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Body Mass Index Is Associated with Proteinuria in Stage 2-3a but not Stage 3b-4 CKD Patients: An Observational Cross-sectional Study

Jianxiao Shen (shenjianxiao@aliyun.com)
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital https://orcid.org/0000-0002-0491-9490

Yipei He
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital

Liqun He
Shuguang Hospital

Yuting Li
Shuguang Hospital

Xiaonong Chen
Shanghai Jiao Tong University Medical School Affiliated Ruijin Hospital

Yaowen Xu
Shanghai Jiao Tong University Medical School Affiliated Ruijin Hospital

Yueyi Deng
longhua hospital

Yi Chen
longhua hospital

Shougang Zhuang
Tongji University Dongfang Hospital

Hongwei Gu
Tongji University Dongfang Hospital

Na Liu
Tongji University Dongfang Hospital

Yinghui Qi
Shanghai Punan Hospital

Cheng Qiao
Shanghai Punan Hospital

Feng Ding
Shanghai Jiao Tong University School of Medicine Affiliated Ninth People's Hospital

Shengbin Wu
Shanghai Jiao Tong University School of Medicine Affiliated Ninth People's Hospital

Ai Peng
Tongji University Tenth People's Hospital: Shanghai Tenth People's Hospital
Jiafen Cheng
Tongji University Tenth People's Hospital: Shanghai Tenth People's Hospital
Qisheng Lin
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Shu Li
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Zhen Zhang
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Jingkui Wu
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Chaojun Qi
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Haijiao Jin
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Wanpeng Wang
Lianshui County People's Hospital
Xinghua Shao
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Na Jiang
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Qin Wang
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Xiajing Che
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Shan Mou
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Leyi Gu
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
Zhaohui Ni
Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital

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Abstract

Background: To investigate the relationship between body mass index (BMI) and proteinuria in stage 2-4 chronic kidney disease (CKD) patients.

Methods: This study conducted a multicenter, cross-sectional study of 804 stage 2-4 CKD patients. Multivariate regression analysis, One-way ANOVA and subsequent multiple comparisons analysis were used to explore the relationship between BMI and proteinuria in pre-dialysis CKD patients.

Results: Among stage 2-4 CKD patients, those with excessive proteinuria accounted for 85.32% of the total. BMI was an independent risk factor for the presence of proteinuria and positively correlated with the volume of proteinuria. Subgroup studies suggested that in stage 2-3a CKD patients, BMI was closely related to the presence and volume of proteinuria. However, in stage 3b-4 CKD patients, there was non-association between BMI and proteinuria. Furthermore, in stage 2-3a but not stage 3b-4 CKD patients, those with obesity (BMI≥ 28 kg/m^2) had higher levels of proteinuria, compared with those with normal weight (BMI< 24 kg/m^2) and overweight (24 kg/m^2≤ BMI < 28 kg/m^2).

Conclusion: BMI is associated with the presence and volume of proteinuria in patients with early stage (stage 2-3a) CKD but not late stage (stage 3b-4) CKD. This result suggests that only in early stage CKD patients, weight control is beneficial for reducing proteinuria.

Trial registration: ChiCTR-INR-17014069**,** Registered December 21, 2017.

Background

Body mass index, or BMI is a mostly widely used metric for obesity calculation [1–3]. A high BMI is associated with development of kidney disease and proteinuria in the general population [4]. This association is reversed among chronic kidney disease (CKD) patients, recent studies reported slower progression of kidney disease and lower risk for cardiovascular disease in pre-dialysis CKD patients with high BMI [5–11]. However, few research pays attention to the link between proteinuria and BMI in CKD patients. Therefore, we examined the association between proteinuria, measured by 24-hour proteinuria [12], and bodyweight, measured by BMI, in pre-dialysis CKD patients.

Methods

Study design

The study was based on the data obtained from our multicenter cross-sectional observational survey, which conducted at eight hospitals in Shanghai city from July 2017 to June 2018.

Participants

Recruitment

CKD patients who have at least one face-to-face outpatient encounter with a nephrologist in one of our clinical research centers including Renji Hospital of Shanghai Jiao Tong University School of Medicine, Shuguang Hospital of Shanghai University of Tranditional Chinese Medicine, Ruijin Hospital of Shanghai Jiao Tong University School of Medicine, Longhua Hospital of Shanghai University of Tranditional Chinese Medicine, Dongfang Hospital of Tong Ji University, Punan Hospital, the Ninth People's Hospital of Shanghai Jiao Tong University School of Medicine and the Tenth People's Hospital of Shanghai Tong Ji University will be recruited for this study. Clinicians will initially screen and identify the patients who are interested in participation. Researchers will confirm the eligibility and written informed consent will be obtained from each participant subsequently (Figure 1).

