The Mediating Effects of Metabolic Traits on the Association between Abdominal Obesity and Renal Function in Older Adults

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Abstract

**Backgrounds:** The deleterious effects of abdominal obesity and aging have grown into a global health issue. However, relationships between abdominal obesity and renal function with aging and underlying mechanisms have not been fully elucidated. We aimed to explore associations of abdominal obesity with renal function in older individuals and further investigate potential mechanisms of metabolic traits on them.

**Methods:** We conducted a cross-sectional study of 4,086 participants aged 60-115 years. Generalized linear models were used to quantify dose-response relationships of abdominal obesity with metabolic traits and renal function. Mediation analysis was performed to assess mediating effects of metabolic traits in the associations between abdominal obesity and renal function.

**Results:** We found negative dose-response relationships between waist circumstance and the estimated glomerular rate (eGFR) \( P<0.05 \). Abdominal obesity was associated with a 1.615 (95%CI: 0.647, 2.582) decrease in the eGFR and the decline of renal function with aging was more evident among abdominal obese participants. Significant relationships were observed between abdominal obesity and metabolic traits as well as between metabolic traits and eGFR (all \( P<0.05 \)). Mediation analysis suggested that triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and total cholesterol (TCHO) partially mediated the association between abdominal obesity and eGFR, with a mediation percentage of 3.80% by LDL-C, 25.80% by TG, and 6.00% by TCHO \( P<0.05 \).

**Conclusion:** Our findings suggest individuals of abdominal obesity are more susceptible to the nephrotoxic effect with aging, and highlight the metabolic pathways, especially TG, in the link of abdominal obesity with decreased renal function.

Introduction

With changing dietary habits and sedentary lifestyles, abdominal obesity has become a growing global public health problem, which has been reported to be correlated with the increased risk of multiple diseases (1, 2). Accumulating evidence has suggested that abdominal obesity is increasingly recognized as the driving force of impaired renal function (3). It is reported that obese individuals tended to have a higher prevalence of impaired renal function and increased adiposity might result in structural and functional changes at the nephron level (4-6). However, the associations between abdominal obesity and renal function were mainly conducted among young adults (7-9). Concurrently, the prevalence of renal diseases was reported to increase with aging(10). In China, 119.5 million individuals have suffered from renal diseases and approximately 20% of them are older adults (11). However, there remains limited evidence whether older adults might be more vulnerable to the nephrotoxic effect of abdominal obesity in the process of aging.

The underlying mechanism linking abdominal obesity and impaired renal function is complex and has not yet been fully elucidated. It is reported that metabolic traits may be involved in the process of obesity-induced damage (5, 12). Alterations in metabolic traits can arouse the endoplasmic reticulum stress of adipokine cells, which might generate oxidizing free radicals and lipid peroxidation (13, 14). The development of renal disease is negatively influenced by disorders of metabolic traits and high levels of plasma lipids were suggested to contribute to the dilation of renal mesenterium, leading to glomerular injury (14, 15). However, whether
changes in metabolic traits play potential role in the association between abdominal obesity has not been studied to date.

Understanding the associations and potential mechanisms between abdominal obesity and renal function among older adults is increasingly critical. In the present study, we hypothesized that abdominal obesity can decrease renal function through metabolic traits changes. The study was carried out among 4,621 older adults between 60-115 years old. We assessed the associations of metabolic traits with abdominal obesity and impaired renal function and further investigated the mediating roles of metabolic traits among older adults.

**Methods**

**Study population and data collection**

The study participants originated from three towns (Wuzhuan, Sanshi, and Donglan) in Guangxi, China, and local residents were recruited in a cross-sectional survey established between 2016 and 2018. Each participant underwent detailed structured questionnaire and information such as demographic and socioeconomic characteristics, and lifestyle habits were obtained through face-to-face interview. Education attainment was classified as illiteracy, primary school, and middle school or higher according to self-reported education level. Individuals who had smoked ≥1 cigarettes/day or who had drunk ≥ 1 times/week for at least half a year were identified as cigarette smokers and alcohol drinkers, respectively; otherwise they were separately identified as non-smokers and non-drinkers. After fasting overnight, each participant went through clinical examinations including anthropometric characteristics and provided their fasting venous blood samples for laboratory assays such as fasting glucose and blood lipids (triglyceride [TG], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C], and total cholesterol [TCHO]). Hypertension was defined if measured systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg, or if the participants self-reported having a hospital diagnosis of hypertension or use of antihypertensive medications. Diabetes were defined if measure fasting glucose ≥ 7.0 mmol/L, or if the participants reported a hospital diagnosis of diabetes or use of antidiabetic medications. For this study, residents were included if they were aged ≥60 years and did not have severe illness. Of 4,612 individuals aged 60 to 115 years, our current study was restricted to a total of 4086 subjects with excluding 535 subjects who failed to complete required examinations and reported a history of taking antilipemic drugs. All participants in our study were informed and provided their written consent. The research protocol was approved by the Ethics Committee of Guangxi Medical University.

