# RESEARCH





# Multiple and large simple renal cysts are associated with glomerular filtration rate decline: a cross-sectional study of Chinese population

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# Abstract

**Background** Although simple renal cyst (SRC) is a kind of structural alterations of kidney with age, the relationship between SRC and renal function is still obscure. We investigated the relationship between SRC and renal function in Chinese population.

**Methods** The medical records of 41,842 individuals who underwent physical examinations at the Health Checkup Center at our institution in 2018 were reviewed. According to whether with SRC, they were divided into no-SRC and SRC groups. SRCs were classified into subgroups based on number (< 2 vs.  $\geq 2$ ) and size (< 2 cm vs.  $\geq 2$  cm). Logistic regression was used to examine the relationship between SRC and estimated glomerular filtration rate (eGFR).

**Results** Multinomial logistic regression analysis showed that the adjusted odds ratio (OR) for eGFR slight decline in subjects with SRC was 1.26(95% confidence interval (95% Cl):1.17–1.35, p < 0.001), and the OR for eGFR severe decline was 1.35(95% Cl: 1.16–1.56, p < 0.001) compared with no-SRC. The adjusted OR of SRC number  $\ge 2$  and  $\ge 2$  cm on the risk of eGFR severe decline was the highest (OR:1.68, 95% Cl:1.25–2.23, p < 0.01) of four SRC subgroups.

**Conclusions** SRC is related to eGFR decline, especially when the person with one more SRCs and the size of SRC is more than 2 cm. SRC could be a warning sign for clinicians to judge the decline of renal function.

Keywords Simple renal cyst, Glomerular filtration rate, Kidney function

# Background

The kidney is one of the most susceptible organs to aging [1, 2]. Structural and functional alterations occur in the kidney with age. Kidney function declines with age is mainly manifested as a decline in glomerular filtration

rate (GFR) [3, 4]. Renal cyst is one of the structural alterations of kidney with age. According to the malignant tendency, renal cysts are categorized into four Bosniak classes baes on ultrasound, computed tomography (CT) and/or magnetic resonance imaging (MRI). Bosniak I renal cysts are the most common and are usually called simple renal cysts (SRCs) [5, 6]. On ultrasonic images, SRC is characterized by homogeneous cystic cavity, regular contour, clear boundary, thin smooth wall, no echo, and no septa or calcifications [5]. In the past, it was considered that SRC had no obvious clinical symptoms, low malignant tendency, little impact on body function, and no follow-up was required [5, 6]. Recently, more



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and more researchers believe that SRC is not as simple as previously thought [7-10]. Clinical studies found that the prevalence of SRC increased with age [11]. In the age-related comorbidity population, such as diabetes, arteriosclerosis, hyperuricemia and hypertension, the SRC prevalence is high [7, 8, 12-14].

The relationship between SRC and renal function is still controversial [15-18]. Some scholars such as HJ Chin [19], Ozdemir [18] believe that SRC has nothing to do with the decline of renal function, while other scholars such as Kong X [15], AL-Said J [17] believe that SRC is related to the decline of renal function. Therefore, this study intends to explore the relationship between SRC and renal function in Chinese population through a cross-sectional study.

# Methods

## Study population

The subjects of this cross-sectional study were individuals who underwent physical examinations from January to December 2018 at the Health Check-up Center of The Affiliated People's Hospital of Jiangsu University, which is a tertiary teaching hospital in China. A total of 41,842 participants were collected for this study and fulfilled the following criteria:

Inclusion criteria: (1) age  $\geq$  18 years; (2) no malignant disease, no acute heart failure, no sever disease or infection disease;(3) without pregnancy. Exclusion criteria: (1) not Chinese ethnic origin, (2) a history of disease(PKD), solitary kidney, partial nephrectomy, renal tumor, or ectopic kidney; (3) missing data for other variables. For subjects with multiple physical examinations, only the first exam record was used. The flowchart of subject inclusion is summarized in Fig. 1.

This study was reviewed and approved by the Ethics Committee of The Affiliated People's Hospital of Jiangsu University (ZFPH No: K-20220061-W). Given the retrospective study design, the need for formal consent was waived. The authors complied strictly with the Declaration of Helsinki and covered patient data confidentiality.

# **Clinical variables**

Body mass index (BMI) was calculated based on body weight (kilograms)/height(meters) squared. All data were obtained retrospectively via the hospital electronic database. Basic demographic characteristics, height, weight, systolic blood pressure, diastolic blood pressure, fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), serum creatinine and other data were recorded.

Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or with a positive history of hypertension. Mean blood pressure = (systolic blood pressure  $\pm$  diastolic blood pressure  $\times$  2)/3.