Diagnose criteria

Diagnosis of CKD will be confirmed by an attending nephrologist according to the Diagnosis from Kidney Disease Improving Global Outcomes 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. CKD is defined as abnormalities of kidney structure or function, present for > 3 months, with implications for health. Criteria for CKD is 1) Markers of kidney damage (one or more): a. Albuminuria (albumin ejection rate ≥30 mg/24 hours; albumin to creatinine ratio ≥30 mg/g [≥3 mg/mmol]) b. Urine sediment abnormalities, c. Electrolyte and other abnormalities due to tubular disorders, d. Abnormalities detected by histology, e. Structural abnormalities detected by imaging, f. History of kidney transplantation; 2) Decreased glomerular filtration rate (GFR): GFR < 60 ml/min/1.73 m2 (GFR categories G3a–G5).

Inclusion criteria

To be included in this study, participants must meet the following inclusion criteria: (1) 18 years of age or older, (2) meet clinical criteria of stage 2 to 4 CKD (eGFR 15-89 ml/min/1.73m2).

Exclusion criteria

Participants will be excluded from the study if they (1) demonstrate a malignancy, (2) demonstrate a pregnancy, (3) demonstrate a severe infection (CRP > 6 mg/L), (4) are unable to complete face-to-face encounter, (5) other circumstances deemed inappropriate by the researcher.

Demographic, Anthropometrical, and Clinical Data Collection

Demographic details (age, gender, education) and clinical information (physical activity, medical and medication history) were obtained by questionnaires in clinic or medical ward. Weight and height were measured in light clothing without shoes, and BMI was calculated as weight in kilograms divided by the square of height in meters. Blood pressure was measured by trained nurses using a calibrated manual mercury sphygmomanometer (Yuyue Medical Instruments Co., Ltd., Jiangsu, China) for all participants in a seated position after resting for 5 minutes. The values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded.

Laboratory Tests

Blood samples were obtained from participants after overnight fasting for at least 8h. The 24-hour urine were collected as follows: patients were instructed to empty the bladder in the morning and discard the urine, and from that point onward for 24 hours, all urine was collected in the container. At the end of the 24-hour period, the bladder is emptied, and the urine is saved. First void morning urine samples were also collected. Levels of 24-hour urine protein, serum creatinine, fasting glucose, C-reactive protein (CRP), serum albumin, serum total protein, cholesterol (TC), serum triglyceride (TG), low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C) were measured by using routine laboratory methods. Aliquots of serum were stored at -20 °C while waiting for subsequent assay.

Definitions

The estimated glomerular filtration rate (eGFR) was calculated by the CKD-EPI equation (GFR = a × (serum creatinine/b) c × (0.993) age. The variable a takes on the following values on the basis of race and sex: black (women = 166, men = 163), white/other (women = 144, men = 141). The variable b takes on the following values on the basis of sex: women = 0.7, men = 0.9. The variable c takes on the following values on the basis of sex and creatinine measurement: women (serum creatinine ≤ 0.7 mg/dL = -0.329, serum creatinine > 0.7 mg/dL = -1.209), men (serum creatinine ≤ 0.7 mg/dL = -0.411, serum creatinine > 0.7 mg/dL = -1.209). CKD was classified into the following stages: stage 2 CKD (eGFR 60-89 ml/min/1.73 m^2, stage 3a CKD (eGFR 45-59 ml/min/1.73m^2), stage 3b CKD (eGFR 30-44 ml/min/1.73 m^2) and stage 4 CKD (eGFR 15-29 ml/min/1.73m^2) [13, 14]. Normal weight was defined as BMI < 24 kg/m^2, overweight was defined as 24 kg/m^2 ≤ BMI < 28 kg/m^2, obesity was defined as BMI ≥ 28 kg/m^2 [15]. Abnormal proteinuria was defined as having a 24-hour urinary protein ≥ 120mg [16].

Statistical Analysis

All statistical analysis were performed with SPSS 23.0 software (Chicago, IL, USA). Data are expressed as mean ± standard deviation, or median (25th-75th percentile). For the categorical variables, absolute and relative (%) values were presented. Baseline characteristics of patients with normal proteinuria and abnormal proteinuria were compared, and Student's t test or Wilcoxon rank-sum test was used for analyses of continuous variables and the chi-squared test was used for categorical variables.

Univariate and multivariate logistic regression analysis was performed to examine the influence of the following variables on the presence of proteinuria: gender, age, education attainment, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor antagonists (ARBs), BMI, diabetes mellitus, eGFR, serum albumin, serum total protein, fasting glucose, C-reactive protein, serum total cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein, systolic blood pressure, diastolic blood pressure. The goodness-of-fit of the logistic regression models was assessed by the Hosmer and Lemeshow test. The same logistic regression analyses were conducted in subgroup analysis.

Furthermore, univariate and multiple linear regression analyses were performed to examine the relationships between 24-hour protein and other variables. The odds ratios with 95% CIs, were calculated. One-way ANOVA were used for comparing the 24-hour protein levels among subjects with normal weight, overweight and obesity. Because the distributions of 24-hour protein and cholesterol were skewed, they were log-transformed to obtain a normal distribution. Shapiro-Wilk test was used to assess the normality for log (24-hour protein). A two-tailed p value <0.05 was considered statistically significant.

