Association of Chronic Kidney Disease with Coronary Heart Disease and Stroke Risks in Patients with Type 2 Diabetes Mellitus: An Observational Cross-sectional Study in Hangzhou, China

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Abstract

Background: Chronic kidney disease (CKD) is an independent risk factor for cardiovascular disease (CVD). However, the association between CKD and CVD risk in patients with type 2 diabetes mellitus (T2DM) in China has not yet been well investigated. This study aimed to determine the association of CKD with the risks of coronary heart disease (CHD) and stroke in a Chinese population with T2DM.
Methods: A total of 1401 inpatients with T2DM at the Second Affiliated Hospital of Zhejiang University School of Medicine between April 2008 and November 2013 were included in this study. The CKD-Epidemiology Collaboration equation for Asians was used to classify CKD. The UK Prospective Diabetes Study risk engine was used to estimate the risks of CHD and stroke.
Results: CHD risk was significantly increased with CKD stage (20.1%, 24.8%, and 34.3% in T2DM patients with no CKD, CKD Stage 1–2, and Stage 3–5, respectively; $P < 0.001$ for all). The stroke risk was also increased with CKD stage (8.6%, 12.7%, and 25.4% in T2DM patients with no CKD, CKD Stage 1–2, and Stage 3–5, respectively; $P < 0.001$ for all). Compared with no-CKD group, the odds ratios (*OR*s) for high CHD risk were 1.7 ($P < 0.001$) in the CKD Stage 1–2 group and 3.5 ($P < 0.001$) in the CKD Stage 3–5 group. The corresponding *OR*s for high stroke risk were 1.9 ($P < 0.001$) and 8.2 ($P < 0.001$), respectively.
Conclusion: In patients with T2DM, advanced CKD stage was associated with the increased risks of CHD and stroke.

Key words: Chronic Kidney Disease; Coronary Disease; Stroke; Diabetes Mellitus

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is associated with an increased risk of cardiovascular disease (CVD) mortality.[1] Approximately half of all deaths in T2DM patients are attributable to coronary heart disease (CHD), and 15% are caused by stroke.[2] In addition, the prevalence of diabetic kidney disease among adults with diabetes mellitus is reported to be 34.5%.[3] Annual assessments of urine albumin excretion and estimated glomerular filtration rate (eGFR) are recommended to detect and monitor kidney damage in patients with T2DM.[4] The classification of chronic kidney disease (CKD) is based on both eGFR and urine albumin excretion. In a randomized, controlled, multicenter trial (ADVANCE study), high albuminuria and low eGFR were proved to be independent risk factors for cardiovascular events among T2DM patients.[5] Moreover, in another prospective cohort study in the United States, CKD was confirmed to be associated with an increase in stroke risk.[6]

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However, the association of CKD with the risks of CHD and stroke in Chinese patients with T2DM has seldom been thoroughly investigated. To evaluate these two risks, we chose the UK Prospective Diabetes Study (UKPDS) risk engine, which is a T2DM-specific risk calculator from the UKPDS.[7] A cross-sectional study has shown that the UKPDS risk engine has good feasibility, convergent validity, and sensitivity in predicting CHD risk in Chinese diabetic patients.[8] The present study sought to determine whether CKD was correlated with the CHD and stroke risk scores computed using the UKPDS risk engine in T2DM patients from Zhejiang, China.

METHODS

Subjects

A total of 1401 inpatients with T2DM (802 men and 599 women, aged 58.4 ± 12.9 years [21–94 years]) at the Second Affiliated Hospital of Zhejiang University School of Medicine between April 2008 and November 2013 were enrolled in this cross-sectional study. T2DM was diagnosed according to the WHO (1999) criteria.[9] Individuals with obvious symptoms were diagnosed with diabetes mellitus if one of the following was present: (1) fasting blood glucose (FBG) ≥7.0 mmol/L; (2) plasma glucose ≥11.1 mmol/L at 2 h after an oral glucose tolerance test; or (3) random plasma glucose ≥11.1 mmol/L. The diagnosis was confirmed on another day in patients with atypical symptoms. The duration of diabetes ranged from 0 to 36 years. The exclusion criteria included the following: Type 1 diabetes mellitus; gestational diabetes mellitus; specific types of diabetes attributable to other causes; urinary tract infections; Cushing disease; cancer; hematological diseases including multiple myeloma, leukemia and lymphoma; systemic lupus erythematosus; and the use of drugs those affect urine albumin-to-creatinine radio (UACR) and eGFR. This study was approved by the Ethics Committee of the Second Affiliated Hospital of Zhejiang University School of Medicine (Zhejiang, China). All participants provided informed consent.

