Impact of obesity on renal function in elderly Korean adults: a national population-based cohort study

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Background: Obesity is a well-known risk factor for chronic kidney disease and its progression. However, the impact of obesity on the renal function of the elderly population is uncertain. We investigated the association between obesity and renal outcomes in the elderly.

Methods: We analyzed 130,504 participants from the Korean National Health Insurance Service-Senior cohort. Obesity was classified according to body mass index (BMI), sex-specific waist circumference (WC), and the presence of metabolic syndrome. The primary outcome was renal function decline, defined as a decline in the estimated glomerular filtration rate (eGFR) of at least 50% from baseline or new-onset end-stage renal disease.

Results: During a follow-up period of 559,531.1 person-years (median, 4.3 years), 2,486 participants (19.0%; incidence rate of 4.44 per 1,000 person-years) showed renal function decline. A multivariate Cox proportional hazards model revealed that BMI/WC was not associated with renal function decline. However, the group with metabolic syndrome had a significantly increased risk of renal function decline compared to the group without metabolic syndrome (adjusted hazard ratio [HR], 1.24; 95% confidence interval [CI], 1.13–1.36). Compared with the non-metabolic syndrome group, the adjusted HRs (95% CI) for participants with one through five components were 0.96 (0.84–1.11), 1.10 (0.96–1.27), 1.24 (1.06–1.45), 1.37 (1.12–1.66), and 1.99 (1.42–2.79), respectively (p for trend < 0.001).

Conclusion: In elderly Korean adults, metabolic syndrome and the number of its components were associated with a higher risk of renal function decline, but BMI or WC was not significant.

Keywords: Elderly, Metabolic syndrome, Obesity, Kidney function
Introduction

The number of elderly patients with chronic kidney disease (CKD) is rapidly increasing worldwide due to the aging of the population, an increase in chronic diseases such as diabetes mellitus (DM) and hypertension, and an increase in the survival rate of CKD patients [1,2]. In addition, obesity and metabolic syndrome increase with age, because aging is associated with an increase in abdominal adipose tissue, inflammation, and insulin resistance [3,4]. Obesity in elderly patients with CKD may be both a consequence of underlying conditions and a factor that exacerbates the comorbidities. There might be a close and intricate relationship between obesity and CKD in elderly, suggesting a causal link, but it is not well studied yet.

Previous studies have shown that obesity is associated with the development of proteinuria, impaired renal function, and progression to end-stage renal disease (ESRD) [5-7]. The mechanism is that increased fat mass in obesity causes mesangial expansion and a rise in the renal metabolic requirement, which can lead to glomerular hyperfiltration, glomerular hypertrophy, and a decrease in podocyte density. Obesity also activates the renin-angiotensin system, which leads to the aggravation of DM, atherosclerosis, and hypertension, as well as the onset and exacerbation of CKD [8,9].

However, in elderly or advanced CKD patients, an “obesity paradox” has been reported, in which patients with high body mass index (BMI) have a lower mortality rate compared to patients with normal or low BMI [10,11]. This could be explained by the greater adverse effect of protein energy wasting than the effects of obesity in elderly CKD patients, or the time mismatch with the competitive risk for death. Another reason is that many previous studies defined obesity based on BMI. Since BMI does not easily differentiate between muscle mass and body fat, it is difficult to determine the amount of visceral fat [7,12]. Unlike BMI, when obesity was defined by the waist-to-hip ratio in ESRD patients, the mortality rate was higher in patients with a high waist-to-hip ratio, indicating the importance of central obesity [12,13]. In addition, the elderly may be misclassified as normal or overweight due to kyphosis that occurs with aging [14].

The effect of obesity on renal function in the elderly is not clear. Previous studies have shown conflicting results, and there are only a few studies on Asian subjects. It is not known whether the obesity paradox persists in the renal function of the elderly. In addition, we do not know whether there is a difference in the effect of BMI and waist circumference (WC), which are convenient tools to assess obesity. Due to the increasing concern regarding the potential influence of obesity on the growing elderly population, we conducted a study to examine the correlation between obesity and renal function in the elderly. In this background, we hypothesized that abdominal obesity or metabolic abnormality would affect renal function more than BMI in the elderly. The aim of this study is to evaluate the association between different obesity parameters and renal outcomes in the elderly.

