Living well with chronic kidney disease: ehealth interventions to support self-management in China

Shen, H.

Chapter 3

Prevalence of reduced kidney function, kidney function decline and related risk factors among a primary care population in China: A repeated cross-sectional study

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Abstract

Background

Chronic kidney disease (CKD) poses a severe health and socioeconomic burden, particularly to low-income and middle-income countries. China is the largest low-income and middle-income country with a current population of 1.4 billion. However, only a few studies reported on the prevalence of reduced kidney function and related risk factors among Chinese populations. Also, none of these studies explored the prevalence of kidney function decline and related risk factors, especially in Chinese primary care settings. To bridge this gap, this study aimed to examine the prevalence of reduced kidney function and kidney function decline and explore related risk factors in a Chinese primary care population.

Methods

We conducted a repeated cross-sectional study in a primary health care population in China. Electronic records were included of 18273 adults who underwent routine health check-ups between 2004-2020 in three primary health care centers in Zhengzhou city, Henan Province in China. Follow-up serum creatinine was available for 3314 participants, with a mean follow-up duration of 1.5 years. Reduced kidney function was defined as an estimated glomerular filtration rate (eGFR) of below 60 mL/min per 1.73 m^2. Kidney function decline was defined as a drop in the glomerular filtration rate (GFR) category (≥90 [G1], 60-89 [G2], 45-59 [G3a], 30-44 [G3b], 15-29 [G4], <15 [G5] mL/min per 1.73 m^2) accompanied by a ≥25% drop in eGFR from baseline, or a sustained decline in eGFR of >5 mL/min per 1.73 m^2/y. Rapid eGFR decline was defined as a decline in eGFR of greater than 3 mL/min/1.73m^2/y. The annual eGFR decline was calculated as ($eGFR_{baseline}$-$eGFR_{follow\text{-}up}$)/time (follow-up years). Descriptive statistics and multivariable logistic regressions were used to examine reduced kidney function, kidney function decline and related risk factors.

Results

Of all participants, 3273(17.9%) had reduced kidney function at first measurement. Of the participants with a follow-up, 640 (19.3%) had kidney function decline and 755 (22.8%) had rapid eGFR decline. Multivariable logistic regression analysis showed that female sex (OR 2.208, 95% CI 1.974-2.470), older age (OR 1.051, 95% CI 1.046-1.057), hypertension (OR 0.847, 95% CI 0.719-0.997), overweight (OR 1.162, 95% CI 1.042-1.296), obesity (OR 1.609, 95% CI 1.349-1.919), diabetes (OR 1.229, 95% CI 1.043-1.447), left ventricular hypertrophy (OR 2.123, 95% CI 1.407-3.203), and dyslipidemia (OR 2.478, 95% CI 2.086-2.943) were independent predictors of reduced kidney function. Moreover, older age (OR 1.013, 95% CI 1.002-1.023) and a reduced kidney function at baseline (OR 11.133, 95% CI 7.827-15.836) were independent predictors of kidney function decline.

Conclusions

Our study demonstrated a high prevalence of reduced kidney function and kidney function decline in a Chinese primary care population. Also, the identified associated risk factors can help to identify those who are more likely to experience a reduced kidney function and kidney function decline. To reduce the burden of CKD in China, effective three-level prevention and treatment strategies seem warranted.

INTRODUCTION

Chronic kidney disease (CKD) is a major public health concern [1, 2]. Globally, 698 million individuals are affected by CKD [3]. Also, CKD is associated with adverse outcomes including kidney failure, accelerated cardiovascular disease (CVD) and premature death [4, 5]. In specific, a recent study reported that globally, 1.4 million CVD-related deaths and 25.3 million CVD disability-adjusted life years are attributable to impaired kidney function [3].

The burden of CKD is particularly high in low-income and middle-income countries [6], including China, with an estimated prevalence of 10.8% (120 million adults) [7]. To reduce this burden, the identification of potentially modifiable risk factors for reduced kidney function [8] is essential to enable the prevention of CKD progression in an early stage. Previous evidence indicates that diabetes, hypertension and dyslipidemia can play an important role in the development of reduced kidney function [9, 10]. Also, minimal, moderate, or rapid rates of estimated glomerular filtration rate (eGFR) decline can predict premature mortality [11-13]. Some of the previous studies reported CKD progression and related risk factors [10, 14], yet only a few studies reported on prevalence of reduced kidney function and related CVD risk factors for the Chinese population [15-17]. Also, none of these studies explored the prevalence of kidney function decline and related CVD risk factors, especially in Chinese primary care settings. Related definitions of reduced kidney function and kidney function decline are operationalized based on previous literature [18, 19] and further detailed in Textbox 1.

Better insights into the prevalence of reduced kidney function and kidney function decline in the Chinese primary care population is of vital importance to assess the burden of CKD in Chinese settings. Evidence on the burden of CKD can adequately inform public health policymakers, healthcare professionals, and community members on the impact of CKD. Also, identifying (modifiable) risk factors for reduced kidney function and kidney function decline has practical relevance to developing target effective strategies. Therefore, we performed a repeated cross-sectional study to examine the prevalence of reduced kidney function and kidney function decline and explore related risk factors in China.