Age, sex, smoking status, and duration of diabetes mellitus were recorded. Smoking status was divided into three categories: "current smoker" if the individual had regularly smoked in the past 1 year; "nonsmoker" if the individual had never regularly smoked; and "ex-smoker" if the individual had stopped smoking for at least 1 year.

Height, body weight, waist circumference, and blood pressure were recorded. Height and weight were measured in light indoor clothing and without shoes. Body mass index was calculated as the ratio of weight (kg) and height squared (m²). Waist circumference was measured at the umbilicus at the end of a normal expiration while standing. Diastolic and systolic blood pressures were measured with a standard sphygmomanometer after at least 5 min of supine rest after patients came to the in-patient department. Hypertension was defined as a systolic blood pressure ≥140 mmHg (1 mmHg = 0.133 kpa), diastolic blood pressure ≥90 mmHg, and/or the use of antihypertensive drugs.

Biochemical parameters

Venous blood samples were collected between 6:00 a.m. and 9:00 a.m. after overnight fasting. FBG, creatinine, total cholesterol, triglyceride, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol (HDL-C) were measured using the Beckman Coulter Chemistry Analyzer AU5400 series (Beckman Coulter Biomedical K.K, Tokyo, Japan). Glycosylated hemoglobin (HbA1c) was measured by high-performance liquid chromatography using Tosoh HLC-723G8 (Tosoh Corporation, Yamaguchi 746-0042, Japan). Screening for UACR was performed using a random, spot urine sample, and the results were expressed in milligrams per gram of creatinine. Urine albumin was measured by nephelometry immunoassay with the SIEMENS BN II System (Siemens Healthcare Diagnostics Products GmbH, 35041 Marburg, Germany).

Urine albumin-to-creatinine radio groups

According to the American Diabetic Association classification of microalbuminuria, patients were divided into three groups: normal albumin group, spot UACR <30 mg/g·Cr; microalbuminuria, spot UACR 30–299 mg/g·Cr; and macroalbuminuria, spot UACR ≥300 mg/g·Cr.[10]

Chronic kidney disease subgroups

GFR was calculated using the modified CKD-Epidemiology Collaboration (CKD-EPI) equation for Asians[11] as follows.

For males:

$$SCr \leq 9 \text{ mg/L}; eGFR_{CKD-EPI} = 141 \times (SCr/0.9)^{-0.411} \times 0.993^{Age} \times 1.057$$

$$SCr > 9 \text{ mg/L}; eGFR_{CKD-EPI} = 141 \times (SCr/0.9)^{-1.209} \times 0.993^{Age} \times 1.057$$

For females:

$$SCr \leq 7 \text{ mg/L}; eGFR_{CKD-EPI} = 144 \times (SCr/0.7)^{-0.329} \times 0.993^{Age} \times 1.049$$

$$SCr > 7 \text{ mg/L}; eGFR_{CKD-EPI} = 144 \times (SCr/0.7)^{-1.209} \times 0.993^{Age} \times 1.049$$

Where SCr = Serum creatinine.

The patients were classified into five CKD stages according to the 2002 Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines:[12] Stage 1, kidney damage (indicated by albuminuria ≥30 mg/24 h or 20 mg/L, clinical proteinuria ≥300 mg/24 h or ≥200 mg/L, or a positive dipstick test for proteinuria) and eGFR ≥90 ml·min⁻¹·1.73 m⁻²; Stage 2, kidney damage and eGFR 60–89 ml·min⁻¹·1.73 m⁻²; Stage 3, eGFR 30–59 ml·min⁻¹·1.73 m⁻²; Stage 4, eGFR 15–29 ml·min⁻¹·1.73 m⁻²; and Stage 5, eGFR <15 ml·min⁻¹·1.73 m⁻².