Results

Briefly, 3340 patients with stage 2 to 4 CKD (eGFR 15-89 ml/min/1.73m^2) were included initially. 2075 were excluded from this study due to missing data. 461 were excluded due to infection, pregnancy or malignancy. Finally, 804 patients were enrolled in this study. The underlying kidney diseases of the enrolled patients were as follows: chronic glomerulonephritis (n = 337), diabetic nephropathy (n = 199), nephron-sclerosis (n = 74), polycystic kidney disease (n = 20), other disease (n = 35), and unknown disease (n = 139). Patients a) had at least one face-to-face outpatient encounter with a nephrologist in one of our clinical research center, and not on dialysis or had renal transplant, and b) had all data this study required.

Clinical characteristics of patients, and comparisons between CKD patients with and without proteinuria

Among the 804 stage 2-4 CKD patients (age 55.41±13.75) included in this study, 53.35% of them were male. Six hundred and eighty-six (686, 85.32%) subjects had abnormal proteinuria. Three hundred and fifty-one (351, 43.65%) subjects were taking ACEIs/ARBs before the survey. Table 1 showed the characteristics of 804 patients. Compared with those with normal 24-hour urinary protein, the patients with abnormal 24-hour-urinary had higher values of BMI, ACR, TC, LDL-C and HDL-C as well as lower values of age, serum albumin and serum total protein.

Univariate and multivariate logistic regression analysis of the association between the presence of proteinuria and other factors

As shown in Table 2a, univariate analyses indicated that the presence of abnormal 24-hour urinary protein was significantly and independently related to BMI, ages, serum albumin, serum total protein, TC, LDL-C and HDL-C. However, only age (0.979 (0.964-0.995), p = 0.008), BMI (1.118 (1.050-1.190), p < 0.001), serum albumin (0.915(0.876-0.955), p < 0.001) and TC (1.392(1.153-1.680), p = 0.001) were independently associated with abnormal 24-hour urinary protein in a multivariate logistic regression model.

In subgroup analysis, Table 2b showed that the presence of abnormal 24-hour urinary protein in stage 2-3a CKD (n=479) patients was significantly and independently related to BMI, ages, serum albumin, serum total protein, TC, LDL-C and HDL-C. Several variables including age (0.970 (0.951-0.989), p = 0.002), BMI (1.159 (1.065-1.261), p =0.001), serum albumin (0.920(0.870-0.973), p = 0.004) and TC (1.422(1.116-1.812), p = 0.004) were independently associated with abnormal 24-hour urinary protein in a multivariate

logistic regression model. While in stage 3b-4 CKD (n=325) patients, Table 2c revealed that abnormal 24-hour urinary protein collection was significantly and independently related to serum albumin, TC and LDL-C. Only LDL-C (1.773(1.186-2.652), p = 0.005) were independently associated with abnormal 24-hour urinary protein in a multivariate logistic regression model.

Univariate and multivariate linear regression analysis for correlation between proteinuria and other variables in CKD patients

Table3a presents the results of univariate and multivariate linear regression analysis for the association between proteinuria and other variables. Univariate analysis showed that BMI, TC, $\log_{10}$TG, LDL-C, HDL-C and SBP were positively correlated with 24-hour-protein, while age, eGFR, serum albumin and serum total protein showed an inverse correlation. Then backward stepwise method was applied in order to select variables included in multivariate regression model. The analysis revealed that age, BMI, eGFR, serum albumin, serum total protein, TC and SBP were independently associated with 24-hour-protein (Table 3a).

Subgroup analysis revealed that in CKD stage 2-3a patients, BMI, TC, $\log_{10}$TG, LDL-C, HDL-C and SBP were positively correlated with 24-hour protein, serum albumin and serum total protein showed negative correlation. Then multivariate regression analysis showed that only BMI, serum albumin and TC were independently associated with 24-hour-protein (Table 3b). However, in stage 3b-4 CKD patients, CRP, TC, $\log_{10}$TG, LDL-C, SBP and DBP were positively correlated with 24-hour protein; age, eGFR, serum albumin and serum total protein had negative correlation. Serum total protein, CRP and TC were independently associated with 24-hour-protein with Multivariate regression analysis (Table 3c).

Based on the above robust results that BMI was independently related with proteinuria in CKD patients of different stages, we further compared the 24-hour protein levels among subjects with normal weight, overweight and obesity. The one-way ANOVA and consequent multiple comparisons analysis revealed that log (24-hour protein) in obese individuals (3.08±0.55) were significantly higher than that with normal weight (2.65±0.58) and overweight (2.92±0.59) ($p < 0.0001$ for both) (Figure 2A). Similar results were observed in stage 2-3a CKD patients (Figure 2B). However, no difference was found among stage 3b-4 CKD patients (Figure 2C).