Textbox 1. Definitions of reduced kidney function and kidney function decline.

Reduced kidney function

- An estimated glomerular filtration rate (eGFR) of below 60 mL/min per 1.73 m^2 is a widely used indicator of reduced kidney function [19].
  eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) study equation [20]: $eGFR = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ [if female], where Scr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κor 1, and max indicates the maximum of Scr/κ or 1.

Kidney function decline and rapid eGFR decline

- CKD is categorized in five stages (CKD stages G1–G5) based on the eGFR [19]. Kidney function decline [18, 19] was defined as a drop in the glomerular filtration rate (GFR) category (≥90 [G1], 60-89 [G2], 45-59 [G3a], 30-44 [G3b], 15-29 [G4], <15 [G5] mL/min per 1.73 m^2) accompanied by a ≥25% drop in eGFR from baseline, or a sustained decline in eGFR of >5 mL/min per 1.73 m^2/y. Rapid eGFR decline was defined as a decline in eGFR of greater than 3 mL/min/1.73m^2/y [18, 19]. The annual eGFR decline was calculated as ($eGFR_{baseline}$-$eGFR_{follow\text{-}up}$) /time (follow-up years).

METHODS

Study Design, setting and population

We performed a repeated cross-sectional study and accumulated data of routine health check-ups in a large primary care population between 2004-2020 in three primary health care centers in Zhengzhou City. Zhengzhou, the capital city of one of the biggest provinces in China (Henan), has a population of nearly 10 million. Participants could receive health check-up for several reasons; (1) if they were enrolled in the general practitioner-centered primary care system in the primary health centers at the first time, they had one free health check-up; (2) if they were aged 65 years or older, they had one free annual health check-up; and (3) some people voluntarily received a health check-up when they paid for it.

A total of 69473 residents underwent health check-ups between 2004-2020 in three primary health care centers. Serum creatinine was measured for 18295 residents; electronic records were included of all residents aged ≥ 18 years old (18273 participants). Using the creatinine measurements, we calculated the eGFR using the CKD-EPI study equation [20]. Follow-up data of serum creatinine measurement was available for 3314 participants (18%), with a mean follow-up duration of 1.5 years (study flow diagram in Figure 1). We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement [21] to report our study.

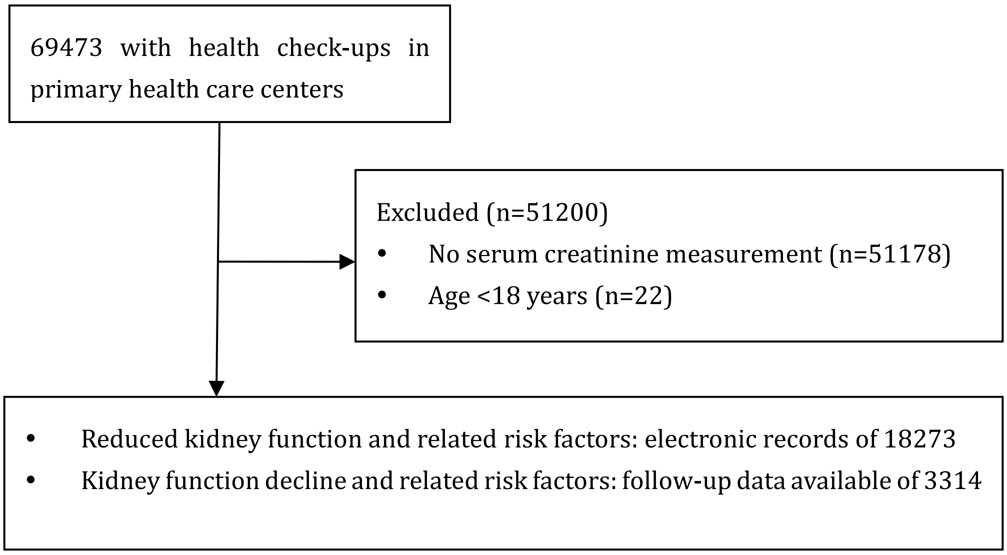

Figure 1. Study flow diagram.

Measurements

The health check-up results were entered into patient health care records by the patients' physicians. The health check-up data include information on demographic characteristics (age, sex), physical examination parameters (height, weight, body temperature, pulse, breathing rate, body mass index and blood pressure), laboratory tests findings (fasting blood glucose, liver function, kidney function and the blood lipids), electrocardiogram (ECG) results and specific diagnoses made by the physicians (e.g. diagnosis of hypertension). No urine tests were performed.

An anonymized database including electronic records was available for analysis. For our study, we extracted data on age, sex, body mass index (BMI), blood pressure (BP), fasting blood glucose, total cholesterol, fasting triglyceride, serum low-density lipoprotein (LDL) cholesterol, serum high-density lipoprotein (HDL) cholesterol, serum creatinine level, ECG test results and the diagnosis made by the physician.

Definitions

Definitions of reduced kidney function and kidney function decline are provided in Textbox 1.