UK Prospective Diabetes Study risk engine

The UKPDS risk engine version 2.0 for windows was used to evaluate CHD and stroke risks. This scale has been validated specifically for patients with diabetes[13] and provides an estimate of the risks for a new CHD event and stroke (fatal and nonfatal).[7] The data used to calculate the UKPDS risk scores (available at http://www.dtu.ox.ac.uk/riskengine/download.php) included HbA1c, systolic blood pressure, serum total cholesterol and HDL-C, atrial fibrillation, sex, age, ethnicity, smoking status, and diabetes duration. The

risks of CHD, fatal CHD, stroke, and fatal stroke were estimated for 10 years.[7] CHD was defined as the occurrence of a fatal or nonfatal myocardial infarction or sudden death. In this study, cases with risk higher than 20% were classified into the high-risk group whereas those with a risk score lower than 20% were classified into the low-to-moderate risk group.

Statistical analysis

All statistical analyses were performed using SPSS 20.0 (IBM, USA) software. Continuous variables were expressed as mean ± standard deviation, median (25th–75th percentiles), or mean (95% confidence interval [CI]), and categorical variables were reported as percentages. Normally distributed continuous variables were compared using one-way analysis of variance and the least-significant difference test was used for comparisons between pairs of groups. The method of rank transform analysis was used for the data of abnormal distributions and comparisons between pairs of groups were analyzed with Scheffe *post hoc* comparison. Difference between groups were analyzed by the Chi-square test for unordered categorical variables and Fisher's exact test was used if cells had expected count <5. Binary logistic regression analysis was performed to obtain odds ratios (*OR*s) and their 95% *CI*s to predict the presence of high CHD and stroke risks. All statistical tests were two-tailed, and $P < 0.05$ was considered statistically significant.

RESULTS

In this cohort of 1401 patients (802 men and 599 women) with T2DM, 60.9% patients had no CKD, 30.5%

were in CKD Stages 1–2, which suggested mild renal dysfunction, and 8.6% were in Stages 3–5, which suggested moderate-to-severe renal dysfunction. Table 1 compares the clinical and metabolic parameters of patients according to the CKD stages as defined by the KDOQI classification. Patients at higher CKD stages were generally older, had diabetes for a longer duration, had higher systolic blood pressure, and had higher UACR.

Compared to those without CKD, patients in CKD Stages 1–2 and CKD Stages 3–5 had higher risks of CHD, fatal CHD, stroke, and fatal stroke, as calculated by the UKPDS risk engine [$P < 0.001$ for all; Table 2]. As the CKD stage deteriorated, the percentage of individuals with high CHD and stroke risks also increased. The *OR*s of CHD in patients in CKD Stages 1–2 and 3–5, compared with patients without CKD, were 1.7 (95% *CI*, 1.4–2.2) and 3.5 (95% *CI*, 2.3–5.3), respectively [$P < 0.001$ for both; Table 3]. Similarly, the *OR*s for high stroke risk in patients in CKD Stages 1–2 and 3–5 were 1.9 (95% *CI*, 1.4–2.7) and 8.2 (95% *CI*, 5.4–12.5), respectively [$P < 0.001$ for both; Table 3]. The percentage of individuals with high CHD and stroke risks was also increased in the patients with higher UACR [Table 3].

As the UACR elevated, the percentage of individuals with a high risk of CHD and stroke also increased [Table 4]. Compared to patients with normal urinary albumin, the *OR*s of CHD in the microalbuminuria and macroalbuminuria groups were 1.8 (95% *CI*, 1.4–2.4) and 2.0 (95% *CI*, 1.4–2.7), respectively ($P < 0.001$ for both). In the case of stroke risk,

Table 1: Anthropometric and biochemical characteristics of patients with T2DM according to CKD stage

