

# Association Between Neck Circumference and Microalbuminuria in Community Residents

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**Objective:** Neck circumference (NC) represents the subcutaneous fat deposition in the neck and is an effective indicator for evaluating metabolic disorders, such as metabolic syndrome, subclinical atherosclerosis, and non-alcoholic fatty liver disease. Microalbuminuria (MAU) is regarded as a potential sign of systemic endothelial dysfunction and microvascular abnormalities. The aim of this study was to elucidate the association of NC with urine albumin-to-creatinine ratio (UACR) and MAU.

**Methods:** A total of 1882 Shanghai community residents were enrolled (816 men and 1066 women), with age ranging from 40 to 80 years. Anthropometric parameters, including NC, and biochemical indices were measured. MAU was determined if  $30 \text{ mg/g} \leq \text{UACR} < 300 \text{ mg/g}$ . An elevated NC was defined as  $\text{NC} \geq 38.5 \text{ cm}$  for men and  $\text{NC} \geq 34.5 \text{ cm}$  for women.

**Results:** Individuals with an elevated NC had significantly higher prevalence of MAU and UACR values than those with normal NC in both men and women (all  $P < 0.05$ ). The logistic regression analysis showed that there were significant and positive associations between elevated NC and the increasing risk of MAU after adjusting for lipid profile and glycemic indices ( $P = 0.007$  for men and  $P = 0.009$  for women). After further adjusting for blood pressure, elevated NC caused an 69.3% additional risk of MAU in men ( $P = 0.037$ ) and the positive correlation in women disappeared ( $P = 0.131$ ).

**Conclusion:** There was an independent and positive association between elevated NC and the risk of MAU in men in the Chinese community population.

**Chinese Clinical Trial Registry** ([Www.chictr.org.cn](http://www.chictr.org.cn)) **Registration Number:** ChiCTR1900024011.

**Keywords:** neck circumference, microalbuminuria, urine albumin-to-creatinine ratio

## Introduction

Neck circumference (NC), the girth measured just below the thyroid cartilage protrusion, represents the subcutaneous fat deposition in the neck, which is an anthropological parameter for determining obesity (especially upper-body obesity). NC has gradually attracted considerable attention from researchers and clinicians owing to its strengths, including simple measurement procedure, explicit anatomic landmark, and low variability. A growing body of evidence suggested that, similar to waist circumference (WC), NC also acted as a powerful tool in identifying metabolic syndrome,<sup>1,2</sup> assessing subclinical atherosclerosis,<sup>3</sup> screening for non-alcoholic fatty liver disease,<sup>4</sup> and predicting cardiovascular diseases effectively.<sup>5,6</sup>

Microalbuminuria (MAU), which is usually measured using urine albumin-to-creatinine ratio (UACR), is seen at several instances, such as abnormal

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hemodynamics, metabolic disorders, or inflammation,<sup>7</sup> and often indicates systemic endothelial dysfunction and microvascular abnormalities.<sup>8</sup> The occurrence of MAU in patients with hypertension or diabetes is related to the hemodynamic adaptations of glomerular hypertension and hyperfiltration in remnant nephrons owing to glomerular permeability dysfunction.<sup>9,10</sup> In addition, a study has shown that MAU increases the risks of cardiovascular diseases and mortality independently in the general population.<sup>11</sup> MAU is reversible in the early stage of microvascular changes, and it can regress after blood pressure, blood glucose level, obesity, or inflammation are brought under control.<sup>7</sup> Therefore, early detection of MAU and timely control of its cause are essential to prevent the exacerbation in microvascular abnormalities to irreversible atherosclerosis and the occurrence of renal damage.

We obtained the optimal NC cutoff points for metabolic syndrome in a previous study through assessing central obesity using the precise standard-visceral fat area, which was measured utilizing magnetic resonance imaging,<sup>1</sup> and verified its efficiency in determining subclinical atherosclerosis.<sup>3</sup> A study has demonstrated that NC, an index closely linked to cardiovascular diseases, was independently associated with the risk of decreased estimated glomerular filtration rate (eGFR) in the Chinese general population.<sup>12</sup> However, whether NC can also be used to assess the risk of MAU in the Chinese population is yet unknown. Therefore, this study aimed to clarify the association of NC with UACR and MAU in community residents.