Methods

This study was approved by the Institutional Review Boards of Catholic Medical Center (DC20ZISI0013) and the Korean National Health Insurance Service (NHIS) (No. NHIS-2022-2-182) and was conducted according to the Declaration of Helsinki. The informed consent was waived by Institutional Review Boards because of the minimal-risk retrospective study.

Study populations

We used data in the geriatric cohort database of the Korean NHIS-Senior cohort (NHIS-Senior). The NHIS-Senior cohort is a retrospective cohort designed to explore various aspects of changes in the socioeconomic and health status of the elderly and to analyze the risk factors and prognosis of geriatric disease. This is a national cohort containing information of 558,147 individuals selected by 10% simple random sampling among a total of 5.5 million subjects aged 60 years or older in the National Health Information Database (NHID), which stores all the records of healthcare and long-term care services. Data from a self-reported questionnaire (lifestyle, past medical history, and family medical history) and biometric information (blood pressure, anthropometry, and laboratory findings) are included in the NHID because the NHIS offers a national health screening program that includes medical check-ups every 2 years [15].

We included adults 65 years of age and older who under-
went medical examinations in 2009 and 2010 and excluded subjects who had no data on BMI, WC, or metabolic syndrome or subjects who were previously diagnosed with ESRD. A total of 130,504 subjects were analyzed, and they were followed up until December 2015.

**Study measures**

Participants’ height and weight were measured with light clothes and no shoes. BMI was calculated by dividing the weight by the height (kg/m$^2$). WC was measured at the midpoint between the lowest rib and iliac crest by a trained examiner. Demographic variables, such as age, sex, smoking status, alcohol intake, physical activity, and history of comorbidities (cerebrovascular disease, heart disease, hypertension, DM, and dyslipidemia), were assessed using self-reported information. Laboratory variables such as serum hemoglobin, fasting glucose, total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, aspartate aminotransferase, alanine aminotransferase, and proteinuria were measured at fasting status. The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) equation [16]. Proteinuria was detected using a urine dipstick test.

**Definitions of variables**

Obesity was classified according to BMI, sex-specific WC, and metabolic syndrome. Participants were divided into four groups according to the World Health Organization (WHO) Asian BMI classification as follows: underweight (<18.5 kg/m$^2$), normal (18.5–22.9 kg/m$^2$), overweight (23.0–24.9 kg/m$^2$), and obesity (≥25 kg/m$^2$) [17]. Participants were also divided into four groups according to their quartile of sex-specific WCs. Metabolic syndrome was diagnosed when three or more of the following criteria were satisfied: 1) WC ≥ 90 cm for men, ≥85 cm for women; 2) triglycerides ≥ 150 mg/dL; 3) HDL cholesterol < 40 mg/dL for men, <50 mg/dL for women; 4) blood pressure ≥130/85 mmHg or taking antihypertensive drugs; and 5) fasting blood glucose ≥100 mg/L or taking glucose-lowering drugs [18]. Hypertension was defined as a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg, presence of history of hypertension, or current use of medication for hypertension. DM was defined as fasting glucose level ≥126 mg/dL, presence of a history of DM, or current use of medication for DM. Dyslipidemia was defined as total cholesterol ≥240 mg/dL, presence of a history of dyslipidemia, or current use of medication for dyslipidemia.

**Outcomes**

The primary outcome was renal function decline, defined as a decline in the eGFR of at least 50% from baseline or the development of ESRD. If serum creatinine was measured more than three times, follow-up renal function was evaluated with the last measurement. ESRD was defined using the combination of the International Statistical Classification of Diseases and Related Health Problems, 10th revision codes (N18-N19, Z49, Z94.0, Z99.2) and a special code for renal replacement therapy (V001, V003, V005). Renal replacement therapy was limited to cases maintained for more than 3 months. We excluded cases with acute renal failure codes (N17.0, N17.8, N17.9) on the day on which the renal replacement therapy cost code was claimed.