Discussion

CKD is now recognized as a major global public health issue [17, 18, 19]. Persistent proteinuria is one of the major criteria of CKD [20]. To our best knowledge, the present cross-sectional study was the first report from China focusing on bodyweight and proteinuria in pre-dialysis CKD patients. We find that the prevalence rates of proteinuria in stage 2-4 CKD patients were 85.32%.

BMI is a heuristic proxy for human body fat calculated from an individual's weight and height. According to the WHO criteria, a BMI between 18.5 and 25 kg/m^2 may be optimal; a BMI ≥ 25 kg/m^2 may indicate the person is overweight; and a BMI ≥ 30 kg/m^2 suggests the person is obese [21]. However, at the same

BMI, people of Asian ancestry might have greater risk of developing metabolic diseases than people of European ancestry. A BMI of 28 kg/m^2 may identify the risk factors with a specificity of approximately 90% and is recommended as the cut off point for obesity in Asian adults. BMI at 24 was recommended as the cut-off point for overweight [15].

It is not difficult to anticipate a high prevalence of cardiovascular disease, diabetes, hypertension, dyslipidemia, or CKD in normal population with higher BMI [22, 23, 24, 25]. However, there are conflicting findings on the association between bodyweight and CKD in previous studies. Early studies reported obesity is an independent risk factor for the development of kidney disease in the general population and an independent risk factor in developing end stage renal disease [5, 6]. A recent cohort study conducted in United States showed that body mass index levels ≥ 35 kg/m^2 are associated with worse outcomes in patients with earlier stages of CKD, but this association is attenuated in those patients with eGFR < 30 ml/min per 1.73m^2 [6]. Data from Cleveland Clinic's electronic health record showed that, compared to BMI of 18.5-24.9 kg/m^2, overweight or obesity patients are associated with lower risk for cardiovascular, malignancy related and non-cardiovascular/non-malignancy related deaths in pre-dialysis patients [26]. Thus, the relationship between CKD and bodyweight was complicated.

Proteinuria is an important biomarker for screening and diagnosing kidney disease and monitoring disease activity, the response to treatment, and renal prognosis [27]. 24-hour urine protein collection is considered the criterion standard for the diagnosis of proteinuria in CKD [28]. Previous studies revealed bodyweight is positively associated with proteinuria in general population [5]. Similarly, in hypertensive patients, BMI is associated with microalbuminuria [29]. However, few studies tried to figure out the association between bodyweight and proteinuria in different stage CKD patients.

The present cross-sectional observational study focused on the association between bodyweight and proteinuria in pre-dialysis CKD patients. This study demonstrated that bodyweight, assessing by BMI, was positively associated with proteinuria in CKD patients. Subgroup analysis showed the association between bodyweight and proteinuria was significantly in stage2-3a CKD patients, revealing that like general population, there is strong connection between bodyweight and proteinuria in early stage of CKD.

Furthermore, subjects with obesity (BMI ≥ 28 kg/m^2) showed significantly higher level of 24-hour proteinuria than their counterparts with normal weight and overweight. Therefore, we conclude that BMI, is positively associated with proteinuria in Chinese, especially early stage, CKD patients.

The findings of our study also indicated that high BMI might not be independently correlated with proteinuria in late stage CKD patients. A possible explanation for this result might be that renal function is severely damaged in late stage CKD patients, the effect of high bodyweight on proteinuria can be negligible.

Of note, this study had several limitations. First, in spite of having adjusted for confounding factors, the cross-sectional nature does not permit the assessment of an absolute cause-and-effect relationship

between proteinuria and other tested risk factors. To establish such a causal relationship, longitudinal studies in various populations are acquired. Second, 24-hour urine protein was obtained on the basis of single measurement; repeated testing may increase the validity of the results. Third, beside body mass index, other characters as waist circumference may support our current results. Finally, the lifestyle factors are not well characterized in the current study. It is reported that diet quality could affect proteinuria risk independently [30]. Future studies should examine these lifestyle factors in relation to proteinuria and CKD.

Conclusions

Based on the findings from our study, together with other reports, we suggest that reducing body weight with maintaining healthy lifestyle should be recommended to early stage CKD patients to decline proteinuria.

Abbreviations

CKD: Chronic kidney disease; BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; CRP: C-reactive protein; TC: cholesterol; TG: serum triglyceride; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol; ACEIs: angiotensin-converting enzyme inhibitors; ARBs angiotensin II receptor antagonists.