## Materials and Methods

### Study Population

This study recruited Shanghai community residents between 2015 and 2016. All participants completed standardized questionnaires, which included medical history, medications, and personal habits. The exclusion criteria of this study included neck deformity or surgical history, goiter, abnormal thyroid function, and history of cardiovascular diseases, severe hepatic dysfunction, macroalbuminuria (UACR  $\geq$  300 mg/g), malignant tumors, infection status, and hormone-based treatments. Finally, a total of 1882 individuals (816 men and 1066 women) with complete data were included in the study. This study was approved by the Ethics Committee of Shanghai Jiao Tong University Affiliated Sixth People's Hospital (Approval number: 2019–067) and all participants signed the informed consent.

## Anthropometric and Biochemical Measurements

The measurements of anthropometric parameters, including height, weight, WC, and NC were conducted in accordance with the standardized methods described in a previous study.<sup>1</sup> Body mass index (BMI) = weight (kg)/height<sup>2</sup> (m<sup>2</sup>). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured after a minimum 10-min rest and the average of three measurements taken at 3-min intervals was recorded.

After overnight fasting for 10 h, venous blood samples were collected, and blood samples were taken again after 2 h by performing a 75-g oral glucose tolerance test or 100-g steamed bread meal test (for valid diabetic patients). Fasting plasma glucose (FPG), 2-h plasma glucose (2hPG), glycated hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>), fasting insulin, total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), and C-reactive protein (CRP) were measured based on standard methods as previously described.<sup>1</sup> The homeostasis model assessment-insulin resistance index (HOMA-IR) = FPG (mmol/L)  $\times$  fasting insulin (mU/L)/22.5. The sarcosine oxidase-PAP method was used to determine the serum and urine creatinine levels on a 7600–120 Hitachi automatic analyzer (Hitachi, Tokyo, Japan). Urine albumin content was determined using immunonephelometry (BN II System; Siemens, Marburg, Germany). UACR was the ratio of urinary albumin to urine creatinine. The eGFR was calculated by the formula proposed by the Chronic Kidney Disease Epidemiology Collaboration:  $eGFR = 141 \times \min(\text{Scr}/\kappa, 1)^\alpha \times \max(\text{Scr}/\kappa, 1)^{-1.209} \times 0.993^{\text{Age}^\text{c}} \times 1.018$  [if female]  $- 1.159$  [if black], where Scr is serum creatinine,  $\kappa$  is 0.7 for females and 0.9 for males,  $\alpha$  is  $-0.329$  for females and  $-0.411$  for males, min indicates the minimum of Scr/ $\kappa$  or 1, and max indicates the maximum of Scr/ $\kappa$  or 1.<sup>13</sup>

### Diagnosis Criteria

1) Diabetes was diagnosed according to the criteria set by the 2010 American Diabetes Association, FPG  $\geq$  7.0 mmol/L and/or 2hPG  $\geq$  11.1 mmol/L and/or HbA<sub>1c</sub>  $\geq$  6.5%.<sup>14</sup> 2) Based on the 2020 International Society of Hypertension global hypertension practice guidelines, SBP  $\geq$  140 mmHg and/or DBP  $\geq$  90 mmHg or currently receiving antihypertensive therapy were diagnosed as patients with hypertension.<sup>15</sup> 3) Elevated NC was defined as NC  $\geq$  38.5 cm for men and NC  $\geq$  34.5 cm for women in the light of our previous results.<sup>1</sup> 4) MAU was diagnosed

if  $30 \text{ mg/g} \leq \text{UACR} < 300 \text{ mg/g}$ .<sup>16</sup> 5) According to the latest 2020 China Guideline, metabolic syndrome was diagnosed when any of the three following components were present: central obesity (WC  $\geq 90$  cm for men and  $\geq 85$  cm for women); hyperglycemia: FPG  $\geq 6.10$  mmol/L and (or) 2hPG  $\geq 7.80$  mmol/L, and (or) previously diagnosed diabetes; hypertension: SBP  $\geq 130$  mmHg, and (or) DBP  $\geq 85$  mmHg, and (or) previously diagnosed hypertension; hypertriglyceridemia (TG  $\geq 1.70$  mmol/L); low HDL-c (HDL-c  $< 1.04$  mmol/L).<sup>17</sup>