**Statistical analysis**

The study population was divided into four groups according to the WHO Asian BMI classification, into quartiles based on the sex-specific waist, and into two groups according to the presence or absence of a diagnosis of metabolic syndrome. To compare between groups, we used the one-way analysis of variance for continuous variables and the chi-square test for categorical variables. The Cox proportional hazards models were used to calculate the hazard ratios (HRs) and 95% confidence intervals (CIs) of each group for renal function decline. We performed subgroup analyses according to sex, age, DM, hypertension, and eGFR (≥60 mL/min/1.73 m$^2$ or <60 mL/min/1.73 m$^2$). For the participants with baseline eGFR ≥60 mL/min/1.73 m$^2$, we analyzed the risk of incident CKD, defined as an eGFR decrease below 60 mL/min/1.73 m$^2$ at follow-up visit. The Kaplan-Meier survival curves were calculated for renal function decline stratified by obesity-related groups, and the survival curves between groups were compared using the log-rank test. All data analyses were performed using R version 3.3.3 (R Foundation for Statistical Computing) and SAS version 9.4 (SAS Institute Inc.). All tests were two-sid-
ed. In all analyses, a p-value of <0.05 was considered statistically significant.

**Results**

**Baseline characteristics**

Table 1 presents the characteristics of the participants according to their BMI categories. The mean age was 72.4 ± 4.3 years, and 44.3% were male. The mean BMI was 24.1 ± 3.1 kg/m², and the mean WC was 83.7 ± 8.4 cm. The mean eGFR was 78.1 ± 31.4 mL/min/1.73 m². Of the participants, 64.8% had hypertension, 22.7% were diabetic, 8.8% had heart disease, and 27.9% did moderate physical activity for more than 150 min/wk. The underweight group was the oldest and had the least physical activity. On the other hand, the obese group was the youngest among the four groups and generally showed a poor cardiometabolic profile. The obese group had the highest systolic blood pressure, diastolic blood pressure, WC, glucose, total cholesterol, triglyceride, and LDL levels. In addition, the prevalences of hypertension, DM, heart disease, dyslipidemia, and proteinuria were highest, while eGFR and serum HDL levels were lowest in the obese group.

**Obesity parameters and renal function decline**

For the BMI categories of underweight, normal, overweight and obesity, the renal function decline occurred in 75 participants (4.62/1,000 person-years), 776 participants (4.17/1,000 person-years), 624 participants (4.16/1,000 person-years), and 1,011 participants (4.88/1,000 person-years), respectively (Table 2).

A renal function deterioration was observed in 2,486 participants (19.0%, incidence rate 4.44 per 1,000 person-years) during the follow-up period of 559,531.1 person-years (median, 4.3 years). The Kaplan-Meier curve showed a higher incidence of renal function decline in participants with high BMI, high WC, and metabolic syndrome (Fig. 1).

Table 2 represents Cox HRs and 95% CIs for renal function decline according to obesity parameters. Adjusted HRs were not significant for any BMI or WC quartile except for overweight. Table 2 represents Cox HRs for renal function decline according to the status of metabolic syndrome. Metabolic syndrome was significantly associated with renal function decline in the crude and fully adjusted models (HR, 1.24 [95% CI, 1.13–1.36]; model 3). The number of metabolic syndrome components was also associated with an increased risk of renal function decline. When all five components were present, the risk was almost 2.0 times higher (HR, 1.99 [95% CI, 1.42–2.79]; model 3). In addition, as the number of metabolic syndrome components increased, the risk of renal function decline increased (p for trend < 0.001). The presence of metabolic syndrome was also associated with an increased risk of incident CKD (HR, 1.22 [95% CI, 1.10–1.35]).

**Subgroup analysis**

Fig. 2 represents subgroup associations of metabolic syndrome and renal function decline. The increased risk of renal function decline by metabolic syndrome showed similar tendencies between subgroups. In participants with baseline eGFR ≥60 mL/min/1.73 m², there was no association between baseline BMI or WC and incident CKD (data are not shown).

**Discussion**

In this study, we explored the associations between different obesity parameters and renal outcomes in a national population-based cohort of the Korean elderly. We found that neither BMI nor WC was associated with renal function decline, but the presence of metabolic syndrome was independently associated with an increased risk of renal function decline. The number of metabolic syndrome components was gradually and independently associated with renal function decline, and this relationship was similar in different subgroups.