Declarations

Ethics approval and consent to participate

This study was approved by The Ethics Committee of Shanghai Jiaotong University affiliated Renji Hospital (No.2016-070k(c))

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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Authors' Contributions

Zhaohui Ni conceived and designed the study. Jianxiao Shen and Yipei He performed the experiments and wrote the paper. Liqun He, Yuting Li, Xiaonong Chen, Yaowen Xu, Yueyi Deng, Yi Chen, Shougang Zhuang, Hongwei Gu, Na Liu, Yinghui Qi, Cheng Qiao, Feng Ding, Shengbin Wu, Ai Peng, Jiafen Cheng, Qisheng Lin, Shu Li, Zhen Zhang, Jingkui Wu, Chaojun Qi, Haijiao Jin and Wanpeng Wang enrolled the patients. Xinghua Shao, Na Jiang, Qin Wang and Shan Mou reviewed and edited the manuscript. Jianxiao Shen and Yipei He made equal contribution to this article. All authors read and approved the manuscript.

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Tables

Table 1. The comparative between subjects with normal proteinuria and abnormal proteinuria. Mean ± SD or median (interquartile range) for continuous variables and % for categorical variables are presented.

Abbreviations: ACR, albumin to creatinine ratio; ACEIs/ARBs, angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists; eGFR, estimated glomerular filtration rate; CRP, high sensitivity C-reactive protein; TC, serum total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Parameter	Normal proteinuria	Abnormal proteinuria	P-value
24-hour-collection, mg	76.30 (59.83–99.01)	772.7 (350.98–2110.52)	<0.001
ACR, mg/g	17.25 (10.5–25.75)	252.7(76.65–815.72)	<0.001
Male, n(%)	61(51.69%)	368(53.64%)	0.695
Age, years	57.87±12.57	54.99±13.91	0.025
Education Attainment High School or Above, n(%)	57(48.30%)	364(53.06%)	0.402
ACEIs/ARBs, n(%)	48(40.67%)	303(44.16%)	0.480
Body Mass Index	22.55±2.96	23.89±3.62	<0.001
Diabetic Nephropathy, n(%)	22(18.64%)	177(25.8%)	0.096
eGFR, mL/min/1.73m2	53.82±19.62	50.39±20.44	0.091
Serum Albumin, g/L	42.02±4.6	39.12±6.48	<0.001
Serum Total Protein, g/L	69.00±6.80	66.28±8.74	<0.001
Fasting Glucose, mmol/L	5.54±1.09	5.53±1.29	0.931
CRP, mg/L	2.54±1.43	2.76±1.39	0.115
TG, mmol/L	1.75(1.40–2.38)	1.82(1.39–2.56)	0.248
TC, mmol/L	4.59±0.93	5.18±1.47	<0.001
LDL-C, mmol/L	2.59±0.84	3.03±1.17	<0.001
HDL-C, mmol/L	1.18±0.36	1.28±0.47	0.011
SBP, mmHg	134.12±13.49	136.35±16.11	0.11
DBP, mmHg	80.64±9.61	81.86±10.87	0.215

Table 2a. Univariate and multivariate logistic regression analyses for the association between the presence of proteinuria and various variables in all patients enrolled. Independent variables in the multivariate model were chosen using a backward stepwise regression analysis. The goodness-of-fit of the logistic regression models was assessed by the Hosmer and Lemeshow test, and the p value was

0.399. Abbreviations: ACEIs/ARBs, angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists; BMI, body mass index; eGFR, estimated glomerular filtration rate; CRP, high sensitivity C-reactive protein; TC, serum total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Variables	Univariate		Multivariate	
	Odds Ratio (95%CI)	*P*	Odds Ratio (95%CI)	*P*
Male，n(%)	0.925(0.625-1.367)	0.695	—	—
Age, years	0.984(0.970-0.999)	0.036	0.979 （0.964–0.995）	0.008
Education Attainment High School or Above, n(%)	0.846(0.572-1.251)	0.402	—	—
ACEIs/ARBs, n(%)	1.154(0.776-1.716)	0.480	—	—
Body Mass Index	1.122(1.057-1.191)	<0.001	1.118 （1.050–1.190）	<0.001
Diabetic Nephropathy，n(%)	1.517(0.926-2.486)	0.098	—	—
eGFR, mL/min/1.73m2	0.992(0.982-1.001)	0.091	—	—
Serum Albumin, g/L	0.912(0.877-0.949)	<0.001	0.915 （0.876–0.955）	<0.001
Serum Total Protein, g/L	0.959(0.934-0.984)	0.002	—	—
Fasting Glucose, mmo/L	0.994(0.852-1.160)	0.936	—	—
CRP, mg/L	1.123(0.975-1.294)	0.108	—	—
TG, mmol/L	1.136(0.942-1.370)	0.181	—	—
TC, mmol/L	1.436(1.209-1.707)	<0.001	1.392(1.153–1.680)	0.001
LDL-C, mmol/L	1.499(1.217-1.846)	<0.001	—	—
HDL-C, mmol/L	1.760(1.050-2.951)	0.032	—	—
SBP, mmHg	1.009(0.997-1.022)	0.157	—	—
DBP, mmHg	1.011(0.992-1.030)	0.253	—	—

