Relationship between obesity and microalbumin in the urine.

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Abstract
This study aimed to investigate the effect of Overweight (OW)/Obesity (OB) on Microalbuminuria (MAU). According to the level of Urine Albumin-to-Creatinine Ratio (UACR), 1170 cases are divided into the Normal Albumin Urine (NAU) group (men: 398 cases, women: 409 cases) and MAU group (men: 175 cases, women: 188 cases). The clinical data and biochemical indexes of the study participants were obtained. Statistical analysis was performed using the SPSS16.0 software. The result of the multiple linear regression analysis depicted that age, Diastolic Blood Pressure (DBP), Fasting Blood Glucose (FBG), Waist-to-Hip Ratio (WTHR), Waist Circumference (WC), and Waist-to-Height Ratio (WHR) were significantly associated with UACR. After the modification of age, sex, FBG, and DBP, the contribution of different variables to MAU showed that WTHR>WC>WHR. By using the Receiver Operating Characteristic curve (ROC) analysis in the male population, the incidence rates of the areas under the curve of WTHR, WHR, and WC used to predict MAU were 0.68 (95% CI: 0.67-0.70), 0.64 (95% CI: 0.62-0.65), and 0.57 (95% CI: 0.55-0.59), respectively, and the predictive points were 0.52, 0.90, and 91.8 cm. In the female population, the incidence rates of the areas under the curve of WTHR, WHR, and WC used to predict MAU were 0.71 (95% CI: 0.70-0.72), 0.69 (95% CI: 0.68-0.70), and 0.64 (95% CI: 0.62-0.65), respectively, and the predictive points were 0.52, 0.8, and 82.5 cm. The AOB population was at high risk for MAU. WTHR was the best predictor, followed by WC and WHR. The cut-off points in men and women are 0.52, 89.6 cm, and 0.88 and 0.52, 84.5 cm, and 0.84 cm, respectively.

Keywords: Microalbuminuria, Overweight, Obesity.

Introduction
Microalbuminuria (MAU) refers to a urinary albumin excretion rate of 20-200 μg/min, and the routine examination of the urine showed negative for urine protein, and this is often the best window period for clinical treatment and the reversible phase [1]. The incidence of cardiovascular disease and its mortality increased [2]. Numerous studies show that genetic factors, age, hyperglycemia-related metabolic disorders, abnormal polyl metabolism, oxygen-free radical formation, hemodynamic disorders, and hypertension, among others can cause and aggravate kidney damage, particularly hypertension and hyperglycemia [3-10]. However, other risk factors of metabolic syndrome, such as obesity and lipid metabolism disorders, are related to Diabetic Nephropathy (DN), and this result remains controversial domestically and overseas. Therefore, the distribution of people with microalbuminuria was explored, and the correlation between microalbuminuria and anthropometric indices of Obesity (OB), particularly Body Mass Index (BMI), Waist Circumference (WC), Hip Circumference (HC), Waist-to-Hip Ratio (WHR), and Weight to Height ratio (WTHR), in patients at the People’s Hospital in Chengyang District of Qingdao City was investigated. Moreover, the optimal cut-off points of MAU were studied, which provided a theoretical basis for treatment intervention.

Materials and Methods
Participants
According to the level of the Urinary Albumin-to-Creatinine Ratio (UACR), 1170 cases are divided into: 1) the NAU group (807 cases: men, 398 cases and women, 409 cases; UACR that is <30 mg/g) and 2) the MAU group (363 cases: men, 175 cases and women, 188 cases; 30 mg/g that is ≤ UACR<300 mg/g). All participants had no history of smoking, drinking, and liver, kidney, lung, and other critical illnesses. No acute infectious diseases, such as urinary tract infection, respiratory infection, and digestive tract infection, are observed. None of the participants took any drugs that affect glucose or insulin metabolism. A written informed consent was obtained from all participants.

Experimental method
The survey method: A uniform questionnaire was adapted, and questions generally include gender, age, smoking,
Diagnostic criteria

MAU refers to internationally accepted standards for diagnosis and staging based on Mogenson and Wang Haiyan’s fourth edition of Nephrology. The provisional criteria are as follows [11]: 1) NAU (UACR that is <30 mg/g), MAU (30 mg/g that is ≤ UACR<300 mg/g), and Clinical Proteinuria (CP) (UACR that is ≥ 300 mg/g). 2) The factors that affect urinary albumin excretion rate, such as heart failure, urinary tract infection, autoimmune diseases, nephrotoxicity, drug history, ketoacidosis, nephritis, and other chronic diseases, are excluded.