In the general population, high BMI and abdominal obesity are well-known risk factors for renal function decline [19]. However, in the geriatric population, the results are not consistent. de Boer et al. [20] examined the association between obesity and longitudinal change in eGFR in 5,888 adults ≥65 years-old who participated in the community-based Cardiovascular Health Study. They found that obesity assessed by BMI, WC, and fat mass was associated with a decrease in eGFR during 7 years of follow-up [20]. Another study by Madero et al. [21] analyzed the associa-
Table 1. Baseline characteristics according to BMI categories

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>Underweight, BMI &lt;18.5</th>
<th>Normal, BMI 18.5–22.9</th>
<th>Overweight, BMI 23.0–24.9</th>
<th>Obese, BMI ≥25.0</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>130,504</td>
<td>4,103</td>
<td>44,061</td>
<td>34,522</td>
<td>47,818</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>72.4 ± 4.3</td>
<td>74.2 ± 5.2</td>
<td>72.8 ± 4.5</td>
<td>72.2 ± 4.1</td>
<td>71.9 ± 3.9</td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>57,786 (44.3)</td>
<td>2,058 (1.6)</td>
<td>21,610 (16.6)</td>
<td>16,167 (12.4)</td>
<td>17,951 (13.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156.8 ± 9.0</td>
<td>157.2 ± 9.6</td>
<td>157.2 ± 9.2</td>
<td>157.4 ± 8.9</td>
<td>156.0 ± 8.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59.3 ± 9.8</td>
<td>43.3 ± 5.7</td>
<td>52.8 ± 6.8</td>
<td>59.6 ± 6.8</td>
<td>66.5 ± 8.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.1 ± 3.1</td>
<td>17.4 ± 0.9</td>
<td>21.3 ± 1.2</td>
<td>24.0 ± 0.6</td>
<td>27.3 ± 2.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>130.8 ± 16.0</td>
<td>125.1 ± 17.1</td>
<td>128.8 ± 16.2</td>
<td>130.9 ± 15.7</td>
<td>133.0 ± 15.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>78.3 ± 10.0</td>
<td>75.9 ± 10.4</td>
<td>77.3 ± 10.0</td>
<td>78.2 ± 9.8</td>
<td>79.4 ± 9.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>83.7 ± 8.4</td>
<td>69.8 ± 6.5</td>
<td>78.1 ± 6.1</td>
<td>83.9 ± 5.7</td>
<td>89.9 ± 6.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoking</td>
<td>13,748 (10.5)</td>
<td>825 (0.6)</td>
<td>6,236 (4.8)</td>
<td>3,421 (2.6)</td>
<td>3,266 (2.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alcohol</td>
<td>30,796 (23.6)</td>
<td>945 (0.7)</td>
<td>11,125 (8.5)</td>
<td>8,464 (6.5)</td>
<td>10,262 (7.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>4,744 (3.6)</td>
<td>144 (0.1)</td>
<td>1,566 (1.2)</td>
<td>1,284 (1.0)</td>
<td>1,750 (1.3)</td>
<td>0.6169</td>
</tr>
<tr>
<td>Heart disease</td>
<td>11,534 (8.8)</td>
<td>284 (0.2)</td>
<td>3,401 (2.6)</td>
<td>3,104 (2.4)</td>
<td>4,745 (3.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>84,532 (64.8)</td>
<td>1,768 (1.4)</td>
<td>24,520 (18.8)</td>
<td>22,603 (17.3)</td>
<td>35,641 (27.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabets mellitus</td>