**Definition of abdominal obesity**

Waist circumstance (WC) is an index parameter of abdominal obesity proposed by the World Health Organization, which has been shown to correlate more strongly with direct measures of abdominal fat accumulation than other indicators of abdominal obesity (16). The National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) recommended measuring WC in metabolic syndrome definition, emphasizing the importance of WC with metabolic traits. WC was measured by wrapping the tape around the horizontal plane midway between the lowest rib and the iliac crest at the end of a normal expiration.
Participants with WC \( \geq 90 \text{ cm} \) in males and \( \geq 80 \text{ cm} \) in females were defined as the abdominal obesity group which is proposed by the International Diabetes Federation for the Chinese population (17).

**Estimation of renal function**

The estimated glomerular rate (eGFR) is used in the assessment of renal function. The eGFR was calculated using the Chronic Renal Disease Epidemiology Collaboration (CKD-EPI) equation, which is based on the data involving 8254 participants and has less bias than the Modification of Diet in Renal Disease (MDRD) formula(18). The equation for serum creatinine was as follows: 

\[
\text{eGFR (mL/min per 1.73m}^2) = 141 \times \min (\text{SCr}/\kappa \text{ or } 1)^{\alpha} \times \max (\text{SCr}/\kappa \text{ or } 1)^{-0.109} \times 0.993^{\text{age}} \times 1.018 \div [\text{if female}].
\]

In the equations, SCr is serum creatinine (mg/dL), \( \kappa \) is 0.7 for females and 0.9 for males, and the values \( \alpha \) of for males were 0.9 and -0.411, respectively(19).

Serum creatinine concentrations were measured using the sarcosine oxidase method via an automatic analyzer.

**Statistical analysis**

The demographic characteristics of all participants were reported as frequencies (percentages) for categorical variables and means (standard deviation) for continuous variables. We compared their differences according to abdominal obesity status using the Student t-test and Chi-square test, respectively. Regression coefficients (\( \beta \)) and 95% confidence interval (CI) were estimated to explore the associations between abdominal obesity (parameters and status) and eGFR using generalized linear regression models with adjustment for gender, age, ethnicity, marriage, education, income, smoking status, drinking status, physical activity, hypertension, and diabetes. We further used restricted cubic splines to estimate dose-response relationships between WC and eGFR, with the reference value setting at the 10\(^{th}\) percentile and three knots at the 5\(^{th}\), 50\(^{th}\), and 95\(^{th}\) percentiles of WC level.

To assess whether mediating roles of metabolic traits were indicated, we estimated the associations between abdominal obesity and blood lipid levels as well as associations between blood lipid levels and eGFR by conducting multivariate generalized linear regressions models. Then we used the approach of mediation analysis to calculate the total effect, directed effect, indirect (mediating) effect, and proportions mediated by metabolic traits for the association of abdominal obesity with eGFR. The framework for the established associations of abdominal obesity with metabolic traits and renal function has provided a basis for assessing the mediating effect. With the hypothesis of mediation analysis holding, the mediating effect represents the effect of abdominal obesity on eGFR through metabolic traits. Mediating effects were estimated by the following two linear mixed models:

\[
M = a_0 + a_{obesity} X_{obesity} + a_C X_C + e_1
\]

\[
Y = v_0 + v_{obesity} X_{obesity} + v_{lipid} X_{lipid} + v_C X_C + e_2
\]
In the equations, $X_{obesity}$ denotes abdominal obesity indices (WC and status), $M$ denotes the mediators (metabolic traits), $Y$ denotes the outcome (eGFR), $X_C$ denotes confounders, $\nu_{obesity}$ denotes direct effect, and $\alpha_{obesity} \times \nu_{lipid}$ represents mediated effect by metabolic traits. The proportion of mediation by metabolic traits was calculated as the following formula: \[ \text{Prop. Mediated} = \frac{\alpha_{obesity} \times \nu_{obesity}}{\alpha_{obesity} \times \nu_{obesity} + \nu_{obesity}} \times 100. \]