BMI was categorized into underweight (<18.5 kg/m^2), healthy weight (18.5-23.9 kg/m^2), overweight (24-27.9 kg/m^2) and obesity (≥28 kg/m^2) by using the Chinese "Criteria of weight for adults (No. WS/T 428-2013, available on http://www.nhfpc.gov.cn)". Hypertension was defined as an average systolic BP (SBP)≥140mmHg or an average diastolic BP (DBP)≥90mmHg or a diagnosis of hypertension by a physician [22]. Diabetes was defined as a fasting blood glucose level of ≥7.00 mmol/L or a diagnosis of diabetes by a physician [9]. Dyslipidemia was defined as the presence of one or more abnormal serum lipid concentrations according to the Chinese guidelines for the prevention and treatment of dyslipidemia in adults [23]: total cholesterol>6.22 mmol/L; fasting triglycerides>2.26 mmol/L; LDL cholesterol>4.14 mmol/L; HDL cholesterol<1.04 mmol/L. Left ventricular hypertrophy (LVH) was defined as an ECG-aided physician-diagnosis of LVH.

The total number of CVD risk factors [9] per patient was calculated based on the presence of the following: obesity, hypertension, diabetes, dyslipidemia and LVH.

Statistical analysis

All statistical analyses were performed using SPSS version 23 (IBM, Armonk, NY, USA). Descriptive analyses were performed, calculating the mean ± standard deviation (SD), median (interquartile range, IQR) and the proportions of categorical variables as appropriate. Continuous variables were compared using *t*-tests. Categorical variables were compared using Chi-square and Fisher's exact tests, as appropriate.

In the database of electronic records of 18273 adults, data were missing for SBP (0. 1%), DBP (0.1%), BMI (0.3%), fasting blood glucose (1.5%), total cholesterol (0.6%), fasting triglyceride (0.7%), serum LDL cholesterol (19.8%) and serum HDL cholesterol (19.9%). For the follow-up electronic records of 3314 out of the total 18273 participants, data were missing for SBP (0.3%), DBP (0.3%), BMI (0.4%), fasting blood glucose (1.6%), total cholesterol (0.4%), fasting triglyceride (0.5%), serum LDL cholesterol (42.6%) and serum

HDL cholesterol (42.8%). Multiple data imputation was used to handle the missing data [24]. We compared multivariable logistic regression analyses results by using multivariable multiple imputations of 10 imputations and 20 imputations and similar results were found. Hence, we used multivariable multiple imputations with 10 imputations and assumed the data were completely missing at random. The univariable analyses were performed on the complete case data and the multivariable logistic regression analyses were performed on each imputed dataset.

Univariable and multivariable logistic regression analyses were used to explore the association between reduced kidney function and potential risk factors. In the first model, we adjusted for sex and age (per year increase). In the second model, based on the results of univariable analyses and previous literature reporting risk factors of reduced kidney function [10, 25], we additionally adjusted for hypertension (yes versus no), BMI (healthy weight [reference] versus underweight versus overweight versus obesity), diabetes (yes versus no), LVH (yes versus no), dyslipidemia (yes versus no) and the number of CVD risk factors (0 [reference] versus 1-2 versus ≥3). Similarly, we used univariable and multivariable logistic regression analyses to examine the association between kidney function decline and potential risk factors. All tests were two-sided with a significance level of P values<0.05. Also, to account for multiple testing, we used the Bonferroni correction and reported significant associations for which P<0.05/number of comparisons in univariable analyses.

RESULTS

Participant characteristics

Participant characteristics are shown in Table 1 and Table 2. Of all participants, 9213 (50.4 %) were aged ≥70 years and 10756 (58.9%) were female. The mean eGFR from the first measurement was 81.56±25.73 mL/min/1.73m^2.

Prevalence of reduced kidney function and kidney function decline

Of all participants, 3273 (17.9%) had reduced kidney function at first measurement. For people aged ≥60 years old, 3034 (18.8%) had reduced kidney function vs. 239 (10.7%) for people <60 years old (Table 1). Of the participants with a follow-up, 640 (19.3%) had kidney function decline and 755 (22.8%) had rapid eGFR decline (Table 2).

Factors associated with reduced kidney function

Table 1 shows that the following factors were associated with reduced kidney function: sex, age, hypertension, BMI, diabetes, LVH, dyslipidemia and the number of CVD risk factors. After applying the Bonferroni correction, hypertension was no longer significantly associated with reduced kidney function. Using univariable and multivariable logistic regression models, in the final model, female sex, older age, hypertension, overweight, obesity, diabetes, LVH and dyslipidemia were independent predictors of reduced kidney function (Table 3). When considering total cholesterol, fasting triglycerides, LDL cholesterol, HDL cholesterol as separate risk factors, the multivariable logistic regression analysis showed that female sex, older age, hypertension, overweight, obesity, diabetes, LVH, fasting triglyceride>2.26 mmol/L and serum HDL cholesterol<1.04 mmol/L were independent predictors of reduced kidney function (Additional file 1).

Factors associated with kidney function decline

Table 2 shows that the following factors were associated with kidney function decline: a reduced kidney function at baseline, sex, hypertension, dyslipidemia and the number of CVD risk factors. After applying the Bonferroni correction, hypertension and the number of CVD risk factors were no longer significantly associated with kidney function decline. Using univariable and multivariable logistic regression models, in the final model, older age and a reduced kidney function at baseline were independent predictors of kidney function decline (Table 4). When considering total cholesterol, fasting triglycerides, LDL cholesterol, HDL cholesterol as separate risk factors, the multivariable logistic regression analysis showed that older age and a reduced kidney function at baseline were independent predictors of kidney function decline (Additional file 2).