<td>29,588 (22.7)</td>
<td>516 (0.4)</td>
<td>8,298 (6.4)</td>
<td>7,917 (6.1)</td>
<td>12,857 (9.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>26,321 (20.2)</td>
<td>482 (0.4)</td>
<td>7,568 (5.8)</td>
<td>7,204 (5.5)</td>
<td>11,067 (8.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proteinuria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>78.1 ± 31.4</td>
<td>82.6 ± 39.7</td>
<td>80.0 ± 31.4</td>
<td>77.7 ± 31.3</td>
<td>76.2 ± 30.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>13.3 ± 1.5</td>
<td>12.8 ± 1.5</td>
<td>13.2 ± 1.5</td>
<td>13.4 ± 1.4</td>
<td>13.5 ± 1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>104.4 ± 27.5</td>
<td>99.1 ± 25.9</td>
<td>102.3 ± 27.2</td>
<td>104.6 ± 27.3</td>
<td>106.8 ± 27.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>196.1 ± 39.1</td>
<td>186.9 ± 37.2</td>
<td>193.6 ± 38.5</td>
<td>196.8 ± 39.4</td>
<td>198.6 ± 39.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>142.2 ± 84.4</td>
<td>107.7 ± 66.3</td>
<td>129.3 ± 78.2</td>
<td>145.5 ± 87.8</td>
<td>154.5 ± 86.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>54.2 ± 33.0</td>
<td>59.8 ± 38.0</td>
<td>56.0 ± 35.0</td>
<td>53.4 ± 31.5</td>
<td>52.7 ± 31.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>115.6 ± 38.5</td>
<td>108.9 ± 42.3</td>
<td>114.2 ± 38.0</td>
<td>116.2 ± 39.1</td>
<td>1170 ± 38.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>26.3 ± 16.9</td>
<td>27.6 ± 17.6</td>
<td>26.0 ± 16.3</td>
<td>25.7 ± 12.8</td>
<td>26.7 ± 19.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>22.7 ± 15.7</td>
<td>19.2 ± 13.7</td>
<td>20.6 ± 15.2</td>
<td>22.4 ± 14.1</td>
<td>25.0 ± 16.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate intensity PA (&gt;150 min/wk)</td>
<td>36,419 (27.9)</td>
<td>844 (0.6)</td>
<td>11,957 (27.1)</td>
<td>10,305 (29.9)</td>
<td>13,313 (27.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>House income, quintile</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1</td>
<td>20,015 (15.3)</td>
<td>665 (0.6)</td>
<td>6,910 (9.2)</td>
<td>5,140 (7.9)</td>
<td>7,300 (10.2)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>15,159 (11.6)</td>
<td>539 (0.4)</td>
<td>5,229 (4.0)</td>
<td>3,953 (3.0)</td>
<td>5,438 (4.2)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>18,259 (14.0)</td>
<td>563 (0.4)</td>
<td>6,264 (4.0)</td>
<td>4,729 (3.0)</td>
<td>6,703 (3.2)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>25,786 (19.8)</td>
<td>847 (0.6)</td>
<td>8,632 (6.6)</td>
<td>6,857 (5.3)</td>
<td>9,450 (7.2)</td>
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</tr>
<tr>
<td>5</td>
<td>51,285 (39.3)</td>
<td>1,489 (1.1)</td>
<td>17,026 (13.0)</td>
<td>13,843 (10.6)</td>
<td>18,927 (14.5)</td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as number only, mean ± standard deviation, or number (%). Categorical variables: p-value obtained from chi-square test; Non-categorical variables: p-value obtained from analysis of variance.