The diagnostic criteria of metabolic syndrome were based on the 2010 and 2013 editions of the CDS diagnostic criteria was proposed to those who meet 3 or more of the following diagnostic criteria: 1) obesity (BMI is greater than or equal to 25 kg/m²) or central obesity (WC is greater than or equal to 90 cm (men) and 80 cm (women)); 2) hypertension (the confirmed patient is taking a medicine or has an FBG that is greater than 140/90 mmHg); 3) dyslipidemia (the confirmed patient is taking a medicine or has a high TG/low HDL-C in the blood); 4) high blood sugar (the confirmed DM patient is taking a medicine or has an FBG that is greater than or equal to 7.8 mmol/L).

Calculation formula

BMI=weight/height squared (kg/m²). UACR=urinary albumin/creatinine ratio.

Statistical analysis

Continuous variables were expressed by the mean ± standard deviation (M ± SD) using SPSS16.0. The t test was used between the two groups and to compare the rate of χ² test, and the significant level was set to 0.05. The Receiver Operating Characteristic (ROC) curve was used to compare the best points of each obesity index to MAU. The contribution of the obesity index to MAU was analysed via regression analysis.

Results

Comparison of the general information of survey participants

Compared with the normal albuminuria group factors, such as age, FBG, DBP, SBP, SUA, WC, WHR, WTHR, and SUA, all increased in the MAU group compared with the normal albuminuria group. The difference is statistically significant (P<0.05 or P<0.01). However, the difference in LDL, LnTG, HDL, TC, BMI, and HC was not statistically significant (P>0.05). Moreover, the prevalence rate of HG, PHT, and AOB in the MAU group was higher than that in the NAU group, and the difference was statistically significant (P<0.01). The prevalence rate of OB was also higher than that of the NAU group, and the difference was statistically significant (P<0.05). No significant difference in the prevalence of DLP was observed (P>0.05) (Table 1).

Multiple linear stepwise regression analysis

UACR was the dependent variable, and age, gender, BMI, WTHR, WC, WRH, TG, TC, HDL, LDL, SBP, DBP, FBG, and UA were the independent variables. Multiple linear regression analysis was conducted. The results show that P<0.05, and age, DBP, FBG, WTHR, WC, and WRH enter into the model and positively correlated. The other independent variables could not enter the model. After the modification of age, sex, FBG, DBP, and other factors and the contribution to MAU in the abdominal obesity index, WTHR had the largest proportion, followed by WC and finally WHR (Table 2).

The partial correlation between obesity indicators

The correlation between the multi-factor linear correlation analysis of BMI, WTHR, WHR, WC, HC, and other anthropometric indices was tested. After the modification of age, sex, BMI, WTHR, WHR, and WC, results show a positive correlation (P<0.01), and a significantly negative correlation between HC and WHR was observed (P<0.01).

ROC analysis of AOB correlation index for the prediction of MAU

In the male population, by ROC analysis, the WTHR, WHR, and WC predicting incidence rates in the area under the MAU curve were 0.68 (95% CI: 0.67-0.70), 0.64 (95% CI: 0.62-0.65), and 0.57 (95% CI: 0.55-0.59). In the female population, the predicting incidence rates are 0.71 (95% CI: 0.70-0.72), 0.69 (95% CI: 0.68-0.70), and 0.64 (95% CI: 0.62-0.65). The best cut-off points for MAU in the male and female population based on WTHR, WHR, and WC were
predicted to be 0.52, 0.90, and 91.8 cm and 0.52, 0.84, and 82.5 cm, respectively, (Table 3).

### Table 1. Comparison of general information of survey subjects (x̄ ± s).

<table>
<thead>
<tr>
<th></th>
<th>NAU group</th>
<th>MAU group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>807</td>
<td>363</td>
</tr>
<tr>
<td>Age (year)</td>
<td>50.18 ± 13.89</td>
<td>54.98 ± 13.60</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>25.13 ± 3.50</td>
<td>25.11 ± 3.84</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>83.24 ± 10.44</td>
<td>88.48 ± 12.78</td>
</tr>
<tr>
<td>HC (cm)</td>
<td>96.61 ± 8.98</td>
<td>96.94 ± 9.14</td>
</tr>
<tr>
<td>WHR</td>
<td>0.78 ± 0.11</td>
<td>0.90 ± 0.11</td>
</tr>
<tr>
<td>WTHR</td>
<td>0.51 ± 0.06</td>
<td>0.62 ± 0.07</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>127.38 ± 18.95</td>
<td>135.22 ± 22.31</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>81.73 ± 11.49</td>
<td>92.64 ± 11.58</td>
</tr>
</tbody>
</table>