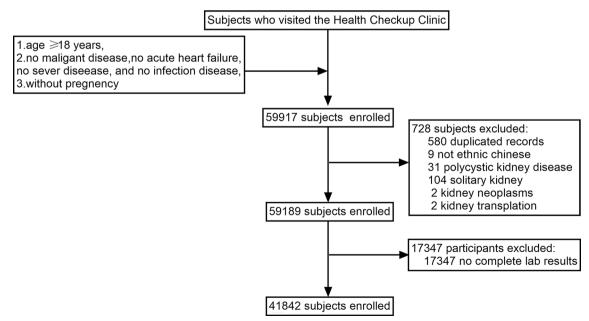


Fig. 1 Flowchart of the enrolled subjects

Diabetes mellitus was defined as  $FPG \ge 7.0 \text{ mmol/L}$  or HbA1c>6.5% or with a positive history of diabetes mellitus.

# **SRC diagnosis**

Ultrasonic diagnosis: According to Bosniak method, SRC was diagnosed on the basis that: (1) round or oval cystic cavity; (2) regular outline of the cystic cavity and clear boundary; (3) homogeneous cystic cavity without separation or calcification;(4) thin and smooth wall without echo, and (5) enhanced echo of the posterior wall [5].

CT diagnosis: CT images showed uniform water attenuation (range -10hu to 20hu), thin and smooth wall, no calcification, septum or mural nodules [5, 20]. If the subject not only had kidney ultrasound record, but also had abdominal CT record, the CT record were prevailed. The subjects with SRC were further stratified according to the maximum diameter of SRC (<2 cm vs.  $\geq$  2 cm) and the number of SRC (<2 vs.  $\geq$  2).

# eGFR calculation

The estimated glomerular filtration rate (eGFR) was calculated by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine Eq. (2009) [21]. The equation is as follows:

for females,

if SCr  $\leq$  0.7 mg/dl, eGFR=144×(SCr/0.7)  $^{-0.329}$ ×(0.993) and if SCr>0.7 mg/dl, eGFR=144×(SCr/0.7)  $^{-1.209}$ ×(0.993)  $^{age}$ ; for males, if SCr  $\leq$  0.9 mg/dl, eGFR=141×(SCr/0.9)

 $^{-0.411}$  × (0.993) <sup>age</sup>,

and if SCr > 0.9 mg/dl, eGFR =  $141 \times (SCr/0.9)$ <sup>-1.209</sup>×(0.993) <sup>age</sup>, where Scr is serum creatinine (mg/dl).

# Statistical analysis

All subjects were divided into no simple renal cyst group (no-SRC group) and simple renal cyst group (SRC group) according to whether they had simple renal cyst. The SRC group was further divided into subgroups based on the number and size of cysts (SRC number <2 and size <2 cm, SRC number <2 and size  $\geq 2$  cm, SRC number  $\geq 2$  and size  $\geq 2$  cm, SRC number  $\geq 2$  and size  $\geq 2$  cm). Categorical variables were presented as counts (percentages). Continuous variables were described as mean  $\pm$  standard deviation or the median (interquartile range) according to normal or skewed distribution. Student's t-test was used to compare between two groups of normally distributed data, and the Mann–Whitney U test was used for skewed

distributions. One-way analysis of variance (ANOVA) test was used to analyze the significance among multigroups. The counting data were tested using Chisquare test. Logistic regression was employed to identify associations between SRC prevalence and eGFR. Using IBM <sup>®</sup> SPSS <sup>®</sup> Statistical version 23.0 (IBM, New York, USA) for statistical analysis. Two tailed *p* value < 0.05 was considered statistically significant. Prism 9.0 (Graphpad, San Diego, CA, USA) was used for plotting graphs.

# Results

## **Baseline characteristics**

According to the inclusion and exclusion criteria, 41,842 subjects were finally included, as shown in Fig. 1. Among them, there were 5758 subjects in the simple renal cyst group (SRC group) and 36,084 subjects in the no simple renal cyst group (no-SRC group). The age of these subjects ranged from 18 to 101 years old with the average of  $50.6 \pm 14.8$  years old. Baseline characteristics are shown in Table 1. Compared to no-SRC group, subjects in SRC group were older, and with higher proportion of males, higher systolic blood pressure, higher diastolic blood pressure, higher TG, higher urea nitrogen, higher serum creatinine, higher uric acid, but lower HDL-C and lower eGFR (p < 0.05).

# SRC and age

In accordance with their ages, subjects were stratified 7 layers: 18–29 years old, 30–39 years old, 40–49 years old, 50–59 years old, 60–69 years old, 70–79 years old, 80 years old and above. The prevalence of SRC in each layer was 4.9%, 7. 3%, 11. 2%, 16. 2%, 18. 8%, 21. 6% and 25.8%, respectively, showing an increasing trend (p<0.001) (Fig. 2). When combining both cyst number and size in the analysis, the increasing trend stood still (Fig. 3).