Table 2b. Univariate and multivariate logistic regression analyses for the association between the presence of proteinuria and various variables in CKD2-CKD3a patients. Independent variables in the multivariate model were chosen using a backward stepwise regression analysis. The goodness-of-fit of the logistic regression models was assessed by the Hosmer and Lemeshow test, and the p value was 0.096. Abbreviations: ACEIs/ARBs, angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists; BMI, body mass index; eGFR, estimated glomerular filtration rate; CRP, high sensitivity C-reactive protein; TC, serum total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Variables	Univariate		Multivariate	
	Odds Ratio (95%CI)	*P*	Odds Ratio (95%CI)	*P*
Male，n(%)	1.112(0.685-1.806)	0.668	—	—
Age, years	0.977（0.960-0.995）	0.013	0.970 （0.951–0.989）	0.002
Education attainment High School or Above, n(%)	0.836（0.519-1.358）	0.475	—	—
ACEIs/ARBs, n(%)	1.046(0.646-1.695)	0.855	—	—
Body Mass Index	1.187(1.095-1.287)	<0.001	1.159 （1.065–1.261）	0.001
Diabetic Nephropathy，n(%)	1.244(0.677-2.287)	0.482	—	—
eGFR, mL/min/1.73m2	1.000(0.982-1.019)	0.986	—	—
Serum Albumin, g/L	0.909(0.866-0.955)	<0.001	0.920 （0.870–0.973）	0.004
Serum Total Protein, g/L	0.955(0.924-0.986)	0.006	—	—
Fasting glucose, mmo/L	0.954(0.781-1.167)	0.648	—	—
CRP, mg/L	1.087(0.916-1.290)	0.339	—	—
TG, mmol/L	1.256(0.961-1.641)	0.095	—	—
TC, mmol/L	1.479(1.194-1.832)	<0.001	1.422(1.116–1.812)	0.004
LDL-C, mmol/L	1.398(1.090-1.793)	0.008	—	—
HDL-C, mmol/L	2.061(1.073-3.958)	0.03	—	—
SBP, mmHg	1.002(0.986-1.017)	0.844	—	—
DBP, mmHg	1.004(0.980-1.028)	0.758	—	—

Table 2c. Univariate and multivariate logistic regression analyses for the association between the presence of proteinuria and various variables in CKD3b-CKD4 patients. Independent variables in the multivariate model were chosen using a backward stepwise regression analysis. The goodness-of-fit of the logistic regression models was assessed by the Hosmer and Lemeshow test, and the p value was 0.533. Abbreviations: ACEIs/ARBs, angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists; BMI, body mass index; eGFR, estimated glomerular filtration rate; CRP, high sensitivity C-reactive protein; TC, serum total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Variables	Univariate		Multivariate	
	Odds Ratio (95%CI)	*P*	Odds Ratio (95%CI)	*P*
Male，n(%)	0.604(0.303-1.205)	0.152	—	—
Age, years	0.996(0.970-1.022)	0.743	—	—
Education Attainment High School or Above, n(%)	0.907(0.461-1.787)	0.778	—	—
ACEIs/ARBs, n(%)	1.343(0.660-2.732)	0.416	—	—
Body Mass Index	1.047(0.954-1.149)	0.335	—	—
Diabetic Nephropathy，n(%)	1.958(0.831-4.617)	0.125	—	—
eGFR, mL/min/1.73m2	0.994(0.956-1.034)	0.77	—	—
Serum Albumin, g/L	0.930（0.869-0.996）	0.037	—	—
Serum Total Protein, g/L	0.967(0.925-1.010)	0.129	—	—
Fasting Glucose, mmo/L	1.019(0.795-1.306)	0.883	—	—
CRP, mg/L	1.229(0.950-1.591)	0.116	—	—
TG, mmol/L	0.995(0.769-1.286)	0.967	—	—
TC, mmol/L	1.373(1.026-1.839)	0.033	—	—
LDL-C, mmol/L	1.773(1.186-2.652)	0.004	1.773 （1.186–2.652）	0.005
HDL-C, mmol/L	1.460(0.618-3.451)	0.389	—	—
SBP, mmHg	1.022(0.999-1.046)	0.061	—	—
DBP, mmHg	1.018(0.987-1.050)	0.254	—	—