Table 1. Participants characteristics and related prevalence of reduced kidney function.

Category	No. of participants	Overall	Participants with eGFR≥60 mL/min per 1.73 m^2 (n=15000)	Participants with eGFR<60 mL/min per 1.73 m^2 (n=3273)	*P -value*
Sex	18273				<0.001
-Female, n %		10756(58.9)	8382(55.9)	2374(72.5)	
Age, mean (SD), years	18273	69.4(10.7)	68.8(10.9)	72.5(9.3)	<0.001
Age (years)					<0.001
-18-39, n %		403(2.2)	395(2.6)	8(0.2)	
-40-59, n %		1815(9.9)	1584(10.6)	231(7.1)	
-60-69, n %		6842(37.4)	5802(38.7)	1040(31.8)	
-≥70, n %		9213(50.4)	7219(48.1)	1994(60.9)	
Hypertension, n %	18250	3321(18.2)	2772(18.5)	549(16.8)	0.024
-Systolic BP, mean (SD), mmHg		129.8(12.2)	129.8(12.1)	129.7(12.4)	0.664
-Diastolic BP, mean (SD), mmHg		76.9(7.7)	76.9(7.8)	76.9(7.4)	0.862
BMI, mean (SD), kg/m^2	18217	24.5(2.9)	24.4(2.9)	24.9(3.2)	<0.001
-Healthy weight (BMI, 18.5-23.9 kg/m^2), n %		8301(45.6)	6998(46.8)	1303(40.1)	<0.001
-Underweight (BMI<18.5 kg/m^2), n %		256(1.4)	222(1.5)	34(1.0)	0.054
-Overweight (BMI, 24-27.9 kg/m^2), n %		7563(41.5)	6181(41.3)	1382(42.5)	0.217
-Obesity (BMI≥28 kg/m^2), n %		2097(11.5)	1563(10.4)	534(16.4)	<0.001
Diabetes (FBG≥7 mmol/L), n %	18005	2395(13.3)	1864(12.6)	531(16.4)	<0.001
-FBG, mean (SD), mmol/L		5.9(2.4)	5.9(2.2)	6.2(3.2)	<0.001

Left ventricular hypertrophy, n %	17293	167 (1)	122(0.9)	45(1.5)	0.002
Dyslipidemia, n %	15541	5053(32.5)	4152(30.6)	901(45.2)	<0.001
-Total cholesterol>6.22 mmol/L	18163	1632(9.0)	1215(8.2)	417(12.8)	<0.001
-Fasting triglyceride>2.26 mmol/L	18153	2893(15.9)	2431(16.2)	462(14.2)	0.002
-Serum LDL cholesterol>4.14 mmol/L	14660	601(4.1)	521(4.0)	80(5.2)	0.019
-Serum HDL cholesterol<1.04 mmol/L	14631	1315 (9)	1150(8.8)	165(10.9)	0.006
No. of CVD risk factors	14568				<0.001
-0, n %		6794(46.6)	6175(48.5)	619(33.8)	
-1, n %		5107(35.1)	4401(34.5)	706(38.6)	
-2, n %		2080(14.3)	1692(13.3)	388(21.2)	
-3, n %		521(3.6)	420(3.3)	101(5.5)	
-4, n %		65(0.4)	50(0.4)	15(0.8)	
-5, n %		1(0)	1(0)	0(0)	

Abbreviations: eGFR: estimated glomerular filtration rate; BP: blood pressure; BMI: body mass index; FBG: fasting blood-glucose; LDL: low-density lipoprotein; HDL: high-density lipoprotein; CVD: cardiovascular disease.

Table 2. Participants characteristics and related presence of kidney function decline.

Category	No. of participants	Overall	No kidney function decline (n=2674)	With kidney function decline (n=640)	*P*-value
Baseline eGFR, mean (SD), mL/min per 1.73 m²	3314		66.9 (20.1)	90.3(41.3)	<0.001
Reduced kidney function at baseline, n %	3314	2172(65.5)	1568(58.6)	604(94.4)	<0.001
Sex	3314				0.001
-Female, n %		2051(61.9)	1693(63.3)	358(55.9)	
Age, mean (SD), years	3314	69.9(9.1)	69.9(9.0)	69.6(9.3)	0.477
Age (years)	3314				0.709
-18-39, n %		15(0.5)	11(0.4)	4(0.6)	
-40-59, n %		307(9.3)	244(9.1)	63(9.8)	
-60-69, n %		1390(41.9)	1116(41.7)	274(42.8)	
-≥70, n %		1602(48.3)	1303(48.7)	299(46.7)	
Hypertension, n %	3304	603(18.3)	469(17.6)	134(21.0)	0.045
-Systolic BP, mean (SD), mmHg		130.2(12.5)	130.2(12.1)	130.2(14.0)	0.981
-Diastolic BP, mean (SD), mmHg		77.4(7.5)	77.5(7.3)	76.9(8.4)	0.141
BMI, mean (SD), kg/m²	3301	24.8 (3.1)	24.9(3.1)	24.6(3.1)	0.076
-Healthy weight (BMI, 18.5-23.9 kg/m²), n %		1323(40.1)	1050(39.4)	273(42.7)	0.129