# SRC and eGFR

As shown in Fig. 4, eGFR of no-SRC, SRC number <2 and size <2 cm, SRC number <2 and size  $\ge 2$  cm, SRC number  $\ge 2$  and size <2 cm and SRC number  $\ge 2$  and size  $\ge 2$  cm were 99.94±17.16 ml/min per 1.73m<sup>2</sup>, 94.71±16.97 ml/min per 1.73m<sup>2</sup>, 94.97±16.78 ml/ min per 1.73m<sup>2</sup> and 91.83±17.72 91.82±17.85 ml/ min per 1.73m<sup>2</sup>, showing a decreasing trend (*p* for trend <0.001), and the eGFR of SRC number  $\ge 2$  and size  $\ge 2$  cm was the lowest of all. eGFR of the two SRC number  $\ge 2$  groups were lower than those of SRC number <2 groups(*p*<0.05). However, there were no statistically significant differences between the two SRC number  $\ge 2$  groups (*p*  $\ge 0.05$ ). And there were no

# Table 1 Characteristics of the study subjects

Variables	Total (N=41,842)	no-SRC (N=36,084)	SRC (N=5758)	F or χ <sup>2</sup>	P value
Male gender	25,971 (62.1)	21,784 (60.4)	4187 (72.7)	321.482	< 0.001
Age(years)	$50.6 \pm 14.8$	49.7±14.6	$56.7 \pm 14.7$	1.896	< 0.001
≥60 years	10,531 (25.2)	8338 (23.1)	2193 (38.1)	591.555	< 0.001
Body mass index(kg/m2)	$22.6 \pm 4.7$	22.7±4.7	$22.6 \pm 4.6$	7.871	0.256
Systolic blood pressure (mmHg)	125.9±18.8	125.3±18.6	$130 \pm 19.5$	27.181	< 0.001
Diastolic blood pressure(mmHg)	76.8±11.6	76.6±11.6	78.5±11.7	0.95	< 0.001
Mean arterial pressure (mmHg)	93.2±13	92.8±13	95.7±13.1	1.00	< 0.001
Hypertension	10,720 (25.6)	8827 (24.5)	1893 (32.9)	184.461	< 0.001
HbA1c (%)	$6.0 \pm 1.0$	5.9±0.9	$6.1 \pm 1.1$	11.54	< 0.001
Albumin(g/L)	$44.7 \pm 2.5$	44.8±2.5	$44.4 \pm 2.5$	0.105	< 0.001
Fasting plasma glucose(mmol/L)	$5.4 \pm 1.4$	$5.3 \pm 1.4$	$5.6 \pm 1.6$	114.133	< 0.001
Diabetes mellitus	2953 (7.0)	2359 (6.5)	576 (10.0)	91.455	< 0.001
HDL-cholesterol (mmol/L)	1.4±0.3	1.4±0.3	$1.3 \pm 0.3$	0.055	< 0.001
LDL- cholesterol (mmol/L)	$2.8 \pm 0.7$	2.8±0.7	$2.8 \pm 0.7$	2.202	0.524
Thyroid stimulating hormone (µIU/mI)	$2.4 \pm 2.1$	2.4±2	$2.3 \pm 2.5$	0.095	0.305
Free triiodothyronine (pmol/L)	$5.4 \pm 0.7$	$5.4 \pm 0.8$	$5.4 \pm 0.7$	1.975	0.105
Free thyroxine (pmol/L)	$10.7 \pm 1.9$	$10.7 \pm 1.9$	$10.7 \pm 1.7$	1.222	0.625
Triglyceride(mmol/L)	$1.68 \pm 1.47$	$1.67 \pm 1.48$	$1.74 \pm 1.40$	0.005	0.001
Total cholesterol (mmol/L)	$4.8 \pm 0.9$	4.8±0.9	4.8±0.9	1.395	0.162
Urea nitrogen (mmol/L)	$5.0 \pm 1.4$	$5.0 \pm 1.4$	$5.2 \pm 1.5$	18.938	< 0.001
Serum creatinine(mg/dl)	$0.80 \pm 0.25$	$0.80 \pm 0.25$	$0.83 \pm 0.22$	0.003	< 0.001
eGFR[ml min <sup>-1</sup> (1.73m <sup>2</sup> ) <sup>-1</sup> ]	99.1±17.3	99.9±17.2	94.0±17.2	0.181	< 0.001
< 60	1376 (3.3)	1115 (3.1)	261 (4.5)		
60-<90	9143 (21.8)	7377 (20.4)	1766 (30.7)		
≥90	31,323 (74.9)	27,592 (76.5)	3731 (64.8)		
Uric acid(µmol/L)	335.6±87.9	334.4±88.2	343.3±85.9	6.474	< 0.001

Data are expressed as mean ± standard deviation or number (percentage)

SRC, simple renal cyst; HDL, high-density lipoprotein, LDL, low-density lipoprotein; HbA1c, glycosylated hemoglobin; eGFR, estimated glomerular filtration rate calculated by the 2009 CKD-EPI formula