Table 3a. Univariate and multivariate linear regression analysis for correlation between 24-hour urinary protein collection and other variables in all subjects. Independent variables in the multivariate model were chosen using a backward stepwise regression analysis where all variables listed in the univariate analysis. Adjust R2 was 0.334, and p<0.001; Abbreviations: ACEIs/ARBs, angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists; BMI, body mass index; eGFR, estimated glomerular filtration rate; CRP, high sensitivity C-reactive protein; TC, serum total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Variables	Univariate		Multivariate		
	r	*P*	B(95%CI)	*t*	*P*
Gender, Male	0.014	0.682	—	—	—
Age, years	0.096	0.006	-0.005 (-0.007–-0.002)	-3.773	<0.001
Education attainment High School or Above	0.05	0.153	—	—	—
ACEIs/ARBs, n(%)	0.004	0.905	—	—	—
Body Mass Index	0.264	<0.001	0.034 (0.024–0.043)	6.747	<0.001
Diabetic Nephropathy	0.044	0.208	—	—	—
eGFR, mL/min/1.73m2	0.095	0.007	-0.002 (-0.004–0.000)	-2.364	0.018
Serum Albumin, g/L	0.45	<0.001	-0.034 (-0.041–-0.027)	-4.508	<0.001
Serum Total Protein, g/L	0.396	<0.001	-0.009(-0.016-–0.001)	-2.345	0.019
Fasting Glucose, mmo/L	0.008	0.831	—	—	—
CRP, mg/L	0.056	0.112	—	—	—
log_{10}TG, mmol/L	0.165	<0.001	—	—	—
TC, mmol/L	0.385	<0.001	0.113 (0.088–0.138)	8.871	<0.001
LDL-C, mmol/L	0.346	<0.001	—	—	—
HDL-C, mmol/L	0.111	0.002	—	—	—
SBP, mmHg	0.106	0.003	0.003(0.00–0.005)	2.359	0.019
DBP, mmHg	0.096	0.006	—	—	—

Table 3b. Univariate and multivariate linear regression analysis for correlation between 24-hour urinary protein collection and other variables in CKD2-CKD3a subjects. Independent variables in the multivariate model were chosen using a backward stepwise regression analysis where all variables listed in the univariate analysis. Adjust R2 was 0.392, and p<0.001; Abbreviations: ACEIs/ARBs, angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; CRP, high sensitivity C-reactive protein; TC, serum total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

Variables	Univariate		Multivariate		
	r	*P*	B(95%CI)	*t*	*P*
Gender, Male	0.01	0.833	—	—	—
Age, years	0.085	0.064	—	—	—
Education Attainment High School or Above	0.044	0.338	—	—	—
ACEIs/ARBs, n(%)	0.009	0.849	—	—	—
Body Mass Index	0.405	<0.001	0.050 (0.037−0.063)	7.679	<0.001
Diabetic Nephropathy	0.003	0.946	—	—	—
eGFR, mL/min/1.73m2	0.041	0.374	—	—	—
Serum Albumin, g/L	0.527	<0.001	-0.034 (-0.041−-0.027)	-9.303	<0.001
Serum Total Protein, g/L	0.444	<0.001	—	—	—
Fasting Glucose, mmo/L	0.071	0.123	—	—	—
CRP, mg/L	0.003	0.943	—	—	—
log_{10}TG, mmol/L	0.179	<0.001	—	—	—
TC, mmol/L	0.396	<0.001	0.094 (0.061−0.127)	5.962	<0.001
LDL-C, mmol/L	0.345	<0.001	—	—	—
HDL-C, mmol/L	0.165	<0.001	—	—	—
SBP, mmHg	0.094	0.04	—	—	—
DBP, mmHg	0.059	0.194	—	—	—

Table 3c. Univariate and multivariate linear regression analysis for correlation between 24-hour urinary protein collection and other variables in CKD3b-CKD4 subjects. Independent variables in the multivariate

model were chosen using a backward stepwise regression analysis where all variables listed in the univariate analysis. Adjust R2 was 0.244, and p<0.001; Abbreviations: ACEIs/ARBs, angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists; BMI, body mass index; eGFR, estimated glomerular filtration rate; CRP, high sensitivity C-reactive protein; TC, serum total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Variables	Univariate		Multivariate		
	r	*P*	B(95%CI)	*t*	*P*
Gender, Male	0.059	0.285	—	—	—
Age, years	0.133	0.017	—	—	—
Education attainment High school or above	0.07	0.209	—	—	—
ACEIs/ARBs, n(%)	0.009	0.849	—	—	—
Body Mass Index	0.84	0.132	—	—	—
Diabetic nephropathy	0.095	0.086	—	—	—
eGFR, mL/min/1.73m2	0.113	0.043	—	—	—
Serum albumin, g/L	0.309	<0.001	—	—	—
Serum Total Protein, g/L	0.31	<0.001	-0.019 (-0.026- −0.013)	-5.627	<0.001
Fasting glucose, mmo/L	0.092	0.097	—	—	—
CRP, mg/L	0.152	0.006	0.057(0.017-0.098)	2.805	0.005
log_{10}TG, mmol/L	0.177	0.001	—	—	—
TC, mmol/L	0.373	<0.001	0.136 (0.097−0.174)	6.951	<0.001
LDL-C, mmol/L	0.351	<0.001	—	—	—
HDL-C, mmol/L	0.043	<0.443	—	—	—
SBP, mmHg	0.111	0.045	—	—	—
DBP, mmHg	0.129	0.02	—	—	—