Characteristics	No CKD (*n* = 853)	CKD Stages 1–2 (*n* = 428)	CKD Stages 3–5 (*n* = 120)	Statistics	P
Male, *n* (%)	508 (59.6)	225 (52.6)	69 (57.5)	$\chi^2 = 5.684$	0.058
Age (years)	56.4 ± 12.5	59.8 ± 12.5*	67.9 ± 12.0*·§	$F = 48.813$	0.000
Duration of DM (years)	6.5 ± 6.2	9.2 ± 6.5*	13.1 ± 7.7*·§	$F = 66.010$	0.000
Weight (kg)	65.4 ± 12.9	63.8 ± 12.1†	64.7 ± 10.9	$F = 2.186$	0.113
BMI (kg/m²)	24.0 ± 3.6	24.0 ± 3.6	24.2 ± 3.1	$F = 0.272$	0.762
WC (cm)	87.8 ± 10.3	87.7 ± 10.3	89.4 ± 9.6	$F = 1.270$	0.281
SBP (mmHg)	132.0 ± 16.9	144.3 ± 21.5*	148.5 ± 24.0*	$F = 76.415$	0.000
DBP (mmHg)	81.0 ± 10.5	83.0 ± 11.8†	81.6 ± 12.7	$F = 4.016$	0.018
FPG (mmol/L)	9.2 ± 3.7	9.8 ± 4.1*	7.7 ± 3.3*	$F = 14.816$	0.000
HbA1c (%)	9.6 ± 2.4	9.8 ± 2.5	8.7 ± 2.3*	$F = 10.915$	0.000
TC (mmol/L)	4.5 (3.8–5.3)	4.5 (3.8–5.4)	4.4 (3.5–5.3)	$F = 1.056$	0.348
TG (mmol/L)	1.5 (1.1–2.1)	1.6 (1.1–2.2)	1.7 (1.3–2.4)*	$F = 3.786$	0.023
HDL–C (mmol/L)	1.2 (1.0–1.4)	1.2 (1.0–1.5)	1.1 (0.9–1.4)*·‡	$F = 4.334$	0.013
LDL–C (mmol/L)	2.8 (2.2–3.5)	2.8 (2.2–3.5)	2.8 (2.1–3.7)*·§	$F = 0.052$	0.949
UACR (mg/g·Cr)	8.9 (5.5–15.1)	125.5 (51.5–508.1)*	450.0 (67.2–2306.2)*	$F = 1430.336$	0.000
Current smoker, *n* (%)	221 (25.9)	84 (19.6)†	17 (14.2)†	$\chi^2 = 12.118$	0.002
Ex–smoker, *n* (%)	101 (11.8)	63 (14.7)	22 (18.3)	$\chi^2 = 4.967$	0.083
AF, *n* (%)	3 (0.4)	5 (1.2)	3 (2.5)†	$\chi^2 = 7.027$	0.023
Hypertension, *n* (%)	502 (58.9)	323 (75.5)*	106 (88.3)*·§	$\chi^2 = 76.939$	0.000

*$P<0.001$; †$P<0.05$, compared to cases without CKD; ‡$P<0.05$; §$P<0.001$ compared to cases in CKD Stages 1–2. Data are expressed as mean ± SD, median (25th–75th percentiles) or percentages. CKD: Chronic kidney disease; DM: Diabetes mellitus; BMI: Body mass index; WC: Waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; HbA1c: Glycosylated hemoglobin; TC: Total cholesterol; TG: Triglyceride; HDL–C: High-density lipoprotein cholesterol; LDL–C: Low-density lipoprotein cholesterol; UACR: Urine albumin–to–creatinine ratio; Cr: Creatinine; AF: Atrial fibrillation; SD: Standard deviation; T2DM: Type 2 diabetes mellitus.

Table 2: Risks of CHD and stroke among patients with T2DM according to CKD stage (%)

Items	No CKD (*n* = 853)	CKD Stages 1–2 (*n* = 428)	CKD Stages 3–5 (*n* = 120)	*F*	*P*
CHD risk	15.2 (9.6–25.3)	20.1 (11.2–33.9)*	28.5 (18.0–48.9)*,†	40.946	0.000
Fatal CHD risk	5.1 (9.6–18.6)	14.6 (7.0–27.9)*	23.2 (12.8–42.7)*,†	52.517	0.000
Stroke risk	4.5 (2.0–10.4)	7.3 (3.0–16.4)*	19.5 (8.6–34.7)*,†	75.408	0.000
Fatal stroke risk	0.6 (0.3–1.5)	1.2 (0.4–2.9)*	3.1 (1.3–6.4)*,†	87.225	0.000

*$P < 0.001$ compared to cases no CKD; †$P < 0.001$ compared to cases in CKD Stages 1–2. Data are expressed as median (25th–75th percentiles). CHD: Coronary heart disease; CKD: Chronic kidney disease; T2DM: Type 2 diabetes mellitus.