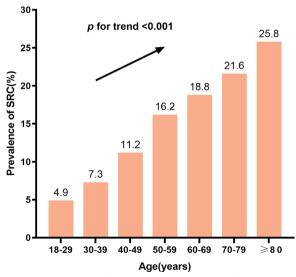
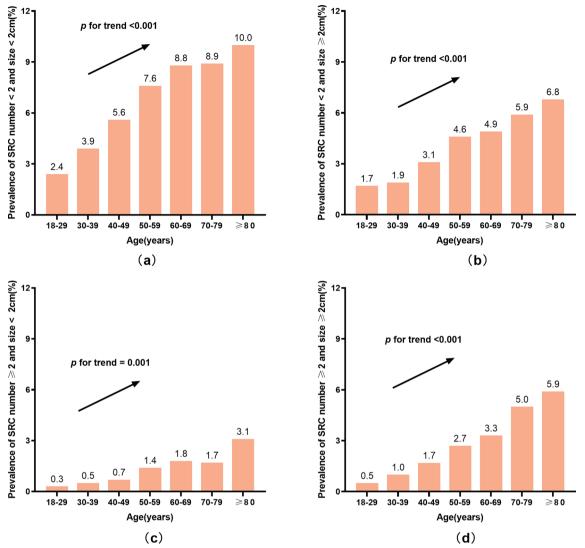


Fig. 2 The prevalence of simple renal cyst (SRC) stratified according to age

statistically significant differences between the two SRC number < 2 either ( $p \ge 0.05$ ).

# Association between SRC and eGFR

A negative association was displayed between the prevalence of SRC and eGFR ( $\beta$ =-0.430, p<0.05) after adjusted for gender, age (per 10 years), systolic blood pressure, fast glucose, serum uric acid and body mass index. In elderly population (age  $\geq$  60 years old), this kind of association was not statically significant ( $\beta$ =- 0.102, p>0.05) after adjusted for clinical influencing factors, even though which was appeared before adjusted ( $\beta$ =- 1.173, p>0.01). The negative association ( $\beta$ =- 0.660, p<0.01) between the prevalence of SRC and eGFR was appeared still in adults (age < 60 years old) after adjusted. It could be noted that the prevalence of SRC showed stronger negative correlation with eGFR in younger adults than in the older adults (Table 2).



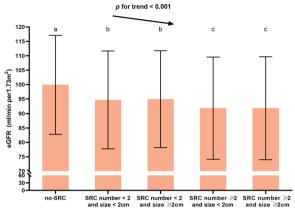
**Fig. 3** The prevalence of simple renal cyst (SRC) combining both cyst number and size. **a** Prevalence of SRC number <2 and size <2 cm. **b** Prevalence of SRC number <2 and size <2 cm. **c** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and size <2 cm. **d** Prevalence of SRC number <2 and s

## Association between SRC and eGFR decline

The association between eGFR decline and SRC was further analyzed. When eGFR slight decline  $(60 \le eGFR < 90 \text{ ml/min per}1.73\text{m}^2)$  and severe decline  $(eGFR < 60 \text{ ml/min per} 1.73\text{m}^2)$  were taken as dependent variables, the parallel line test failed (p < 0.05). Therefore, subsequent studies on the above dependent variables were conducted by multinomial logistic regression analysis instead of ordinal logistic regression analysis (Additional file 1: Table S1).

The presence of SRC was independently associated with eGFR slight decline and severe decline after adjusting for some clinical variables such as older age, gender, hypertension, fasting plasma glucose, uric acid, and triglyceride. Compared with no-SRC, the adjusted odds ratio (OR) for eGFR slight decline in subjects with SRC was 1.26 (95% confidence interval (95%CI): 1.17–1.35, p < 0.001), and the OR for eGFR severe decline was 1.35 (95%CI: 1.16–1.56, p < 0.001), increased by 9% than which of eGFR slight decline (Fig. 5).

After adjusting for clinical variables such as age, gender, hypertension, fasting plasma glucose, uric acid, and triglyceride, the adjusted OR of SRC number  $\geq 2$  and  $\geq 2$  cm on the risk of eGFR severe decline was the highest of all (OR:1.68, 95% CI:1.25–2.23, p < 0.01) (Fig. 6). The association did not change after stratified by age. The adjusted OR of SRC number  $\geq 2$  and  $\geq 2$  cm on the risk of eGFR severe decline was 2.13(CI:1.24–3.67, p < 0.01) in adults



**Fig. 4** Comparisons of eGFR among subjects with simple renal cyst (SRC) and those without SRC (no-SRC). Error bars indicate standard errors. The same letter on the column indicates that the difference is not significant ( $p \ge 0.05$ ), and different letters **a**–**c** indicate that the difference is significant (p < 0.05). *eGFR* estimated glomerular filtration rate calculated by the 2009 CKD-EPI formula

Table 2 Association between the prevalence of SRC and eGFR<sup>a</sup>

	The adults		The elderly		
	β	P value	β	P value	
With SRC	- 0.660	0.003	- 0.102	0.728	

SRC simple renal cyst, eGFR estimated glomerular filtration rate calculated by the 2009 CKD-EPI formula

<sup>a</sup> Adjusted for gender, age, systolic blood pressure, fast glucose, serum uric acid and body mass index

(age < 60 years old), and 1.45(CI:1.02–2.07, p < 0.05) in older (age  $\geq$  60 years old) (Fig. 7).