Data analysis was performed using Statistical Analysis Software (SAS), version 9.4 (SAS Institute, Cary, N.C.), and R version 3.6.1 (R Core Team 2019).

**Results**

**Characteristics of the study population**

Of 4,086 participants, 1225 (29.98%) participants were identified with abdominal obesity in the present study (presented in Table 1). Approximately, most of the participants were female (67.57%) and the mean age was 70.18 years which ranged from 60 to 115 years. In comparison with non-abdominal obese individuals, participants with abdominal obesity were more likely to be female, less educated, smokers and alcohol drinkers, and had higher values of waist to height ratio (WHR), body mass index (BMI), and waist to hip ratio (WHR), as well as a higher proportion of history of hypertension and diabetes ($P<0.05$).
Table 1
General characteristics of study population (n=4086)

| Characteristics              | Total | Non-abdominal obesity | Abnormal obesity | P   |
|------------------------------|-------|------------------------|------------------|-----|
| No. participants            | 4,086 | 2,861                  | 1,225            |     |
| Gender, female, n (%)       | 2,761 (67.57) | 1,572 (54.94) | 889 (72.57) | <0.01 |
| Age (years)                 | 70.18±7.62 | 70.13±7.53 | 70.28±7.84 | 0.57 |
| Height (cm)                 | 152.57±9.35 | 152.71±9.29 | 152.26±9.48 | 0.16 |
| Weight (kg)                 | 51.28±9.61 | 48.45±8.08 | 57.88±9.66 | <0.01 |
| BMI (kg/m²)                 | 21.95±3.21 | 20.70±2.41 | 24.88±2.93 | <0.01 |
| WHR                         | 0.87±0.06 | 0.84±0.05 | 0.92±0.05 | <0.01 |
| WHtR                        | 0.51±0.06 | 0.48±0.04 | 0.57±0.04 | <0.01 |
| Education, n (%)            |       |                       |                  |     |
| Illiterate                  | 1,914 (46.84) | 1,261 (44.07) | 653 (53.31) | <0.01 |
| Primary school              | 1,365 (33.41) | 987 (34.50) | 378 (30.86) |     |
| Middle school or higher     | 807 (19.75) | 613 (21.43) | 194 (15.83) |     |
| Annual income, n (%)        |       |                       |                  |     |
| <10000 RMB                  | 1,567 (38.35) | 1,147 (40.10) | 420 (34.30) | <0.01 |
| 10000~30000 RMB             | 1,088 (26.63) | 749 (26.20) | 339 (27.70) |     |
| >=30000 RMB                 | 1,431 (35.02) | 965 (33.70) | 466 (38.00) |     |
| Smoking, n (%)              | 3,454 (84.53) | 2,354 (82.28) | 1,100 (89.80) | <0.01 |
| Alcohol drinking, n (%)     | 3,154 (77.19) | 2,132 (74.52) | 1,022 (83.43) | <0.01 |
| Hypertension, n (%)         | 2,095 (51.27) | 1,342 (46.91) | 753 (61.47) | <0.01 |
| Diabetes, n (%)             | 270 (6.61) | 154 (5.38) | 116 (9.47) | <0.01 |
| Metabolic traits            |       |                       |                  |     |
| LDL_C (mmol/L)              | 3.27±0.91 | 3.21±0.92 | 3.40±0.89 | <0.01 |
| TG (mmol/L)                 | 1.24±0.67 | 1.14±0.59 | 1.48±0.79 | <0.01 |
| HDL_C (mmol/L)              | 1.57±0.35 | 1.60±0.35 | 1.48±0.31 | <0.01 |
| TCHO (mmol/L)               | 5.39±1.07 | 5.33±1.08 | 5.54±1.04 | <0.01 |
| eGFR(mL/min per 1.73m²)     | 86.30±16.19 | 86.78±15.86 | 85.15±16.9 | <0.01 |

Abbreviations: BMI, body mass index; WHR, waist to hip ratio; WHtR, waist to height ratio; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; TCHO, total cholesterol; eGFR, estimated glomerular rate. Participants with waist circumstance ≥ 90 cm in males and ≥ 80 cm in females were defined as abdominal obesity group. Smoking individuals included current and
ever smokers. Data are presented as n (%), for categorical variables, mean ± SD for continuous variables. P values were estimated by Student's t-test for continuous variables according to the data distribution and Chi-square test for categorical variables.