## Statistical Analysis

The data were analyzed using SPSS 20.0 version. Continuous variables are shown as mean  $\pm$  standard deviation (ones with a normal distribution) and median (interquartile range; ones with a skewed distribution). Categorical variables are expressed as number (percentage). Normal, skewed, and categorical variables were compared using Student's *t*-test, Wilcoxon rank-sum test, and chi-square test, respectively. Logistic regression analysis was conducted to analyze the association between MAU and NC after adjusting for age, lipid profiles, CRP, eGFR, lipid-lowering therapy, NC cutoff, glycemic indices, diabetes, antidiabetic therapy, blood pressure, hypertension, antihypertensive therapy, metabolic syndrome and BMI or WC. All reported *P*-values were two-tailed, and a *P*-value  $< 0.05$  was considered statistically significant.

## Results

### Clinical Characteristics of the Study

#### Participants

The total population had a median age of 61 (57–65) years (ranging from 40 to 80 years), a median NC of 35.0 (32.8–37.7) cm [38.0 (36.0–39.8) cm for men and 33.4 (31.8–34.8) cm for women], and a median UACR of 7.90 (5.17–14.55) mg/g. The prevalence of MAU was 11.2% (210/1882). As listed in Table 1, the values of NC were significantly higher in individuals with MAU in both men and women [38.9 (37.2–40.8) versus 37.9 (36.0–39.7) cm,  $P = 0.004$  in men and 34.0 (32.3–35.8) versus 33.3 (31.7–34.7) cm,  $P = 0.001$  in women]. Moreover, participants with MAU had higher values of BMI, WC, SBP, DBP, FPG, 2hPG, HbA<sub>1c</sub>, fasting insulin, HOMA-IR, CRP, and UACR and proportions of hypertension (all  $P < 0.05$ ) than the participants without MAU, and there were no significant differences between two groups in the values of TC, LDL-c, and eGFR (all  $P > 0.05$ ),

irrespective of gender. Furthermore, individuals with MAU had a higher TG ( $P < 0.001$ ) and a lower HDL-c ( $P = 0.003$ ) than those without MAU, in women.

### Comparison of MAU in Different NC Groups

The participants were divided into different groups according to gender and NC levels. There were 460 individuals with normal NC, 356 individuals with elevated NC in men and 735 individuals with normal NC, and 331 individuals with elevated NC in women. As shown in Figure 1, the prevalence of MAU in men was 6.74% (31/460) and 12.36% (44/356) for those with normal and elevated NC, respectively, demonstrating that the prevalence significantly increased in those with elevated NC ( $P = 0.007$ ). Similarly, in women, participants with elevated NC had higher prevalence of MAU than those with normal NC (18.13% versus 10.20%,  $P < 0.001$ ). Furthermore, UACR of individuals with elevated NC were also significantly higher than those with normal NC in both men and women [7.09 (4.49–13.73) versus 6.35 (4.45–10.14) mg/g,  $P = 0.021$  for men; 10.47 (6.71–21.79) versus 8.62 (5.64–15.21) mg/g,  $P < 0.001$  for women; Figure 2].

