sodium, and then increased blood volume and blood pressure. Some findings suggested that activation of the RAAS is responsible for the occurrence and development of hypertension caused by SRCs.[25–27] The enlarged cysts may cause local ischemia via local tissue and/or renal artery compression, thereby activating the RAAS, increasing the release of renin, and resulting in hypertension. In addition, a large cyst presses against or occupies normal kidney tissues, leading to loss of multiple nephrons, abnormal structure, and functional changes. The changes in renal tubule function can lead to water and sodium retention, thus elevating blood pressure. At the same time, a decrease of renal enzymes can result in myocardial contractility, altered heart rate, and increased peripheral vascular resistance, thus leading to increased blood pressure. Thus, there are several possible mechanisms by which a SRC could cause hypertension.

Our studies had numerous strengths. First, we investigated the relationship between SRC and hypertension in a large population, thus reducing risk of bias due to small sample size. We also examined the influence of the number, bilaterality, and size of SRCs on hypertension. Our findings provide a theoretical basis for removal of SRCs as an intervention to normalize blood pressure, an intervention that could have a large impact on public health. Second, we considered many potential confounding factors. In particular, we performed univariate and multivariate analyses that controlled for multiple confounders, and we also used subgroup analysis and propensity score matching that also considered multiple confounders. The results of these analyses confirmed a relationship between SRC and hypertension. Third, we established a comprehensive scoring system to examine the effect of SRC subtype on hypertension.

This study also had some limitations, even though we investigated the prevalence and relationship of hypertension and SRC in a large sample. All blood pressure measurements were from a single date for each patient. Although most studies that screen for the prevalence of hypertension use this method, it can lead to an overestimate of hypertension, and thus obscure the true relationship between a SRC and hypertension. In addition, due to the limitations of this retrospective study, we only considered smoking status as current smoking or not. Because this was a retrospective study, we could not establish a causal relationship between SRC and hypertension. Moreover, this was a single-center study of individuals receiving routine physical examinations in the province of Hebei, so the results may not be applicable to other populations. We are therefore planning a large multicenter prospective study to examine the causal relationship of SRC and clinically diagnosed hypertension. We accounted for the presence of missing or lost data using multiple imputation, and the results were similar before and after this procedure. Finally, we only enrolled patients with the three most common subtypes of SRCs to reduce variability of the scoring system. We suggest enrollment of patients with more subtypes of SRC to develop a more refined scoring system.

5 | CONCLUSIONS

We found that a SRC was an independent risk factor for hypertension and a positive correlation between SRC load and hypertension. In particular, the risk of hypertension increased gradually with the size, number, and location of a SRC. Our results thus suggest that a SRC may be a reversible cause of hypertension. Careful follow-up or excision should be considered for a patient who presents with a SRC and hypertension.

AUTHOR CONTRIBUTIONS

CONFLICT OF INTEREST

There are no conflicts of interest.

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SUPPORTING INFORMATION

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