The mean values for metabolic traits (LDL-C, TG, HDL-C, and TCHO) and eGFR for all participants were 3.27, 1.24, 1.57, 5.39 mmol/L, and 86.30 mL/min per 1.73m$^2$ respectively. Levels of LDL-C, TG, and TCHO (mean: 3.40, 1.48, 5.54 mmol/L) were significantly higher in abdominal obese participants than those with non-abdominal obesity (mean: 3.21, 1.14, 5.33 mmol/L). Abdominal obese participants tended to have lower levels of HDL-C ($P<0.05$). Meanwhile, lower levels of eGFR was observed in participants with abdominal obesity (mean: 85.15 vs. 86.78 mL/min per 1.73m$^2$, $P<0.05$), compared to those with non-abdominal obesity.

**Association between abdominal obesity and renal function**

The dose-response association of WC with renal function was present in Figure 1. We visually observed a negative dose-response relationship between WC and renal function ($P<0.05$). When WC gradually increased, estimates changes of eGFR showed a monotonous decreasing trend. Results of Figure 2 indicated that participants with abdominal obesity had a 1.615 (95% CI: 0.647 to 2.582) decrease in eGFR (mL/min per 1.73m$^2$), compared to those with non-abdominal obesity after adjusting for potential covariates. Additionally, we investigated whether the effect of abdominal obesity on renal function is influenced by the aging of older adults, and found that the downward trends for eGFR with increased age were more significant in individuals with abdominal obesity, compared to non-abdominal obese participants (presented in Figure 2).

**Abdominal obesity-metabolic traits and metabolic traits-renal function**

Significant positive relationships were observed between WC and levels of LDL-C, TG, and TCHO, and a negative relationship was observed between WC and HDL-C in both crude and adjusted models (shown in Table 2). Compared to those with non-abdominal obesity, participants with abdominal obesity had a 0.128 (95% CI: 0.065 to 0.19), 0.294 (95% CI: 0.249 to 0.339), 0.129 (95% CI: 0.056 to 0.203) mmol/L increase in LDL-C, TG, and TCHO, respectively, and had a -0.129 (95% CI: -0.152 to -0.105) mmol/L decrease in HDL-C, with adjustment for potential confounders (all $P<0.05$).
Table 2
Associations between WC and metabolic traits (n=4086)

| Metabolic traits (mmol/L) | Estimated changes in metabolic traits by WC | Estimated changes in metabolic traits by abdominal obesity status |  |
|--------------------------|------------------------------------------|---------------------------------------------------------------|---|
|                          | β (95% CI)                                | P value | Non-abdominal obesity | Abdominal obesity | P value |
| LDL_C                    |                                          |         |                     |                   |         |
| Crude                    | 0.010(0.007,0.013)                        | <0.001  | 0(referent)          | 0.185(0.124,0.246) | <0.001  |
| Adjusted                 | 0.010(0.006,0.013)                        | <0.001  | 0(referent)          | 0.128(0.065,0.190) | <0.001  |
| TG                       |                                          |         |                     |                   |         |
| Crude                    | 0.023(0.020,0.025)                        | <0.001  | 0(referent)          | 0.333(0.289,0.377) | <0.001  |
| Adjusted                 | 0.020(0.018,0.023)                        | <0.001  | 0(referent)          | 0.294(0.249,0.339) | <0.001  |
| HDL_C                    |                                          |         |                     |                   |         |
| Crude                    | -0.009(-0.010,-0.008)                     | <0.001  | 0(referent)          | -0.122(-0.145,-0.100) | <0.001  |
| Adjusted                 | -0.009(-0.010,-0.008)                     | <0.001  | 0(referent)          | -0.129(-0.152,-0.105) | <0.001  |
| TCHO                     |                                          |         |                     |                   |         |
| Crude                    | 0.012(0.008,0.015)                        | <0.001  | 0(referent)          | 0.210(0.139,0.282) | <0.001  |
| Adjusted                 | 0.010(0.006,0.014)                        | <0.001  | 0(referent)          | 0.129(0.056,0.203) | <0.001  |

Abbreviations: WC, waist circumstance; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; TCHO, total cholesterol; β, the regression coefficient, CI, confidence interval.