### The Association of MAU with NC and Other Measurements

As shown in Table 2, taking MAU as the dependent variable and NC elevation as the independent variable for logistic regression analysis, there were significant and positive associations between elevated NC and the increased risk of MAU in both men and women [odds ratio (OR) = 1.952 (1.205–3.161),  $P = 0.007$  for men and OR = 1.875 (1.291–2.725),  $P = 0.001$  for women] after adjusting for age, TG, HDL-c, LDL-c, CRP, eGFR and lipid-lowering therapy in model 1. In model 2, although further adjustments were made for glycemic indices on the basis of model 1, elevated NC remained positively correlated with the increased risk of MAU ( $P = 0.007$  for men and 0.009 for women). If we further adjusted for blood pressure related indices in model 3 and metabolic syndrome in model 4, the results showed that elevated NC brought about an additional 69.3% risk of MAU in men [OR = 1.693 (1.031–2.781),  $P = 0.037$ ] and the positive correlation between elevated NC and risk of MAU in women disappeared ( $P = 0.131$ ). Further adjusting for BMI based on model 4 did not change the

**Table 1** Characteristics of the Study Participants

Variable	Men		P	Women		P
	MAU			MAU		
	No (n = 741)	Yes (n = 75)		No (n = 931)	Yes (n = 135)	
Age (years)	62 (56–66)	62 (56–66)	0.844	61 (57–65)	62 (58–65)	0.011
Height (cm)	170.0 (166.0–173.0)	169.0 (165.0–172.0)	0.436	158.0 (154.5–161.0)	158.0 (155.0–163.0)	0.142
Weight (kg)	70.1 (64.2–76.7)	73.0 (67.3–79.5)	0.008	58.3 (53.4–64.5)	62.6 (56.3–68.6)	< 0.001
BMI (kg/m <sup>2</sup> )	24.57 ± 3.02	25.73 ± 2.84	< 0.001	23.76 ± 3.16	25.07 ± 3.52	< 0.001
WC (cm)	87.0 (82.0–93.0)	93.0 (85.0–96.5)	< 0.001	81.0 (76.0–87.0)	85.0 (78.0–92.0)	< 0.001
NC (cm)	37.9 (36.0–39.7)	38.9 (37.2–40.8)	0.004	33.3 (31.7–34.7)	34.0 (32.3–35.8)	0.001
SBP (mmHg)	134 (123–146)	144 (130–156)	< 0.001	128 (117–140)	139 (127–154)	< 0.001
DBP (mmHg)	80 (74–87)	83 (77–92)	0.004	75 (69–82)	78 (72–85)	0.001
FPG (mmol/L)	5.85 (5.45–6.53)	6.07 (5.49–7.28)	0.033	5.78 (5.42–6.32)	6.01 (5.54–7.09)	< 0.001
2hPG (mmol/L)	7.72 (6.07–9.73)	8.61 (6.93–13.15)	0.008	7.50 (6.14–9.78)	8.46 (6.65–11.86)	< 0.001
HbA <sub>1c</sub> (%)	5.7 (5.4–6.1)	5.9 (5.6–6.4)	< 0.001	5.8 (5.5–6.1)	6.1 (5.7–6.8)	< 0.001
Fasting insulin (mU/L)	8.40 (5.84–12.18)	10.62 (6.63–14.97)	0.006	9.38 (6.65–12.99)	11.08 (8.13–15.79)	< 0.001
HOMA-IR	2.24 (1.56–3.45)	2.89 (1.76–4.78)	0.001	2.45 (1.70–3.56)	3.12 (2.12–4.59)	< 0.001
TC (mmol/L)	5.06 (4.49–5.72)	5.24 (4.69–5.69)	0.124	5.58 (5.01–6.30)	5.61 (4.96–6.21)	0.420
TG (mmol/L)	1.46 (1.04–2.21)	1.62 (1.12–2.80)	0.135	1.38 (0.97–1.94)	1.56 (1.21–2.24)	< 0.001
HDL-c (mmol/L)	1.23 (1.08–1.45)	1.16 (0.95–1.39)	0.078	1.50 (1.29–1.76)	1.42 (1.19–1.65)	0.003
LDL-c (mmol/L)	3.13 ± 0.80	3.30 ± 0.71	0.084	3.42 ± 0.85	3.41 ± 0.78	0.912
CRP (mg/L)	0.82 (0.38–1.64)	1.11 (0.67–2.10)	0.009	1.00 (0.50–1.76)	1.27 (0.67–3.12)	0.002
eGFR (mL/min/1.73 m <sup>2</sup> )	93.89 (86.98–100.26)	95.31 (84.26–104.11)	0.592	97.19 (91.65–102.12)	98.68 (92.36–103.96)	0.200
UACR (mg/g)	6.04 (4.31–9.77)	60.65 (41.11–126.11)	< 0.001	8.05 (5.60–12.45)	51.25 (36.39–98.35)	< 0.001
Hypertension, n (%)	415 (56.0)	56 (74.7)	0.002	400 (43.0)	95 (70.4)	< 0.001
Diabetes, n (%)	198 (26.7)	28 (37.3)	0.058	211 (22.7)	59 (43.7)	< 0.001
Metabolic syndrome, n (%)	327 (44.1)	45 (60.0)	0.010	292 (31.4)	69 (51.1)	< 0.001
Lipid-lowering therapy, n (%)	40 (5.4)	2 (2.7)	0.418	76 (8.2)	13 (9.6)	0.617
Antidiabetic therapy, n (%)	74 (10.0)	11 (14.7)	0.231	70 (7.5)	24 (17.8)	< 0.001
Antihypertensive therapy, n (%)	201 (27.1)	28 (37.3)	0.079	226 (24.3)	60 (44.4)	< 0.001