Table 3: Presence and *OR*s of high risks of CHD and stroke according to CKD groups

Stages	High CHD risk		High stroke risk	
	n (%)	*OR* (95% *CI*)	*n* (%)	*OR* (95% *CI*)
No CKD (*n* = 853)	317 (37.2)	–	90 (10.6)	–
CKD Stages 1–2 (*n* = 428)	216 (50.5)	1.7 (1.4–2.2)*	79 (18.5)	1.9 (1.4–2.7)*
CKD Stages 3–5 (*n* = 120)	81 (67.5)	3.5 (2.3–5.3)*	59 (49.2)	8.2 (5.4–12.5)*

*$P < 0.001$ compared to cases no CKD. The 10-year CHD and stroke risks were estimated using the UK prospective diabetes study risk engine, and individuals were categorized as having low (<10%), intermediate (10–20%) or high (>20%) 10-year risk. *OR*s were calculated with binary logistic regression analysis. CHD: Coronary heart disease; CKD: Chronic kidney disease; *OR*: Odds ratio; *CI*: Confidence interval; UACR: Urine albumin–to–creatinine ratio; –: Not applicable.

Table 4: Presence and *OR*s of high risks of CHD and stroke according to UACR value

Items	High CHD risk		High stroke risk	
	n (%)	*OR* (95% *CI*)	*n* (%)	*OR* (95% *CI*)
Normal (*n* = 862)	326 (37.8)	–	99 (11.5)	–
Microalbuminuria (*n* = 337)	178 (52.8)	1.8 (1.4–2.4)*	81 (24.0)	2.4 (1.8–3.4)*
Macroalbuminuria (*n* = 202)	110 (54.5)	2.0 (1.4–2.7)*	48 (23.8)	2.4 (1.6–3.5)*

*$P < 0.001$ compared to cases with normal UACR. The 10-year CHD and stroke risks were estimated using the UK prospective diabetes study risk engine, and individuals were categorized as having low (<10%), intermediate (10–20%) or high (>20%) 10-year risk. *OR*s were calculated with binary logistic regression analysis. CHD: Coronary heart disease; UACR: Urine albumin–to–creatinine ratio; *OR*: Odds ratio; *CI*: Confidence interval; –: Not applicable.

the *OR*s for the above UACR groups were 2.4 (95% *CI*, 1.8–3.4) and 2.4 (95% *CI*, 1.6–3.5), respectively ($P < 0.001$ for both).

Age is known to be one of the traditional risk factors of CHD.[7] As shown in Figures 1 and 2, both risks of CHD and stroke were increased gradually with age.

DISCUSSION

In this study, we examined the association of CKD with risks of CHD and stroke in Chinese patients with T2DM. Our results showed that patients in more advanced CKD stages were generally older, with longer diabetes duration, higher systolic blood pressure, and higher UACR. Furthermore, with development in the CKD stage, the percentage of patients with atrial fibrillation and hypertension also increased. We also noticed that as the CKD progressed, the percentage of current smokers decreased and the percentage of ex-smokers increased, that may be attributed to efforts to educate the patients to quit smoking. In terms of CVD risks, worsening CKD stage was associated with increasing risks of CHD and stroke.

Of the 1401 T2DM patients in this study, 8.6% had evidence of advanced CKD, defined as an eGFR <60 ml·min⁻¹·1.73 m⁻²