Participants with WC ≥ 90 cm in males and ≥ 80 cm in females were defined as abdominal obesity group. Models were adjusted for gender, age, education, income, smoking status, drinking status, hypertension, and diabetes, and included towns as a random effect. P values were estimated in mixed linear models using WC as a continuous variable and abdominal obesity status as a categorical variable.

We found that renal function showed a downward trend when LDL-C, TG, and TCHO levels gradually increased (all P<0.05) (shown in Table 3). With adjustment for potential confounders, each one-unit increase in LDL-C, TG, and TCHO was associated with a -0.555(95% CI: -1.024 to -0.086), -1.576(95% CI: -2.216 to -0.935), and -0.817(95% CI: -1.217 to -0.418) changes in eGFR (mL/min per 1.73m²), respectively (all P<0.05). Yet, the adjustment of potential confounders substantially affect the association of renal function with HDL-C, and we did not observe significant alterations of eGFR with HDL-C levels in adjusted models (P>0.05).
| Metabolic traits (mmol/L) | Estimated changes in renal function by tertiles of metabolic traits | Changes in renal function by continuous metabolic traits | P value for trend |
|--------------------------|-------------------------------------------------|----------------------------------------------------|------------------|
|                         | Tertile1 β (95% CI) | Tertile2 β (95% CI) | Tertile3 β (95% CI) |                                    |
| LDL_C                   | <2.8                | 2.8-3.6             | >=3.6               |                                |
| Crude                   | 0(referent)         | -1.539(-2.764,-0.315) | -0.991(-2.222,0.24) | -0.672(-1.21,-0.134) | 0.014 |
| Adjusted                | 0(referent)         | -1.584(-2.644,-0.524) | -1.168(-2.242,-0.094) | -0.555(-1.024,-0.086) | 0.020 |
| TG                      | <0.88               | 0.88-1.27           | >=1.27              |                                |
| Crude                   | 0(referent)         | -1.758(-2.971,-0.545) | -2.478(-3.68,-1.277) | -1.399(-2.129,0.668) | <0.001 |
| Adjusted                | 0(referent)         | -1.045(-2.09,-0.001) | -2.353(-3.404,-1.301) | -1.576(-2.216,-0.935) | <0.001 |
| HDL_C                   | <1.40               | 1.40-1.67           | >=1.67              |                                |
| Crude                   | 0(referent)         | 0.782(-0.438,2.003)  | 1.081(-0.115,2.277)  | 2.073(0.651,3.495) | 0.004 |
| Adjusted                | 0(referent)         | 0.225(-0.826,1.277)  | 0.208(-0.833,1.249)  | 0.322(-0.921,1.564) | 0.612 |
| TCHO                    | <4.88               | 4.88-5.77           | >=5.77              |                                |
| Crude                   | 0(referent)         | -1.053(-2.265,0.159) | -1.42(-2.625,-0.214) | -0.646(-1.105,-0.187) | 0.006 |
| Adjusted                | 0(referent)         | -1.099(-2.144,-0.054) | -1.877(-2.926,-0.828) | -0.817(-1.217,-0.418) | <0.001 |

Abbreviations: LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; TCHO, total cholesterol; eGFR, estimated glomerular rate; β, the regression coefficient, CI, confidence interval.

Models were adjusted for gender, age, education, income, smoking status, drinking status, hypertension, and diabetes, and included towns as a random effect. P value for trend was conducted by assigning the median value to each tertile of metabolic traits levels and treated as a continuous variable.