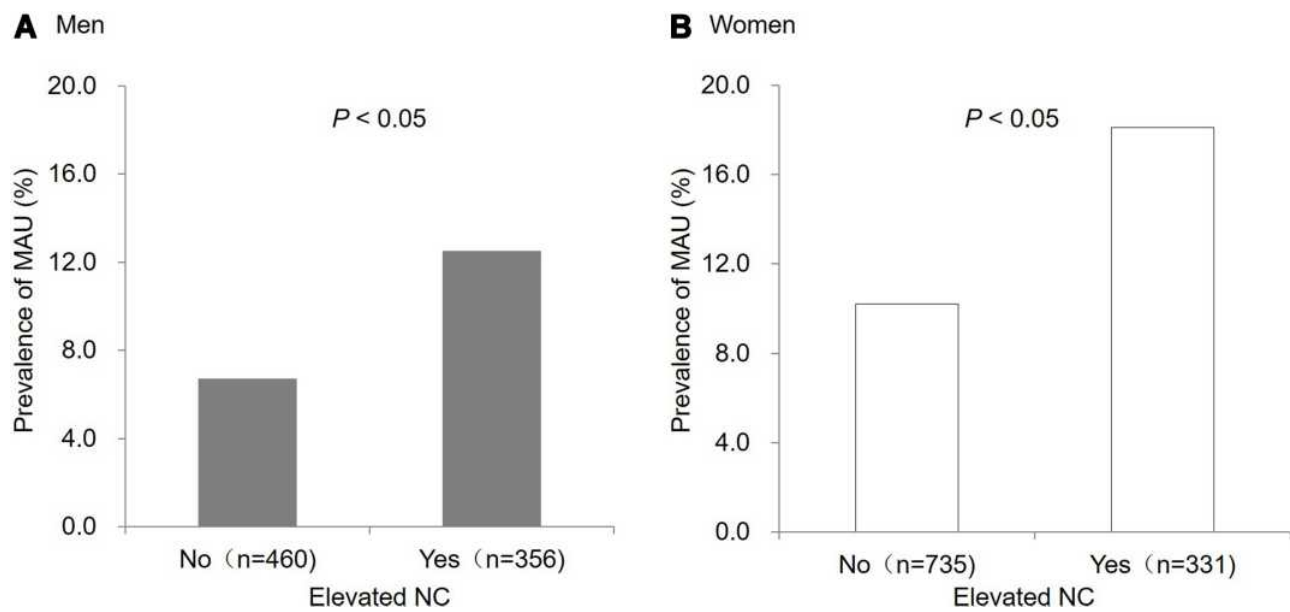
**Note:** Data were expressed as mean ± standard deviation for normally distributed variables or the median (interquartile range) for skewed-distribution variables.