-Underweight (BMI<18.5 kg/m^2), n %		48(1.5)	35(1.3)	13(2.0)	0.172
-Overweight (BMI, 24-27.9 kg/m^2), n %		1449(43.9)	1178(44.3)	271(42.4)	0.399
-Obesity (BMI≥28 kg/m^2), n %		481(14.6)	399(15.0)	82(12.8)	0.165
Diabetes (FBG≥7 mmol/L), n %	3260	569(17.5)	473(18.0)	96(15.3)	0.111
-FBG, mean (SD), mmol/L		6.1(2.5)	6.1 (2.5)	6.1(2.3)	0.482
Left ventricular hypertrophy, n %	3061	24(0.8)	20(0.8)	4(0.7)	0.941
Dyslipidemia, n %	2265	1093(48.3)	894(50.4)	199(40.6)	<0.001
-Total cholesterol>6.22 mmol/L	3300	356(10.8)	294(11.0)	62(9.7)	0.339
-Fasting triglyceride>2.26 mmol/L	3296	530(16.1)	429(16.1)	101(15.9)	0.894
-Serum LDL cholesterol>4.14 mmol/L	1862	52(2.8)	45(3.1)	7(1.7)	0.113
-Serum HDL cholesterol<1.04 mmol/L	1857	222(12.0)	183(12.7)	39(9.4)	0.066
No. of CVD risk factors	2050				0.041
-0, n %		635(31.0)	472(29.4)	163(36.9)	
-1, n %		887(43.3)	707(44.0)	180(40.7)	
-2, n %		422(20.6)	345(21.5)	77(17.4)	
-3, n %		96(4.7)	76(4.7)	20(4.5)	
-4, n %		10(0.5)	8(0.5)	2(0.5)	

Abbreviations: eGFR: estimated glomerular filtration rate; BP: blood pressure; BMI: body mass index; FBG: fasting blood-glucose; LDL: low-density lipoprotein; HDL: high-density lipoprotein; CVD: cardiovascular disease.

Table 3. Factors associated with reduced kidney function.

Analysis	Univariable		Model 1		Model 2	
	OR (95% CI)	*P -value*	OR (95% CI)	*P -value*	OR (95% CI)	*P -value*
Female	2.085(1.918-2.266)	<0.001	2.185(2.008-2.377)	<0.001	2.208(1.974-2.470)	<0.001
Age (per year increase)	1.038(1.034-1.042)	<0.001	1.040(1.036-1.045)	<0.001	1.051(1.046-1.057)	<0.001
Hypertension	0.889(0.804-0.983)	0.022			0.847(0.719-0.997)	0.046
Body mass index						
-Healthy weight (BMI, 18.5-23.9 kg/m^2)	Reference				Reference	
-Underweight (BMI<18.5 kg/m^2)	0.825(0.572-1.191)	0.305			0.932(0.606-1.434)	0.750
-Overweight (BMI, 24-27.9 kg/m^2)	1.202(1.106-1.306)	<0.001			1.162(1.042-1.296)	0.007
-Obesity (BMI≥28 kg/m2)	1.833(1.635-2.056)	<0.001			1.609(1.349-1.919)	<0.001
Diabetes (FBG≥7 mmol/L)	1.361(1.225-1.511)	<0.001			1.229(1.043-1.447)	0.014
Left ventricular hypertrophy	1.726(1.224-2.435)	0.002			2.123(1.407-3.203)	<0.001
Dyslipidemia	2.572(2.348-2.816)	<0.001			2.478(2.086-2.943)	<0.001
No. of CVD risk factors						
-0	Reference				Reference	
-1-2	2.316(2.090-2.566)	<0.001			1.207(0.982-1.482)	0.073
-≥3	3.109(2.542-3.801)	<0.001			0.945(0.605-1.474)	0.801

Abbreviations: OR: odds ratio; CI: confidence interval; BMI: body mass index; FBG: fasting blood-glucose; LDL: low-density lipoprotein; HDL: high-density lipoprotein; CVD: cardiovascular disease. Model 1 was adjusted for sex and age; Model 2 adjusted for sex, age, hypertension, body mass index, diabetes and left ventricular hypertrophy, dyslipidemia and no. of CVD risk factors.

Table 4. Factors associated with kidney function decline.