# Discussion

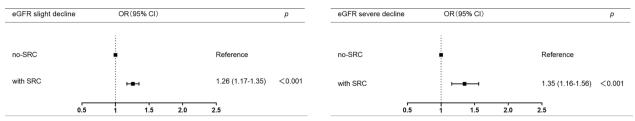
SRCs are common renal cysts and commonly asymptomatic. With the advances in imaging technology, more and more SRCs are incidentally found during imaging examination for other reasons [6]. Due to different races, different complications, different imaging methods used, and other factors, the prevalence of SRC varies between 4.2% to 55% [22-24]. The detection rate of SRC by CT or MRI is higher than that by ultrasound [25]. The prevalence of SRC in the physical examination population is 7.7–10.5% [15, 26], and the prevalence of SRC in individuals with diabetes mellitus, hypertension is 21.1% [27] and 20.3% [28], respectively. The prevalence of SRC increases with age, and is reported to be up to 31.9% in the elderly [12]. The prevalence of SRC in this study was 13.8%, slightly higher than the study carried out by Chinese scholar Kong X et al. [15]. The reason is possibly caused by the fact that our study included CT examination results, which improved the detection rate. Our results showed the prevalence of SRC increased with age, which was consistent with previous studies. Concerning SRC number and size, the increasing trend with age stood still.

Some scholars hold the view that SRC could be a variant of "normal" [29], which has no special significance in clinical diagnosis or treatment and does not need follow-up [6, 30]. However, other scholars believe that SRC could be a kind of variant "without known pathologic associations" but for "with unknown pathologic associations" [31]. And its clinical significance still needs to be explored [12, 24, 32, 33]. SRC, simple renal cyst may not be as simple as we think. As early as 1977, a study by Baert L et al. [34] pointed out that before the identification of SRC by imaging, there had been microstructural changes in the kidney, including the formation of diverticula and micro-cysts. His study found that all kidneys of adults and elderly people had diverticula on the distal tubule, the number increasing with age. This change is consistent with our result that the prevalence of SRC increases with age.

SRC is not only related to aging, but also related to hypertension [8, 28], diabetes [12], arteriosclerosis[7] and hyperuricemia [13]. In this study, we also found that the blood pressure, fasting plasma glucose, blood lipid, uric acid and serum creatinine in SRC group were higher than those in no-SRC group (p < 0.001), and eGFR in SRC group was lower than those in no-SRC group (p < 0.001).

The relationship between SRC and renal function is still controversial [15–18]. Some studies consider that SRC has nothing to do with the reduced renal function [18, 19], while others suggest that SRC is related to the decline of renal function [15, 17]. In this study, the presence of SRC was independently associated with eGFR slight decline and severe decline after adjustment. Analyzing SRCs with characteristics of both number and size, four SRC subgroups were all independently associated with eGFR slight decline and severe decline when other clinical variables were not adjusted (Additional file 2: Fig. S1). After adjusting for clinical variables, all four SRC subgroups were associated with eGFR slight decline, but were not all statistically associated with eGFR severe decline. The association of SRC number < 2 and size  $\geq 2$  cm and eGFR severe decline was not statistically significant. Except for "single large cyst", the OR on risk of eGFR severe decline was gained with the increase of SRC number and diameter. Among four SRC subgroups, the adjusted OR of SRC number  $\geq 2$  and  $\geq 2$  cm on the risk of eGFR severe decline was the highest of all (OR:1.68, 95% CI:1.25–2.23, p<0.01). The association did not change after stratified by age, even though it was attenuated in older layer.





**Fig. 5** The association of eGFR decline and SRC. Adjusted by age, gender, hypertension, fasting plasma glucose, uric acid, and triglyceride. eGFR slight decline, $60 \le eGFR < 90 \text{ ml/min per1.73m}^2$ ; eGFR severe decline, eGFR < 60 ml/min per1.73m<sup>2</sup>. OR odds ratio, CI confidence interval, eGFR estimated glomerular filtration rate calculated by the 2009 CKD-EPI formula, SRC simple renal cyst

eGFR slight decline	OR (95% CI)		p	eGFR severe decline	OR(95% CI)	p
no-SRC	•	Reference		no-SRC	÷	Reference
SRC number<2 and size<2cm	⊢∎→	1.29(1.16-1.42)	<0.001	SRC number<2 and size<2cm		1.27(1.03-1.57) 0.029
SRC number<2 and size≥2cm	<b>⊢</b> ∎i	1.19(1.04-1.37)	0.010	SRC number<2 and size≥2cm	<b>⊢_</b> ∎I	1.20(0.91-1.57) 0.205
SRC number≥2 and size<2cm	<b>—</b>	1.34(1.07-1.36)	0.011	SRC number≥2 and size<2cm		<b>1.53(0.99 -2.38)</b> 0.057
SRC number≥2 and size≥2cm	n <b>ii</b>	1.24(1.06-1.46)	0.008	SRC number≥2 and size≥2cm	· · · · · · · · · · · · · · · · · · ·	1.68(1.25-2.23) 0.001
0.5	1 1.5 2.0	2.5		0.5	1 1.5 2.0	2.5