**Abbreviations:** MAU, microalbuminuria; BMI, body mass index; WC, waist circumference; NC, neck circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; 2hPG, 2-h plasma glucose; HbA<sub>1c</sub>, glycated hemoglobin A<sub>1c</sub>; HOMA-IR, homeostasis model assessment-insulin resistance index; TC, total cholesterol; TG, triglyceride; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio.

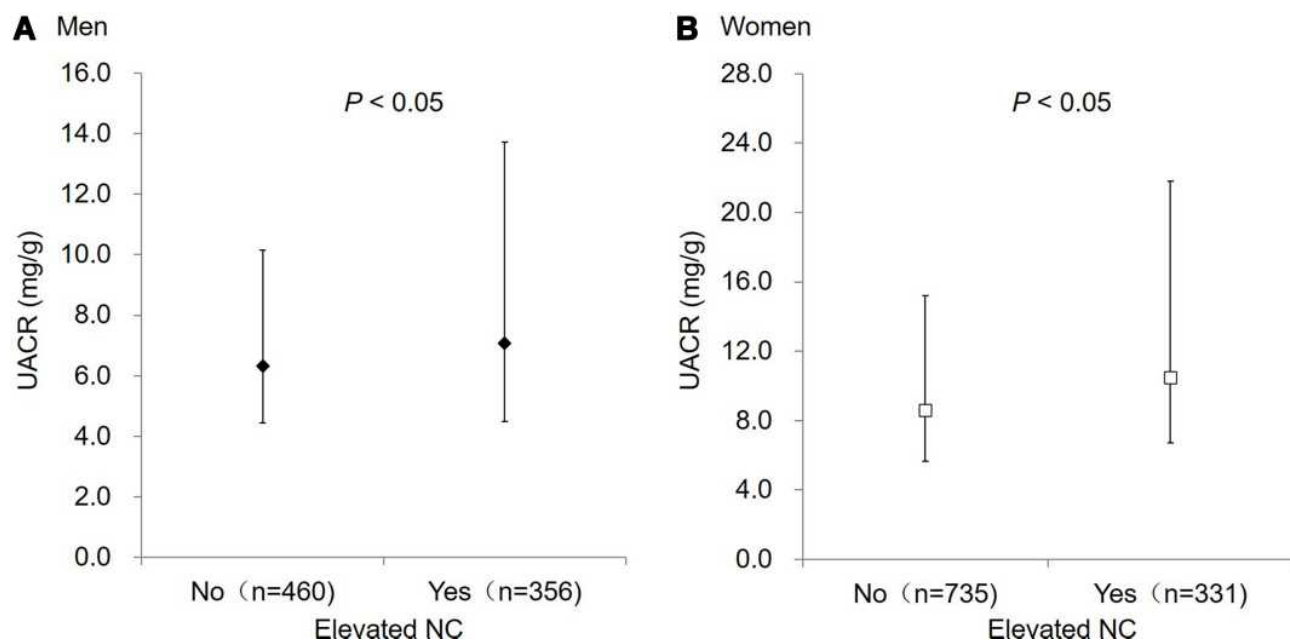
association between elevated NC and risk of MAU in men ( $P = 0.037$ ). However, the positive association in men disappeared after further adjusting for WC on the basis of model 4 ( $P = 0.449$ )

## Discussion

This study found that the average UACR value and prevalence of MAU in participants with elevated NC were significantly increased in the community population. There



**Figure 1** Prevalence of MAU according to elevated NC groups in men (A) and women (B).  
**Abbreviations:** MAU, microalbuminuria; NC, neck circumference.



**Figure 2** Distribution of UACR according to elevated NC groups in men (A) and women (B).  
**Abbreviations:** UACR, urine albumin-to-creatinine ratio; NC, neck circumference.

was a positive correlation between elevated NC and the risk of MAU in men, independent of confounding factors, including renal function, lipid profiles, glycemic indices, and blood pressure. However, elevated NC did not contribute to MAU risk independent of metabolic factors in women.