Mediation analysis

Results of Table 4 showed that associations between abdominal obesity and eGFR were partially mediated by LDL-C, TG, and TCHO, the mediating effect of which were -0.064 (95%CI: -0.145,-0.001), -0.421 (95% CI: -0.644,-0.230), and -0.101 (95%CI: -0.186,-0.030), respectively. Similar results were found for mediating effects of LDL-C, TG, and TCHO on the relationships between WC and eGFR decline. Among these significant mediators, TG was found to be the strongest mediator. The percentage of mediation of TG to decrease renal function associated with abdominal obesity were 22.4% for WC, and 25.8% for abdominal obesity status.
Table 4
Mediating effects of metabolic traits on associations between abdominal obesity and renal function (n=4086)

| Variables                          | LDL_C         | TG            | HDL_C         | TCHO          |
|------------------------------------|---------------|---------------|---------------|---------------|
| Abdominal obesity parameter (WC)   |               |               |               |               |
| Total effect $\beta$ (95% CI)      | -0.122(-0.167,-0.070) | -0.117(-0.169,-0.060) | -0.115(-0.167,-0.060) | -0.117(-0.166,-0.060) |
| Direct effect $\beta$ (95% CI)     | -0.118(-0.163,-0.060) | -0.09(-0.144,-0.040) | -0.118(-0.170,-0.060) | -0.109(-0.157,-0.060) |
| Mediating effect $\beta$ (95% CI)  | -0.004(-0.010,-0.002) | -0.026(-0.041,-0.010) | 0.002(-0.009,0.010) | -0.007(-0.013,-0.003) |
| Prop. mediated % ($P$ value)       | 3.4($P=0.040$) | 22.4 ($P<0.001$) | *             | 6.20($P<0.001$) |
| Abdominal obesity status (yes/no)  |               |               |               |               |
| Total effect $\beta$ (95% CI)      | -1.621(-2.566,-0.680) | -1.611(-2.550,-0.670) | -1.613(-2.567,-0.660) | -1.650(-2.644,-0.660) |
| Direct effect $\beta$ (95% CI)     | -1.557(-2.505,-0.630) | -1.190(-2.133,-0.190) | -1.609(-2.570,-0.660) | -1.549(-2.545,-0.550) |
| Mediating effect $\beta$ (95% CI)  | -0.064(-0.145,-0.001) | -0.421(-0.644,-0.230) | -0.004(-0.170,0.170) | -0.101(-0.186,-0.030) |
| Prop. mediated % ($P$ value)       | 3.8($P=0.046$) | 25.8($P=0.002$) | 0.10($P=0.970$) | 6.00 ($P<0.001$) |

Abbreviations: WC, waist circumstance; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; TCHO, total cholesterol; eGFR, estimated glomerular rate; $\beta$, the regression coefficient, CI, confidence interval. Participants with WC ≥ 90 cm in males and ≥ 80 cm in females were defined as abdominal obesity group. Models were adjusted for gender, age, education, income, smoking status, drinking status, hypertension, and diabetes, and included towns as a random effect. The mediation analysis was performed to identify the proportion of a statistical relationship between abdominal obesity and eGFR that occurs through changes in the metabolic traits using a sum or product coefficient method. *Proportion mediated cannot be calculated due to opposite signs between direct effect and mediating effect.

Discussion
As we have known, the potential mechanism of metabolic traits in relating abdominal obesity to renal function is firstly investigated in older adults aged 60 to 115 years. Our results showed that individuals with abdominal obesity were more prone to renal function decline with aging. Significant relationships were observed between abdominal obesity and metabolic traits, as well as between metabolic traits and renal function. Metabolic traits, including LDL-C, TG, and TCHO, were significant mediators for the associations of abdominal obesity indices with eGFR, and the mediating role of TG was stronger than the other two metabolic traits. These results suggested that individuals of abdominal obesity are more susceptible to nephrotoxic effect in the process of aging, and the metabolic traits partly mediated the association of abdominal obesity with renal function.

These findings have substantial implications, as abdominal obesity has long been a major risk factor for public health. Most studies describing the adverse effects of abdominal obesity were carried out in younger populations (20, 21). Elisabeth et al. found that obese individuals at the age of 20 had a two-fold increase in the risk of chronic renal disease when compared to participants with normal weight (7). However, obesity and aging are independent risk factors for multiple conditions. In older adults, abdominal obesity confers a higher risk of impaired physical function and relevant outcomes (22). Our study highlights the public health concern regarding renal function damage induced by abdominal obesity in older adults, and provides important clues for the underlying mechanism. Effective measures are urgently needed for older adults with abdominal obesity, highlighting the priority in reducing the levels of TG to decrease impaired renal function related to abdominal obesity with aging.