**Fig. 6** The association of eGFR decline and SRC four combinates. Adjusted by age, gender, hypertension, fasting plasma glucose, uric acid, and triglyceride. eGFR slight decline,  $60 \le eGFR < 90$  ml/min per1.73m<sup>2</sup>; eGFR severe decline, eGFR < 60 ml/min per1.73m<sup>2</sup>. OR odds ratio, Cl confidence interval, eGFR estimated glomerular filtration rate calculated by the 2009 CKD-EPI formula, SRC simple renal cyst

## age< 60 years old

eGFR slight decline	OR(95% CI)		p	eGFR severe decline	OR(95% CI)		p
no-SRC		Reference		no-SRC	÷	Reference	
SRC number<2 and size<2cm	<b>⊢</b> ∎1	1.39(1.21-1.60)	<0.001	SRC number<2 and size<2cm		1.52(1.05-2.21)	0.027
SRC number<2 and size≥2cm		1.19(0.98-1.44)	0.073	SRC number<2 and size≥2cm	<b>⊢_</b> ∎I	1.32(0.80-2.19)	0.282
SRC number≥2 and size<2cm		1.46(1.04-2.05)	0.027	SRC number $\geqslant$ 2 and size<2cm H		→ 1.60(0.65-3.90)	0.305
SRC number≥2 and size≥2cm		1.28(0.99-1.64)	0.051	SRC number $\geqslant$ 2 and size $\geqslant$ 2cm	· · · · · · · · · · · · · · · · · · ·	2.13(1.24-3.67)	0.006
0.5 1	1.5	2.0 2.5		0.5	1 1.5 2.0 2.5 3.0 3.5	4.0	

#### age $\geq$ 60 years old

eGFR slight decline OR (95% CI)		p	eGFR severe decline	OR (95% CI)		p
no-SRC	Reference		no-SRC	÷	Reference	
SRC number<2 and size<2cm	1.16(1.00-1.34)	0.051	SRC number<2 and size<2cm		1.07(0.82-1.41)	0.607
SRC number<2 and size≥2cm	1.18(0.98-1.42)	0.077	SRC number<2 and size≥2cr	m ••	1.13(0.80-1.58)	0.487
SRC number≥2 and size<2cm ↓	⊣ 1.27(0.94-1.72)	0.118	SRC number≥2 and size<2cr	m 🕂 💼 🗖	1.47(0.87 -2.48)	0.151
SRC number≷2 and size≷2cm	1.21(0.98-1.49)	0.083	SRC number≥2 and size≥20	m 🗕	<b>⊣</b> 1.45(1.02-2.07)	0.039
0.5 1 1.5	2.0 2.5		0.5	1 1.5 2.0	0 2.5	

**Fig. 7** The association of eGFR decline and SRC four combinates stratified by age. Adjusted by gender, hypertension, fasting plasma glucose, uric acid, and triglyceride. eGFR slight decline,  $60 \le eGFR < 90 \text{ ml/min per1.73m}^2$ ; eGFR severe decline, eGFR <  $60 \text{ ml/min per1.73m}^2$ ; OR odds ratio, Cl confidence interval; eGFR estimated glomerular filtration rate calculated by the 2009 CKD-EPI formula, SRC simple renal cyst

The following factors may explain the association between SRC and renal function decline. The association between SRC and renal function may be related to the aging process and primary renal diseases, which are accompanied by an increased number and enlarged size of cysts. SRC originated from distal convoluted tubule or collecting duct, and its precursor structure, renal tubular diverticulum or microcyst, is considered to be secondary

to nephron loss [34]. With the advancing age and the occurrence of kidney diseases, the mass of renal cortex decreases, and nephrons losing increase the workload of the remaining nephrons, and may lead to hypertrophy or proliferation of renal tubular cells, leading to the formation of cysts [11]. On the other hand, some studies have shown the prevalence of SRC is related to the increased renin release which due to renal ischemia caused by cyst expansion [28, 35]. With the stimulation of renin angiotensin aldosterone system, the elevated blood pressure leads to endothelial dysfunction and microvascular ischemia, glomerulosclerosis, loss of nephron, and decline of renal function, which in turn causes the occurrence of renal cyst [36, 37]. The presence of SRC and the increase of SRC number or larger diameter will aggravate renal ischemia, because the effect of cyst expansion is more serious. Therefore, it is more likely to generate higher internal hydrostatic pressure to compress the surrounding renal tissue, leading to renal ischemia.