Albuminuria is one of the earliest markers of glomerular diseases and an important indicator of poor renal prognosis. The guideline updated by The Kidney Disease: Improving Global Outcomes (KDIGO) organization in 2013 summarized the relationship between increased proteinuria and a variety of important outcomes,

**Table 2** Logistic Regression Analysis Showing the Variables Associated with MAU

Variables	Men		Women	
	OR (95% CI)	P	OR (95% CI)	P
Multivariate Model 1				
Age	–	–	1.079 (1.037–1.124)	< 0.001
eGFR	–	–	1.036 (1.012–1.061)	0.004
CRP	–	–	1.042 (1.002–1.084)	0.042
NC cutoff	1.952 (1.205–3.161)	0.007	1.875 (1.291–2.725)	0.001
Multivariate Model 2				
HbA <sub>1c</sub>	1.340 (1.119–1.605)	0.001	1.612 (1.356–1.917)	< 0.001
NC cutoff	1.954 (1.201–3.178)	0.007	1.658 (1.132–2.428)	0.009
Multivariate Model 3				
HbA <sub>1c</sub>	1.320 (1.095–1.590)	0.004	1.512 (1.265–1.806)	< 0.001
SBP	1.022 (1.009–1.036)	0.001	1.031 (1.020–1.043)	< 0.001
NC cutoff	1.693 (1.031–2.781)	0.037	–	–
Antihypertensive therapy	–	–	1.587 (1.058–2.380)	0.025
Multivariate Model 4				
HbA <sub>1c</sub>	1.320 (1.095–1.590)	0.004	1.512 (1.265–1.806)	< 0.001
SBP	1.022 (1.009–1.036)	0.001	1.031 (1.020–1.043)	< 0.001
NC cutoff	1.693 (1.031–2.781)	0.037	–	–
Antihypertensive therapy	–	–	1.587 (1.058–2.380)	0.025

**Notes:** Model 1 included age, TG, HDL-c, LDL-c, CRP, eGFR, lipid-lowering therapy and NC cutoff. Model 2 included age, TG, HDL-c, LDL-c, CRP, eGFR, lipid-lowering therapy, NC cutoff, HbA<sub>1c</sub>, HOMA-IR, diabetes and antidiabetic therapy. Model 3 included age, TG, HDL-c, LDL-c, CRP, eGFR, lipid-lowering therapy, NC cutoff, HbA<sub>1c</sub>, HOMA-IR, diabetes, antidiabetic therapy, SBP, DBP, hypertension and antihypertensive therapy. Model 4 included age, TG, HDL-c, LDL-c, CRP, eGFR, lipid-lowering therapy, NC cutoff, HbA<sub>1c</sub>, HOMA-IR, diabetes, antidiabetic therapy, SBP, DBP, hypertension, antihypertensive therapy and metabolic syndrome.

**Abbreviations:** MAU, microalbuminuria; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein; NC, neck circumference; HbA<sub>1c</sub>, glycated hemoglobin A<sub>1c</sub>; SBP, systolic blood pressure; TG, triglyceride; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment-insulin resistance index; DBP, diastolic blood pressure.

including all-cause mortality, cardiovascular disease, kidney failure, and acute kidney injury for the first time, revealed that MAU (UACR 30–299 mg/g) had indispensable clinical significance in both diabetic and nondiabetic participants, and assigned great importance to the laboratory measurement of UACR.<sup>18,19</sup>

Recently, some studies have explored the relationships between traditional anthropometric indicators and MAU.<sup>20–24</sup> A cross-sectional study involving 8600 community residents over the age of 40 in China investigated the relationships between BMI, WC, body fat content, and UACR. The results showed that after adjusting for age, gender, physical activity, FPG, TG, LDL-c, HbA<sub>1c</sub>, HOMA-IR, and SBP, taking the lowest quartile of BMI and WC as reference, the risk of MAU in the highest quartile of BMI and WC increased by 65% and 73%, respectively.<sup>20</sup> Another Chinese study conducted in 341 newly diagnosed type 2 diabetes patients demonstrated that the prevalence of MAU increased with an increase in visceral fat index. The risk of MAU increased by 94% per one standard deviation increase in the visceral fat