(Stage 3 or higher). A national cross-sectional survey in China in 2012 showed that the prevalence of CKD (defined as an eGFR <60 ml·min⁻¹·1.73 m⁻² or the presence of albuminuria) was 10.8%, and that diabetes was the major cause of CKD.[14] The prevalence of advanced CKD in the present study is lower than that reported in a Hong Kong study, which found a prevalence of 15.8% of advanced CKD in T2DM patients[15] and that reported in western countries such as Norway (10.2%)[16] and the USA (17.7.0%),[3] but similar to the prevalence rate reported in the mainland of China.[17,18] Two studies in Chinese individuals with T2DM showed that the prevalence of advanced CKD was 6%[17] and 10.5% in hospitalized patients.[18] In our study, 30.5% of patients were in CKD Stages 1–2, and a total of 39.1% of our patients had renal impairment. UACR measurements showed that 14.4% of all patients had macroalbuminuria, and 24.1% had microalbuminuria. These rates are similar to those in a study in urban Chinese patients with T2DM, which reported that the frequency of CKD (eGFR <60 ml·min⁻¹·1.73 m⁻²) and albuminuria (UACR ≥30 mg/g·Cr) was 31.0% and 28.9%.[19] A study in an Asian hypertensive population with T2DM showed that the prevalence of macro- and micro-albuminuria was 18.8% and 39.8%, respectively.[20] Differences in sample selection, study populations, and eGFR evaluation methods might account
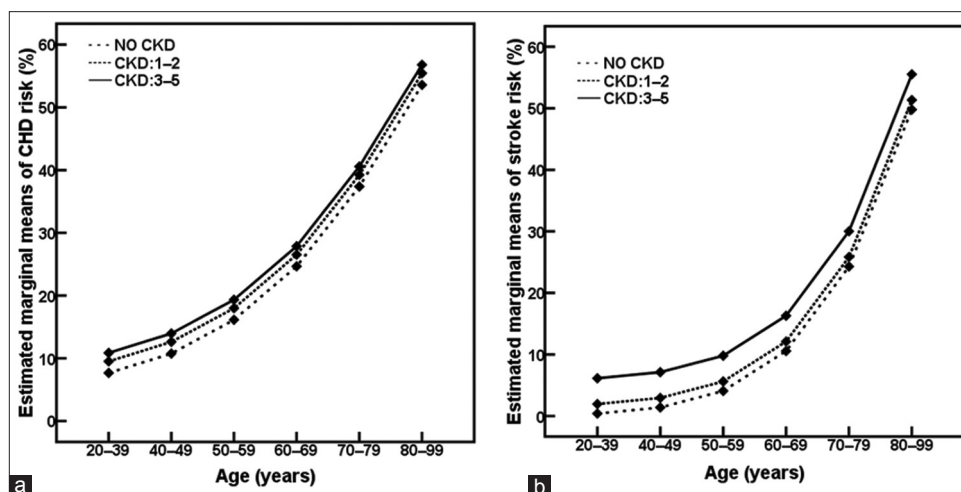
Figure 1: Age-related changes in risks of coronary heart disease (CHD, a) and stroke (b) according to chronic kidney disease (CKD) stage. $P < 0.001$ compared among age groups at the same CKD stage.
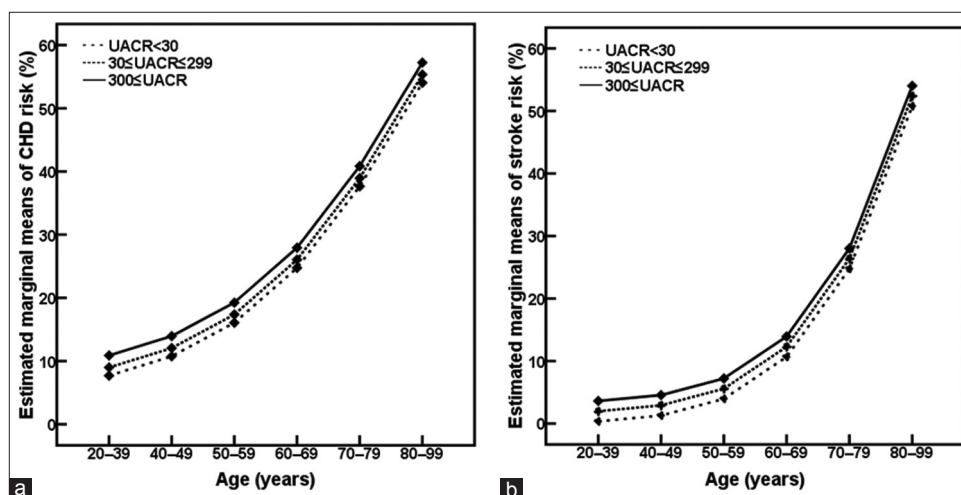
Figure 2: Age-related changes in risks of coronary heart disease (CHD, a) and stroke (b) according to urine albumin-to-creatinine ratio (UACR). $P < 0.001$ compared among age groups at the same UACR level.

for the variation in the prevalence of CKD and albuminuria among different studies.

With aggravation of CKD, the risks of CHD and stroke, as calculated using the UKPDS risk engine, increased correspondingly. The mean CHD risks were 20.1%, 24.8%, and 34.3% among patients with no CKD, CKD Stage 1–2, and CKD Stage 3–5, while the corresponding stroke risks were 8.6%, 12.7%, and 25.4%, respectively. Similar results were obtained for the risks of fatal CHD and fatal stroke. Several comparable findings have been reported. Recently, a prospective cohort study in multi-ethnic Asian adults showed that decreased eGFR and increased albuminuria were independently associated with incident CVD. The *OR*s of CVD and all-cause mortality were 1.54 and 2.21, respectively, in patients with eGFRs of <45 versus ≥60 ml·min⁻¹·1.73 m⁻², and 2.81 and 2.34, respectively, in patients with UACRs of ≥300 versus <30 mg/g·Cr.[21] In an earlier study in the general population, a 2-fold increase in urine albumin concentration was found to be associated with a 1.29-fold increase in the risk for cardiovascular mortality.[22] It was reported