To sum up, this study believes that SRC has a certain correlation with the decline of eGFR. The greater the number and diameter of SRC, the lower the eGFR may be. This study has some limitations. 1. This study is a cross-sectional study that limits causal inference: we see correlations, but we cannot confirm the direction or causal relationship of these correlations. 2. Although this study included some abdominal CT results, the imaging basis of most subjects was ultrasound. Although renal ultrasound is a reliable tool for estimating renal length, it is not as sensitive as CT or MRI, so some smaller cysts may be missed in the study.3. The subjects of the study are ethnic Chinese. Whether the results of this study are applicable to other ethnic groups needs further research. 4. In this study, molecular genetic tests were not performed on every subject, especially the SRC group, to exclude PKD. Some people in our study may have PKD. In the follow-up, further studies were conducted to explore the causal relationship between SRC and eGFR decline.

# Conclusions

In conclusion, we believe that SRC is related to the decrease of eGFR, especially when the person with one more SRCs and the diameter of the biggest SRC is more than 2 cm. SRC may be a warning sign for clinicians to judge the decline of renal function.

#### Abbreviations

SRC	Simple renal cyst
OR	Odds ratio
CI	Confidence interval
eGFR	Estimated glomerular filtration rate
CT	Computed tomography
MRI	Magnetic resonance imaging

PKD Polycystic kidney disease BMI Body mass index FPG Fasting plasma glucose HbA1c Glycosylated hemoglobin TC Total cholesterol TG Triglyceride HDL-C High-density lipoprotein cholesterol CKD-FPI Chronic Kidney Disease Epidemiology Collaboration ANOVA One-way analysis of variance

# Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s40001-023-01552-2.

Additional file 1: Table S1. The adjusted OR of clinical variables on the risk of eGFR decline on the basis of multinomial logistic regression (OR, 95% CI).

Additional file 2: Figure S1. The unadjusted OR of SRC four combinates on the risk of eGFR decline. eGFR slight decline,  $60 \le eGFR < 90$  ml/min per1.73m<sup>2</sup>; eGFR severe decline, eGFR < 60 ml/min per1.73m<sup>2</sup>; OR odds ratio, Cl confidence interval, eGFR estimated glomerular filtration rate calculated by the 2009 CKD-EPI formula, SRC simple renal cyst.

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#### Author contributions

CJ contributed to the study design, acquisition, analysis and interpretation of data, drafting and revising the article, and final approval of the version to be published. LW, ZZY, YM, BZ and XHP contributed to revising the article for important intellectual content and final approval of the version to be published. CHZ contributed to acquisition of data and final approval of the version to be published. WHZ contributed to conception and design, analysis and interpretation of data, revising the article for important intellectual content, and final approval of the version to be published. All authors read and approved the final manuscript.

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#### Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

# Declarations

#### Ethics approval and consent to participate

This study was approved by the ethical review committee of The Affiliated People's Hospital of Jiangsu University waived off the requirement for informed consent and approved the study (ZFPH No: K-20220061-W). All subject records and data were deidentified and anonymized prior to analysis. This study was conducted in accordance with the Declaration of Helsinki.

# **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare that they have no competing interests.

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#### References

- Lee G, Uddin MJ, Kim Y, Ko M, Yu I, Ha H. Pgc-1a, a potential therapeutic target against kidney aging. Aging Cell. 2019. https://doi.org/10.1111/ acel.12994.
- Wang X, Bonventre J, Parrish A. The aging kidney: increased susceptibility to nephrotoxicity. Int J Mol Sci. 2014;15(9):15358–76.
- Wang M, Sun X, Zhang W, Zhang Q, Qian J, Chen W, et al. Frailty and the risk of kidney function decline in the elderly population: the rugao longevity and ageing study. Nephrol Dial Transplant. 2021;36(12):2274–81.
- Denic A, Mathew J, Lerman LO, Lieske JC, Larson JJ, Alexander MP, et al. Single-nephron glomerular filtration rate in healthy adults. N Engl J Med. 2017;376(24):2349–57.
- Bosniak MA. The current radiological approach to renal cysts. Radiology. 1986;158(1):1–10.
- Silverman SG, Pedrosa I, Ellis JH, Hindman NM, Schieda N, Smith AD, et al. Bosniak classification of cystic renal masses, version 2019: an update proposal and needs assessment. Radiology. 2019;292(2):475–88.
- Wu H, Chang Y, Wu I, Lu F, Chang C, Yang Y, et al. Simple renal cysts are associated with increased arterial stiffness in a taiwanese population. Hypertens Res. 2019;42(7):1068–73.
- Lu N, Hu P, Wang J, Yan W, He Z, Xu T, et al. Simple renal cysts are associated with 24-month prognosis of patients with type b aortic dissection and hypertension. Can J Cardiol. 2019;35(11):1499–504.
- Hélénon O, Crosnier A, Verkarre V, Merran S, Méjean A, Correas JM. Simple and complex renal cysts in adults: classification system for renal cystic masses. Diagn Interv Imaging. 2018;99(4):189–218.
- Tatar E, Ozay E, Atakaya M, Yeniay PK, Aykas A, Okut G, et al. Simple renal cysts in the solitary kidney: are they innocent in adult patients? Nephrology (Carlton). 2017;22(5):361–5.
- Hommos MS, Glassock RJ, Rule AD. Structural and functional changes in human kidneys with healthy aging. J Am Soc Nephrol. 2017;28(10):2838–44.
- Wei L, Xiao Y, Xiong X, Li L, Yang Y, Han Y, et al. The relationship between simple renal cysts and renal function in patients with type 2 diabetes. Front Physiol. 2020. https://doi.org/10.3389/fphys.2020.616167.
- Han Y, Zhang M, Lu J, Zhang L, Han J, Zhao F, et al. Hyperuricemia and overexcretion of uric acid increase the risk of simple renal cysts in type 2 diabetes. Sci Rep. 2017. https://doi.org/10.1038/s41598-017-04036-6.
- Lee Y, Kim MS, Cho S, Kim SR. Association between simple renal cysts and development of hypertension in healthy middle-aged men. J Hypertens. 2012;30(4):700–4.
- Kong X, Ma X, Zhang C, Su H, Gong X, Xu D. Increased risk of kidney damage among chinese adults with simple renal cyst. Int Urol Nephrol. 2018;50(9):1687–94.
- Qiu W, Jiang Y, Wu J, Huang H, Xie W, Xie X, et al. Simple cysts in donor kidney contribute to reduced allograft function. Am J Nephrol. 2017;45(1):82–8.
- 17. Al-Said J, Brumback MA, Moghazi S, Baumgarten DA, O'Neill WC. Reduced renal function in patients with simple renal cysts. New York, NY; 2004.
- Ozdemir AA, Kapucu K. The relationship between simple renal cysts and glomerular filtration rate in the elderly. Int Urol Nephrol. 2017;49(2):313–7.
- Chin HJ, Ro H, Lee HJ, Na KY, Chae DW. The clinical significances of simple renal cyst: is it related to hypertension or renal dysfunction? Kidney Int. 2006;70(8):1468–73.
- O'Connor SD, Silverman SG, Ip IK, Maehara CK, Khorasani R. Simple cystappearing renal masses at unenhanced ct: can they be presumed to be benign? Radiology. 2013;269(3):793–800.
- 21. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009.
- Laucks JSP, Mclachlan MS. Aging and simple cysts of the kidney. Br J Radiol. 1981;54(637):12.