Analysis	Univariable		Model 1		Model 2	
	OR (95% CI)	*P -value*	OR (95% CI)	*P -value*	OR (95% CI)	*P -value*
Female	0.736(0.618-0.876)	0.001	0.735(0.617-0.875)	0.001	0.867(0.715-1.050)	0.143
Age (per year increase)	0.997(0.987-1.006)	0.477	0.996(0.987-1.006)	0.435	1.013(1.002-1.023)	0.018
Reduced kidney function at baseline	11.834(8.382-16.709)	<0.001			11.133(7.827-15.836)	<0.001
Hypertension	1.244(1.003-1.543)	0.047			1.074(0.746-1.545)	0.701
Body mass index						
-Healthy weight (BMI, 18.5-23.9 kg/m^2)	Reference				Reference	
-Underweight (BMI<18.5 kg/m^2)	1.414(0.738-2.710)	0.297			1.133(0.558-2.302)	0.729
-Overweight (BMI, 24-27.9 kg/m^2)	0.886(0.735-1.069)	0.208			0.913(0.744-1.122)	0.389
-Obesity (BMI≥28 kg/m2)	0.791(0.603-1.039)	0.092			1.035(0.701-1.529)	0.862
Diabetes (FBG≥7 mmol/L)	0.834(0.656-1.060)	0.138			0.907(0.637-1.292)	0.588
Left ventricular hypertrophy	0.833(0.284-2.446)	0.740			0.771(0.241-2.465)	0.660
Dyslipidemia	0.819(0.671-0.999)	0.049			0.921(0.628-1.349)	0.670
No. of CVD risk factors						
-0	Reference				Reference	
-1-2	0.847(0.691-1.038)	0.109			0.887(0.570-1.382)	0.595
-≥3	0.918(0.584-0.444)	0.713			0.923(0.320-2.661)	0.882

Abbreviations: OR: odds ratio; CI: confidence interval; BMI: body mass index; FBG: fasting blood-glucose; LDL: low-density lipoprotein; HDL: high-density lipoprotein; CVD: cardiovascular disease. Model 1 was adjusted for sex and age; Model 2 adjusted for sex, age, hypertension, body mass index, diabetes and left ventricular hypertrophy, dyslipidemia and no. of CVD risk factors.

DISCUSSION

This study explored the prevalence of reduced kidney function and kidney function decline in a large, urban Chinese primary care population. Results revealed a prevalence of reduced kidney function of 17.9% and a prevalence of kidney function decline of 19.3%. The prevalence of rapid eGFR decline was 22.8%. Female sex, older age, hypertension, overweight, obesity, diabetes, LVH and dyslipidemia were independent predictors of reduced kidney function. Moreover, older age and a reduced kidney function at baseline were independent predictors of kidney function decline.

Prevalence of reduced kidney function and kidney function decline

The prevalence of reduced kidney function that we found was similar to the 12-23% reported in previous studies in the elderly Chinese population based on health check-up data [15-17]. Our study population was relatively old (69.4±10.7 years). For other countries, the prevalence of reduced kidney function in older people was reported to be 37.1% to 61.7% (Germany; age>70 years old) [26], 19.6% (Brazil; aged ≥60 years) [27] and 11.2% (Australia; mean age of 62 years old) [28]. These discrepancies found may partially be explained by differences in the equations to estimate GFR [26], characteristics of the populations and the setting. Our study was conducted in a primary care setting, while other studies were conducted in community settings; patients could suffer from a chronic illness. This could also explain why we found a higher prevalence of kidney function decline and rapid eGFR decline compared to a previous Chinese community-based population study reporting normal kidney function at baseline [18]. Additionally, the prevalence of rapid eGFR decline in our study was higher than the reported 16% in a community-based cohort of ambulatory elderly individuals in the United States [29]. This could also be explained by the fact that we included data of both participants with and without reduced kidney function at baseline; people with reduced kidney function at baseline would more likely have kidney function decline. Also, the disparity in quality of and access to health care between areas in China could lead to the higher prevalence of kidney function decline in our study. For instance, the previous study was conducted in Beijing with better health care resources than our study setting [18].

Factors associated with reduced kidney function and kidney function decline

We found that diabetes was independently associated with reduced kidney function, which is consistent with a previous study [30]**.** The Global Burden of Disease study suggested that diabetes affects 6.6% of the overall (all-age) Chinese population [31]. Moreover, LVH was revealed as a risk factor for reduced kidney function, which corroborates previous findings [9]. Notably, hypertension, which is a key risk factor of LVH [32], was associated with a lower risk of reduced kidney function in the current study. This could be explained by the use of antihypertensive medications in patients with reduced kidney function in our population. People with reduced kidney function may have been undertreated for CKD and also already treated for hypertension. In the past twenty years, a noteworthy increase in the prevalence of hypertension in the Chinese population has occurred; hypertension affects nearly 23.2% of Chinese adults [33]. Future studies with information on participants' medication use are needed to explore this question further.

Female sex was shown as a risk factor for reduced kidney function, which corroborates previous findings [7]. However, in contrast, other studies indicated that being male is an independent risk factor for reduced kidney function [34]. Future studies can clarify the association between gender difference and reduced kidney function by considering lifestyle differences, such as dietary protein intake, salt, smoking and alcohol intake [35]. Additionally, overweight and obesity were associated with an increased risk of reduced kidney function in our study. Previous data also linked overweight and obesity to reduced kidney function [30, 36] and CKD progression [37]. Overweight and obesity are widely prevalent and are major public health concerns [38, 39].