Previous studies reported that obesity to be a risk factor for kidney diseases and positive associations were observed between obesity and the risk of kidney disease (8, 23). The eGFR describes the flow rate of filtered fluid through the renal and the decline in eGFR is indicative of early-onset renal damage that may precede the progression of renal disease (24). Agreeing with our results, Wang and his colleagues performed a meta-analysis and reported a positive relationship between obesity and increased risk of impaired renal function (25). Chang et al. found that higher WC was related to the decline of eGFR in a dose-dependent manner in young adults (9). However, eGFR at the age of 90 years was reported to decrease 50% compared to young people (26). In the present study, we found that the downward trends for eGFR with increased age were more significant in older adults with abdominal obesity, indicating older adults are more susceptible to nephrotoxic effect of abdominal obesity along with aging.

The biological mechanisms by which abdominal obesity contribute to renal function decline remained unclear, but metabolic traits are thought to be of importance (12, 27). A study of NHANES in the US adults reported that an increase in TG was associated with obesity in white men and women of all ages (28). Consistent with prior studies, our results reported significant associations between abdominal obesity and metabolic traits (LDL-C, TG, HDL-C, and TCHO) in the older adults. In addition, a growing body of studies reported that blood lipid disorders were associated with a reduction in the amount of glomerular injury and altered lipid metabolism contributes to the progression of renal diseases (29-31). Wahl and his colleagues reported that patients with impaired renal function had higher levels of LDL than those controls, and hypertriglyceridemia was found to be associated with nephrotic syndrome (27). Studies carried out in several animal models also demonstrated that blood lipid disorders were associated with a reduction in the amount of glomerular injury. When rats treated with antilipemic agents, serum cholesterol was reduced and the amount of renal injury diminished (32,
The method of mediation analysis has been widely used to explore the potential mechanisms in population-based studies in the past few years (34). Our results of mediation analysis show that metabolic traits (LDL-C, TG, and TCHO), especially TG, might be the intermediate pathways underlying decreased renal function caused by abdominal obesity. Accumulation of lipids might result in the stimulation of inflammatory response such as activation of monocytes and macrophages, which promote the release of pro-inflammatory cytokines and reduced glomerular filtration rate and renal failure (27, 35). In the present study, the mediating effect of metabolic traits was found to be partly mediated, indicating that other pathways such as DNA methylation and genomic imprinting might be involved in the abdominal obesity-associated impaired renal function. To find more biomarkers comprehensively explicating potential biological pathways, future studies based on mediation is warranted.

Several strengths should be acknowledged. First, this study with a relatively large-scale population aged 60 to 115 years enables us to establish a relationship between abdominal obesity and renal function in the process of aging. Second, we used a mediation analysis to investigate the underlying mechanism for the effect of abdominal obesity on renal function. The application of mediation analysis has been proven to offer important clues and forward steps for further research of biological molecular pathways. Finally, concerning the bias of confounding factors, multivariate linear mixed models were carried out to ensure the greatest likelihood of reduced bias, with adjustment for gender, age, ethnicity, marriage, education, income, smoking status, drinking status, physical activity. The limitation of our study is that the nature of cross-sectional design has not been able to establish a causal link between abdominal obesity and renal function decline, and further in vivo and vitro researches are urgently needed to verify our findings and to explore biological pathway for the effect of abdominal obesity on renal function in older adults.

**Conclusions**

Our results indicate that individuals with abdominal obesity were more susceptible to renal disease with aging, and effective precautions are urgently needed to prevent older adults from damage to renal function. The metabolic traits pathway might be a potential mechanism for the link between abdominal obesity and renal function decline, providing an important clue for further research.

**Declarations**

**Ethics approval and consent to participate**

All participants in our study were informed and provided their written consent. The research protocol was approved by the Ethics Committee of Guangxi Medical University. All procedures performed in the study were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declarations and its later amendments.

**Consent for publication**

Not applicable
Availability of data and materials

The datasets for the current study is available from the corresponding author on reasonable request.

Competing interest

The authors declare that they have no competing interests.

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Author Contributions

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