- Mosharafa AA. Prevalence of renal cysts in a middle-eastern population: an evaluation of characteristics and risk factors. BJU Int. 2008;101(6):736–8.
- 24. Song BG, Park YH. Presence of renal simple cysts is associated with increased risk of abdominal aortic aneurysms. Angiology. 2020;71(5):465–70.
- 25. Al-Said J, Charles OW. Reduced kidney size in patients with simple renal cysts. Kidney Int. 2003;64(3):1059–64.
- Ozveren B, Onganer E, Türkeri LN. Simple renal cysts: prevalence, associated risk factors and follow-up in a health screening cohort. Urol J. 2016;13(1):2569–75.
- Chen J, Ma X, Xu D, Cao W, Kong X. Association between simple renal cyst and kidney damage in a chinese cohort study. Ren Fail. 2019;41(1):600–6.
- Lee C, Yang Y, Wu J, Chang Y, Huang Y, Lu F, et al. Multiple and large simple renal cysts are associated with prehypertension and hypertension. Kidney Int. 2013;83(5):924–30.
- 29. Pandharipande PV, Herts BR, Gore RM, Mayo-Smith WW, Harvey HB, Megibow AJ, et al. Rethinking normal: benefits and risks of not reporting harmless incidental findings. J Am Coll Radiol. 2016;13(7):764–7.
- 30. Israel GM, Bosniak MA. An update of the bosniak renal cyst classification system. Urology. 2005;66(3):484–8.
- Brown SD. Should incidental simple renal cysts be considered normal variants and ignored in radiologic reports? Review of a proposed framework. J Am Coll Radiol. 2016;13(10):1169.
- 32. Simms RJ, Ong ACM. How simple are "simple renal cysts"? Nephrol Dial Transplant. 2014;29(suppl 4):iv106–12.
- Giannopoulos S, Kokkinidis DG, Avgerinos ED, Armstrong EJ. Association of abdominal aortic aneurysm and simple renal cysts: a systematic review and meta-analysis. Ann Vasc Surg. 2021. https://doi.org/10.1016/j.avsg. 2021.01.075.
- Baert L, Steg A. Is the diverticulum of the distal and collecting tubules a preliminary stage of the simple cyst in the adult? J Urol. 1977;118(5):707–10.
- 35. Pedersen JF, Emamian SA, Nielsen MB. Simple renal cyst: relations to age and arterial blood pressure. Br J Radiol. 1993;66(787):581–4.
- Terada N, Arai Y, Kinukawa N, Yoshimura K, Terai A. Risk factors for renal cysts. BJU Int. 2004;93(9):1300–2.
- van Varik BJ, Vossen LM, Rennenberg RJ, Stoffers HE, Kessels AG, de Leeuw PW, et al. Arterial stiffness and decline of renal function in a primary care population. Hypertens Res. 2017;40(1):73–8.

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