Previous studies suggested that dyslipidemia mostly develops along with kidney function decline in patients with CKD, even in the early stages. It is also the major risk factor for CVD in patients with CKD [40]. In our study, the prevalence of dyslipidemia was 32.5%, which is similar to a previous survey [36]. We also demonstrated that dyslipidemia was associated with reduced kidney function. Thompson *et al*. found that reduced kidney function was independently associated with lower concentrations of HDL cholesterol and higher concentrations of triglycerides in an Australian population [25]. Similarly, in our study, the proportion of low HDL cholesterol was higher in participants with reduced kidney function than in participants without reduced kidney function. However, the proportion of high fasting triglyceride was lower in participants with reduced kidney function than in participants without reduced kidney function. This could be explained by the use of anti-dyslipidemia medications in patients with reduced kidney function in our population. Nevertheless, the high proportion of high fasting triglyceride still deserves medical attention due to its notable consequences.

Strengths and limitations

Our study has several strengths. To our knowledge, this study is the first primary care population-based study in China to examine the prevalence of kidney function decline and rapid eGFR decline. Also, our study has a large sample size and conducts analyses based on real-world data.

Nevertheless, several limitations should be noted. First, as our study focused on people with health check-up records, information concerning urine tests (e.g. data of albuminuria), the usage of medications such as anti-hypertensive, anti-diabetic and anti-dyslipidemia drugs, self-reported history such as smoking and alcohol use of people and socioeconomic status were not available. Secondly, as participants aged 65 years or older had one free annual health check-up, the entire study population was relatively old. Therefore, the prevalence of reduced kidney function and kidney function decline can be overestimated. Also, these findings may not generalize to the younger population. Third, the serum creatinine measurement was available for 18273 (26.3%) of 69473 people and the follow-up data were available for 3314 (18%) of 18273 people. The related reasons for the lack of data were unknown and could influence the results. For instance, patients with more severe kidney impairment may go for health check-ups more frequently. A prospective cohort study can be conducted for further exploration.

Implications for future research initiatives

To reduce the substantial burden of CKD in the Chinese primary care population, an effective prevention and treatment health care system is needed. For instance, three-level prevention and treatment programs are being developed in Chinese settings [41]. These programs often include primary prevention and treatment, which focuses on targeted screening to achieve early detection of CKD in at-risk groups (e.g. people with diabetes); secondary prevention and treatment, which focuses on the referral of those identified as pre-existing CKD to community hospitals and aims to slow disease progression; tertiary prevention and treatment, which aims to avoid or delay dialysis or kidney transplantation for patients with advanced CKD.

To enhance the development of three-level prevention and treatment system in Chinese settings, we suggest the following initiatives. First, we advise future researchers to implement (online) training and education such as e-learning on CKD prevention and treatment to increase public and health care professional awareness about CKD and its risk factors. Also, considering the risk factors of reduced kidney function are mostly related to lifestyle-related factors such as overweight, lifestyle interventions are needed to support individuals' self-management and improve their health behaviors. As there is an enormous shortage of healthcare professionals in China [42], electronic health (eHealth)-based lifestyle interventions are more accessible and widely used [43]. Second, to support the referral of patients with kidney impairment to a nephrologist in a secondary or tertiary hospital, national guidelines should be developed for medical specialists such as the referral criteria adopted in the Netherlands [44]. Also, an improved primary healthcare system supporting the implementation of integrated approaches can help manage the increasing burden of CKD [45], for instance, the Innovative Care for Chronic Conditions (ICCC) proposed by the World Health Organization (WHO) [46].

CONCLUSIONS

The high prevalence of reduced kidney function and kidney function decline indicates that CKD is a severe public health problem in China. Female sex, older age, hypertension, overweight, obesity, diabetes, LVH and dyslipidemia were independent predictors of reduced kidney function, and older age, a reduced kidney function at baseline to kidney function decline. To reduce the substantial CVD risk and CKD burden in Chinese primary care populations, three-level preventive and treatment programs need to be developed and enhanced. Important strategies would include an (online) education and training program to promote awareness of CKD, widely and accessible (eHealth-based) lifestyle interventions, national guidelines for referral of identified patients to a nephrologist and improving the primary healthcare systems to support the implementation of integrated approaches.

Authors' contributions

HS led the conception and design of this study and is the main contributor in writing this manuscript. HS and WW participated in data collection and analysis. WW, RK, PB, XC, EB, XL and NC contributed to the conception and design of the study and editing of this manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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Additional file 1. Factors associated with reduced kidney function.