Figures

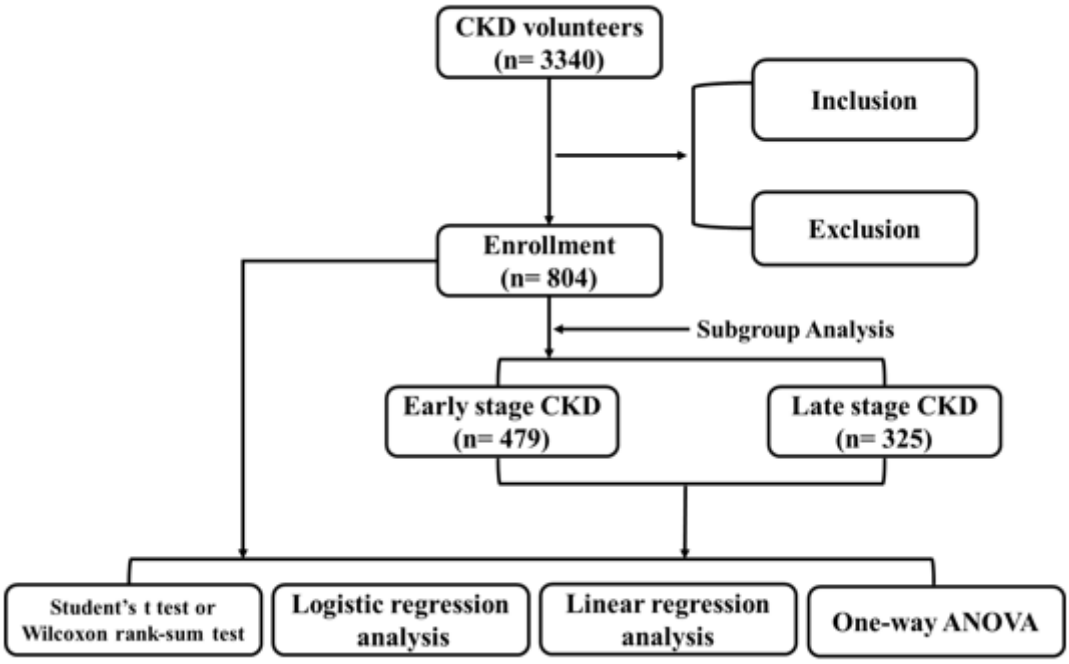

Figure 1

The flow chart of the observational cross-sectional study trial of chronic kidney disease Patients.

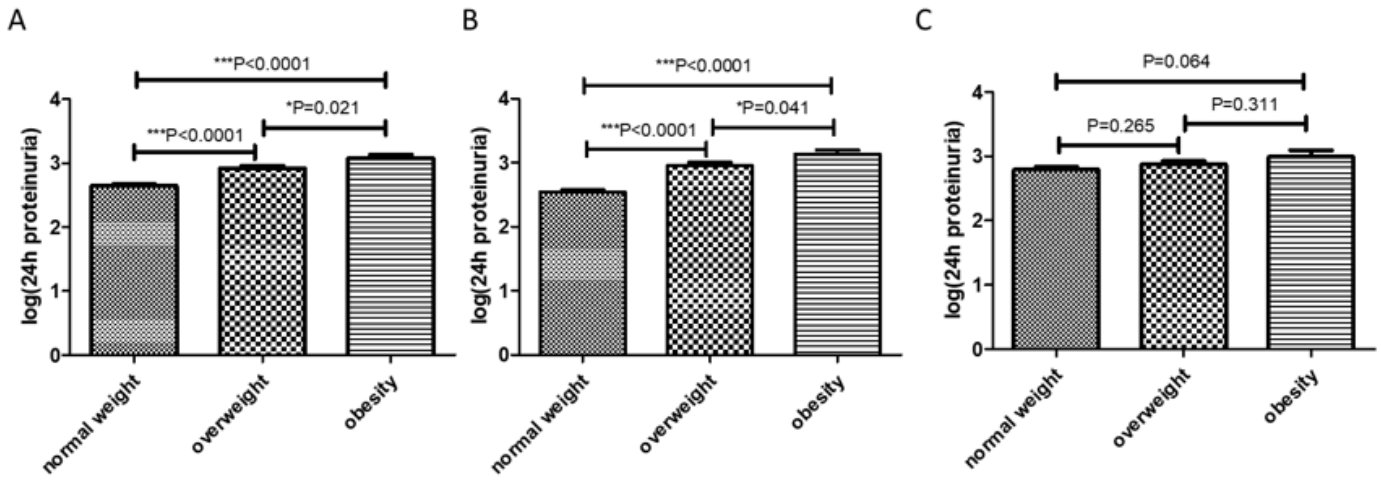

Figure 2

Comparison of 24-hour urinary protein values among CKD patients with normal weight (BMI < 24kg/m2), overweight (24 kg/m2 ≤ BMI < 28 kg/m2) and obesity (BMI ≥ 28 kg/m2). (A) stage 2-4 CKD patients; (B) stage 2-3a CKD patients; (C)stage 3b-4 CKD patients.

Supplementary Files

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