### Table 2. Multiple linear stepwise regression analysis.

<table>
<thead>
<tr>
<th>Items</th>
<th>Regression coefficient (B)</th>
<th>Standard regression coefficient (Std. B)</th>
<th>t values</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant t</td>
<td>-5.387</td>
<td>-8.312</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WHR</td>
<td>0.06</td>
<td>0.09</td>
<td>2.71</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>WC</td>
<td>0.24</td>
<td>0.13</td>
<td>3.686</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>WRS</td>
<td>0.3</td>
<td>0.21</td>
<td>5.123</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FBG</td>
<td>0.33</td>
<td>0.47</td>
<td>8.621</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP</td>
<td>0.49</td>
<td>0.33</td>
<td>6.199</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Table 3. ROC analysis of AOB correlation index for prediction MAU.

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UACR (male)</td>
</tr>
<tr>
<td>WTHR</td>
<td>0.52</td>
</tr>
<tr>
<td>WHR</td>
<td>0.9</td>
</tr>
<tr>
<td>WC</td>
<td>91.8 cm</td>
</tr>
</tbody>
</table>

Notes: AUC area under curve

### Discussion

In the recent years, studies have shown that MAU is significantly associated with the risk factors of cardiovascular disease, known as the MS component [12]. The study on adults in the Huayang and Cao Yang community in Shanghai showed that the detection rate of MAU increased significantly with the combination of multiple factors in cardiovascular and cerebrovascular diseases, particularly in cases of hypertension and hyperglycemia. Studies conducted by Chen et al. [13] show that the risk of chronic kidney disease and MAU in patients with MS was significantly higher than in patients without MS [14]. Moreover, studies by Abdul-Ghani et al. [15] depicted that Type 2 Diabetes Mellitus (T2DM) patients with MS had higher rates of MAU and massive proteinuria than in patients without MS. However, only few clinical studies that are related to OB and MAU are available domestically or overseas, particularly those related to AOB and MAU. Weisinger et al. [16] reported for the first time the association between severe OB and proteinuria. Glomerular hypertrophy and focal segmental glomerulosclerosis are presented. Hsu et al. [17] conducted a retrospective study of 320252 healthy volunteers and showed that 1471 patients developed end-stage renal disease. After the modification of other factors, we found participants with a greater BMI are at high risk for end-stage renal disease compared with patients with a normal BMI. The incidence rates in patients with OW who are at high risk for
end-stage renal disease were 1.87, 3.57 at one-degree OB, 6.12 at two-degree OB, and 7.07 at three-degree OB. Thus, PHT detection and follow-up program are needed. The data also confirmed that OB is associated with impaired renal function. In 5897 patients with normal renal function, PHT patients were monitored for 5 years after chronic renal failure [18]. The normal BMI was 28%, the OW 31%, and the OB 34%. OW and OB are considered risk factors for chronic renal insufficiency. In a study conducted by Chagnac et al. [19], 8 patients with severe OB but without renal impairment were studied, and the renal function was improved when the BMI was reduced to 32.1 kg/m².

The above-mentioned studies did not depict the correlation between AOB and MAU. At the same time, most of the studies were performed in patients with renal insufficiency or advanced renal disease, with a minimal discussion of the MAU study. Based on the contribution to MAU size of the abdominal obesity index, such as WC, WHR, and WTHR, WTHR is the largest contributor among these indicators, and the cut-off point of prediction is 0.52, followed by WC and WHR. The cut-off points for men and women were 89.6 cm and 0.88 and 84.5 cm and 0.84 cm, respectively. The WC of the patient should be improved as much as possible, particularly the relative height of WC, and the control of the point of prediction may reduce or delay the occurrence and development of MAU. Hadja et al. [20] showed that in 297 cases serum TG level is an independent predictor of the occurrence and progression of Type 1 Diabetes Mellitus (T1DN). Some studies suggest that dyslipidemia is significantly correlated with the onset and progression of DN, and they interact with each other and form a vicious cycle [21]. No association between dyslipidemia and MAU was found in this study. However, because this study is a cross-sectional study, the relationship between them is impossible to determine. Thus, a follow-up intervention is needed to determine the association of these risk factors with MAU.

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Conflict of Interest

All authors have no conflict of interest regarding this paper.

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