Analysis	Univariable		Model 1		Model 2	
	OR (95% CI)	*P -value*	OR (95% CI)	*P -value*	OR (95% CI)	*P -value*
Female	2.085(1.918-2.266)	<0.001	2.185(2.008-2.377)	<0.001	2.171(2.140-2.203)	<0.001
Age (per year increase)	1.038(1.034-1.042)	<0.001	1.040(1.036-1.045)	<0.001	1.070(1.067-1.074)	<0.001
Hypertension	0.889(0.804-0.983)	0.022			1.369(1.109-1.689)	0.003
Body mass index						
-Healthy weight (BMI, 18.5-23.9 kg/m^2)	Reference				Reference	
-Underweight (BMI<18.5 kg/m^2)	0.825(0.572-1.191)	0.305			0.933(0.578-1.507)	0.778
-Overweight (BMI, 24-27.9 kg/m^2)	1.202(1.106-1.306)	<0.001			1.139(1.005-1.289)	0.041
-Obesity (BMI≥28 kg/m2)	1.833(1.635-2.056)	<0.001			1.508(1.193-1.905)	0.001
Diabetes (FBG≥7 mmol/L)	1.361(1.225-1.511)	<0.001			1.299(1.042-1.618)	0.020
Left ventricular hypertrophy	1.726(1.224-2.435)	0.002			2.702(1.723-4.238)	<0.001
Total cholesterol>6.22 mmol/L	1.628(1.447-1.833)	<0.001			1.279(0.963-1.700)	0.089
Fasting triglyceride>2.26 mmol/L	0.845(0.759-0.941)	0.002			0.730(0.577-0.922)	0.008
Serum LDL cholesterol>4.14 mmol/L	3.423(3.010-3.893)	<0.001			1.224(0.864-1.734)	0.254
Serum HDL cholesterol<1.04 mmol/L	1.274(1.072-1.514)	0.006			1.793(1.414-2.273)	<0.001
No. of CVD risk factors						
-0	Reference				Reference	
-1-2	1.226(1.092-1.377)	0.001			0.915(0.714-1.173)	0.483
-≥3	1.439(1.168-1.773)	0.001			0.689(0.391-1.214)	0.197

The total number of CVD risk factors per patient was calculated based on the presence of the following: obesity, hypertension, diabetes, abnormal total cholesterol, abnormal fasting triglycerides, abnormal LDL cholesterol, abnormal LDL cholesterol and LVH. Abbreviations: OR: odds ratio; CI: confidence interval; BMI: body mass index; FBG: fasting blood-glucose; LDL: low-density lipoprotein; HDL: high-density lipoprotein; CVD: cardiovascular disease. Model 1 was adjusted for sex and age; Model 2 adjusted for sex, age, hypertension, body mass index, diabetes and left ventricular hypertrophy, total cholesterol>6.22 mmol/L, fasting triglyceride>2.26 mmol/L, serum LDL cholesterol>4.14 mmol/L, serum HDL cholesterol<1.04 mmol/L and no. of CVD risk factors.

Additional file 2. Factors associated with kidney function decline.

Analysis	Univariable		Model 1		Model 2	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Female	0.736(0.618-0.876)	0.001	0.735(0.617-0.875)	0.001	0.848(0.697-1.031)	0.099
Age (per year increase)	0.997(0.987-1.006)	0.477	0.996(0.987-1.006)	0.435	1.013(1.002-1.024)	0.016
Reduced kidney function at baseline	11.834(8.382-16.709)	<0.001			11.193(7.863-15.933)	<0.001
Hypertension	1.244(1.003-1.543)	0.047			1.218(0.875-1.695)	0.241
Body mass index						
-Healthy weight (BMI, 18.5-23.9 kg/m^2)	Reference				Reference	
-Underweight (BMI<18.5 kg/m^2)	1.414(0.738-2.710)	0.297			1.125(0.554-2.286)	0.744
-Overweight (BMI, 24-27.9 kg/m^2)	0.886(0.735-1.069)	0.208			0.910(0.740-1.119)	0.371
-Obesity (BMI≥28 kg/m2)	0.791(0.603-1.039)	0.092			1.174(0.803-1.718)	0.408
Diabetes (FBG≥7 mmol/L)	0.834(0.656-1.060)	0.138			0.997(0.714-1.392)	0.987
Left ventricular hypertrophy	0.833(0.284-2.446)	0.740			0.871(0.276-2.751	0.814
Total cholesterol>6.22 mmol/L	0.868(0.651-1.159)	0.338			1.277(0.849-1.921)	0.239
Fasting triglyceride>2.26 mmol/L	0.998(0.789-1.263)	0.988			1.290(0.904-1.839)	0.160
Serum LDL cholesterol>4.14 mmol/L	0.767(0.424-1.387)	0.379			0.821(0.388-1.739)	0.605
Serum HDL cholesterol<1.04 mmol/L	0.808(0.587-1.112)	0.189			0.926(0.618-1.387)	0.708
No. of CVD risk factors						
-0	Reference				Reference	
-1-2	0.850(0.691-1.045)	0.122			0.727(0.505-1.047)	0.087
-≥3	0.863(0.604-1.234)	0.419			0.606(0.264-1.393)	0.237

The total number of CVD risk factors per patient was calculated based on the presence of the following: obesity, hypertension, diabetes, abnormal total cholesterol, abnormal fasting triglycerides, abnormal LDL cholesterol, abnormal LDL cholesterol and LVH. Abbreviations: OR: odds ratio; CI: confidence interval; BMI: body mass index; FBG: fasting blood-glucose; LDL: low-density lipoprotein; HDL: high-density lipoprotein; CVD: cardiovascular disease Model 1 was adjusted for sex and age; Model 2 adjusted for sex, age, hypertension, body mass index, diabetes and left ventricular hypertrophy, total cholesterol>6.22 mmol/L, fasting triglyceride>2.26 mmol/L, serum LDL cholesterol>4.14 mmol/L, serum HDL cholesterol<1.04 mmol/L and no. of CVD risk factors.