that cardiovascular mortality was found to be two to three times higher in patients with Stage 3 or higher CKD than in individuals without renal dysfunction.[23,24] In addition, a prospective study in the Netherlands showed that there appears to be no threshold effect in the association of albuminuria with cardiovascular risk, unlike the nonlinear relationship between eGFR and cardiovascular risk.[25] In a population with diabetes, a prospective study in Australia showed that the multivariate-adjusted hazard ratio for cardiovascular events was 2.48 for every 10-fold increase in the baseline UACR, and 2.20 for every halving of baseline eGFR.[5] Moreover, patients with both UACR >300 mg/g·Cr and eGFR <60 ml·min⁻¹·1.73 m⁻² had an obviously higher risk of cardiovascular events compared with patients with normal GFR and UACR, but no evidence of an interaction between the effects of increased UACR and decreased eGFR was found.[5]

While the impact of CKD on CVD risk is less understood, data from epidemiological studies indicate that reduced eGFR and increased UACR are independent risk factors for stroke.[26] A cohort study in Taiwan (China) reported that

beyond the traditional cardiovascular risk factors, CKD was a risk factor for stroke.[27]

Furthermore, we defined "high risk" as a CHD or stroke risk of above 20%. The *OR*s of high CHD risk were 1.7–3.5 times higher in patients with CKD than in patients with normal kidney function. Similarly, the *OR*s of high stroke risk were 1.9–8.8 times higher in patients with renal impairment than in those without renal impairment. As expected, increasing UACR was associated with a 1.8–2.0-fold increase in CHD risk. Moreover, the stroke risk was 2.4–2.4 times higher in patients with micro- or macro-albuminuria than in patients with normal urine albumin. It has been suggested that there exist racial differences in albuminuria, kidney function, and stroke risk. High UACR is independently associated with high stroke risk in black people, and reduced eGFR is more closely associated with the incident stroke risk in white people.[28,29] Furthermore, the Chronic Renal Insufficiency Cohort study recently reported that compared to eGFR, albuminuria is a better predictor of stroke risk in patients with CKD.[30]

Although the exact mechanism is not clear, hypertension, left ventricular hypertrophy, dyslipidemia, low-grade inflammation, increased activity of the renin – angiotensin system, sympathetic nervous system activity, and deficiency of active Vitamin D have been implicated as the mechanisms that mediate the relationship between CKD and CVD risks.[31] Furthermore, it has been confirmed that increased UACR and impaired eGFR are independently and additively associated with increased CHD risk.[32] Similar results have been found in studies on stroke risk.[31] In addition, a multicenter, observational, prospective cohort study in China indicates that renal insufficiency is an important independent predictor of cardiovascular outcome in patients with acute STEMI.[33]

There are some limitations to our study. In this study, we measured renal impairment through UACR and eGFR. Both these indexes have been used to evaluate the occurrence and development of renal dysfunction in patients with diabetes.[32,34,35] However, a retrospective analysis of biopsy data has indicated that approximately 8% of Chinese T2DM patients may have co-existing diabetic nephropathy and nondiabetic renal disease.[36] Such comorbidities may affect prognosis and treatment, and the evaluation of CHD and stroke risks. In general, diabetic nephropathy is diagnosed on the basis of the duration of diabetes, UACR, and eGFR rather than renal biopsy. As we excluded urinary tract infections, systemic lupus erythematosus, and hepatitis B virus-associated nephropathy, we considered our results would still be reliable. Second, this is a cross-sectional study, and a further prospective study is required to investigate the development and progression of nephropathy and its association with CVD events.

In conclusion, the present study showed that worsening CKD stage in patients with T2DM was associated with increases in risks of CHD and stroke. CHD and stroke risks were greater in T2DM patients with CKD than those without CKD. Similar results were found for UACR as patients with increased UACR were proven with a higher proportion of high risks of CHD and stroke. The assessments of CKD stages could be useful in identifying T2DM patients with high risks of CHD and stroke.

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Conflicts of interest

There are no conflicts of interest.

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