index, revealing the predictive ability of visceral fat index in MAU.<sup>21</sup> A study based on the Korean National Health and Nutrition Examination Survey 2011–2014 data (19,331 participants, ≥ 19 years old) found that compared to individuals with normal BMI, overweight/obese individuals possessed an additional risk of approximately 50% of increased UACR value.<sup>22</sup> A longitudinal population-based cohort involving 26,960 participants in the REGARDS study demonstrated that there was no significant association between elevated BMI and the incidence of end-stage renal disease. Those with elevated WC had a 3.97-fold increased risk of end-stage renal disease. However, after adjusting for obesity-related comorbidities and baseline values of UACR and eGFR, this correlation disappeared.<sup>23</sup> The results from the study conducted by Dittmann et al showed that there was a U-shaped association between WC and MAU in the German general population, suggesting that both obese and very thin people had an increased risk of renal insufficiency.<sup>24</sup> Although the results on the relationships between the traditional anthropological indicators such as BMI, WC, and MAU were

slightly discrepant because of the differences in study population and diagnostic criteria, most of the studies suggested that the systemic or visceral fat accumulation reflected by BMI or WC were positively correlated with the prevalence of MAU.

As an anthropological indicator of obesity proposed in recent years, NC was revealed to be associated with MAU in few studies.<sup>25–27</sup> A small sample study in South Africa comprising 101 black African men and 99 women showed that after adjusting for confounding factors, a significant and positive correlation between NC and MAU was observed only in women ( $\beta = 0.52$ ,  $P < 0.01$ ).<sup>25</sup> Another study from Taiwan in 177 consecutive patients who visited the outpatient department of cardiology found that after adjusting for age and creatinine, there was no significant correlation between NC and MAU in men and NC was significantly and positively correlated with MAU in women, with higher linear regression correlation coefficient than BMI and WC.<sup>26</sup> The results of the abovementioned studies are inconsistent as a result of differences in the study population and design; moreover, there is a lack of evidence from the Chinese population. In this study, we found that elevated NC was independently and positively correlated with the risk of MAU after adjusting for age, lipid profile, and glycemic indices. The correlation disappeared in women and remained in men after further adjusting for blood pressure. In other words, elevated NC was an independent determinant for MAU in men, irrespective of lipid profile, glycemic indices, and blood pressure.

Owing to the difference in study population size, the associations between NC and MAU in men and women are inconsistent. In this study, we only observed the independent association between elevated NC and MAU in men after adjusting for blood pressure, lipid profile, glycemic indices, CRP, and other metabolic factors. The difference in the absolute content of upper-body subcutaneous fat between men and women may account for the results in our study. Upper-body subcutaneous fat has been considered to be the main reservoir of circulating non-esterified fatty acids (NEFAs). NEFAs affected the production of vascular nitric oxide, enhanced endothelial dysfunction, and impaired vascular reactivity. In addition, the renal uptake of NEFAs in the proximal tubules also caused tubulointerstitial inflammation and fibrosis.<sup>28,29</sup>

There are some limitations in the current study. Given the single-center study design, the conclusions of this study need to be verified in a multi-center, large-cohort study. Another limitation is the fact that it is a cross-sectional study; therefore, the predictive efficiency of NC

on the development of MAU needs to be verified using longitudinal studies in the future. In addition, the study population had higher prevalence of diabetes and hypertension than the general population and further studies in a general population are needed to confirm the findings.

## Conclusion

In the Chinese community population, there was an independent and positive association between elevated NC and the risk of MAU only in men.

## Data Sharing Statement

The data that support the findings of this study are available on request from the corresponding author (Yuqian Bao, yqbao@sjtu.edu.cn). The data are not publicly available due to privacy or ethical restrictions.

## Ethical Approval and Informed Consent

The study was approved by the Ethics Committee of Shanghai Jiao Tong University Affiliated Sixth People's Hospital, and all procedures were performed in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The study methods and potential risks were fully explained to all participants, and each participant provided a written informed consent prior to enrollment.

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## Disclosure

The authors declare no potential conflicts of interest.

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