ALT, alanine transferase; AST, aspartate transaminase; BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PA, physical activity; SBP, systolic blood pressure.
Table 2. The association between obesity markers and the risk of renal disease progression

<table>
<thead>
<tr>
<th>Variable</th>
<th>Observed</th>
<th>Events</th>
<th>Person-year</th>
<th>Incidence rate/1,000 person-years</th>
<th>Model 1</th>
<th></th>
<th></th>
<th></th>
<th>Model 2</th>
<th></th>
<th></th>
<th></th>
<th>Model 3</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HR (95% CI)</td>
<td>p for trend</td>
<td>HR (95% CI)</td>
<td>p for trend</td>
<td>HR (95% CI)</td>
<td>p for trend</td>
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<tr>
<td><strong>BMI</strong></td>
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<td></td>
</tr>
<tr>
<td>Underweight, reference</td>
<td>4,103</td>
<td>75</td>
<td>16,248</td>
<td>4.62</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td>0.87 (0.68–1.10)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td>0.81 (0.64–1.04)</td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>Normal</td>
<td>44,061</td>
<td>776</td>
<td>186,229</td>
<td>4.17</td>
<td>0.83 (0.66–1.05)</td>
<td></td>
<td></td>
<td></td>
<td>0.83 (0.65–1.05)</td>
<td></td>
<td></td>
<td></td>
<td>0.74 (0.57–0.96)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>34,522</td>
<td>624</td>
<td>149,907</td>
<td>4.16</td>
<td>0.80 (0.63–1.02)</td>
<td></td>
<td></td>
<td></td>
<td>0.83 (0.65–1.05)</td>
<td></td>
<td></td>
<td></td>
<td>0.74 (0.57–0.96)</td>
<td></td>
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</tr>
<tr>
<td>Obese</td>
<td>47,818</td>
<td>1,011</td>
<td>207,147</td>
<td>4.88</td>
<td>0.94 (0.75–1.19)</td>
<td></td>
<td></td>
<td></td>
<td>0.97 (0.76–1.23)</td>
<td></td>
<td></td>
<td></td>
<td>0.83 (0.63–1.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sex-specific WC</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Quartile 1, reference</td>
<td>30,427</td>
<td>523</td>
<td>128,710</td>
<td>4.06</td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td>&lt;0.001</td>
<td>0.94 (0.83–1.06)</td>
<td></td>
<td></td>
<td></td>
<td>0.92 (0.81–1.05)</td>
<td></td>
<td>0.009</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>29,645</td>
<td>509</td>
<td>127,862</td>
<td>3.98</td>
<td>0.95 (0.84–1.07)</td>
<td></td>
<td></td>
<td></td>
<td>0.94 (0.83–1.06)</td>
<td></td>
<td></td>
<td></td>
<td>0.92 (0.81–1.05)</td>
<td></td>
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</tr>
<tr>
<td>Quartile 3</td>
<td>36,890</td>
<td>687</td>
<td>159,181</td>
<td>4.32</td>
<td>1.02 (0.91–1.15)</td>
<td></td>
<td></td>
<td></td>
<td>0.99 (0.88–1.11)</td>
<td></td>
<td></td>
<td></td>
<td>0.96 (0.84–1.09)</td>
<td></td>
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<tr>
<td>Quartile 4</td>
<td>33,542</td>
<td>767</td>
<td>143,779</td>
<td>5.33</td>
<td>1.28 (1.14–1.43)</td>
<td></td>
<td></td>
<td></td>
<td>1.09 (0.98–1.23)</td>
<td></td>
<td></td>
<td></td>
<td>1.04 (0.90–1.21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MetS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>(–), reference</td>
<td>98,450</td>
<td>1,675</td>
<td>423,228</td>
<td>3.96</td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td>&lt;0.001</td>
<td>1.5 (1.38–1.63)</td>
<td></td>
<td></td>
<td></td>
<td>1.53 (1.40–1.67)</td>
<td></td>
<td>1.24 (1.13–1.36)</td>
</tr>
<tr>
<td>(+)</td>
<td>32,054</td>
<td>811</td>
<td>136,304</td>
<td>5.95</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.53 (1.40–1.67)</td>
<td></td>
<td></td>
<td></td>
<td>1.24 (1.13–1.36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>No. of MetS components</strong></td>
<td>130,504</td>
<td>2,486</td>
<td>559,531</td>
<td>4.44</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0, reference</td>
<td>21,052</td>
<td>301</td>
<td>91,035</td>
<td>3.31</td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td>&lt;0.001</td>
<td>1.09 (0.95–1.26)</td>
<td></td>
<td></td>
<td></td>
<td>0.96 (0.84–1.11)</td>
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<tr>
<td>1</td>
<td>39,575</td>
<td>614</td>
<td>170,442</td>
<td>3.60</td>
<td>1.08 (0.94–1.24)</td>
<td></td>
<td></td>
<td></td>
<td>1.09 (0.95–1.26)</td>
<td></td>
<td></td>
<td></td>
<td>0.96 (0.84–1.11)</td>
<td></td>
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</tr>
<tr>
<td>2</td>
<td>37,823</td>
<td>760</td>
<td>161,751</td>
<td>4.70</td>
<td>1.41 (1.23–1.61)</td>
<td></td>
<td></td>
<td></td>
<td>1.38 (1.21–1.59)</td>
<td></td>
<td></td>
<td></td>
<td>1.10 (0.96–1.27)</td>
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</tr>
<tr>
<td>3</td>
<td>22,824</td>
<td>547</td>
<td>97,263</td>
<td>5.62</td>
<td>1.69 (1.47–1.94)</td>
<td></td>
<td></td>
<td></td>
<td>1.73 (1.50–2.01)</td>
<td></td>
<td></td>
<td></td>
<td>1.24 (1.06–1.45)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>8,041</td>
<td>220</td>
<td>34,000</td>
<td>6.47</td>
<td>1.95 (1.64–2.32)</td>
<td></td>
<td></td>
<td></td>
<td>2.09 (1.74–2.52)</td>
<td></td>
<td></td>
<td></td>
<td>1.37 (1.12–1.66)</td>
<td></td>
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</tr>
<tr>
<td>5</td>
<td>1,189</td>
<td>44</td>
<td>5,041</td>
<td>8.73</td>
<td>2.67 (1.95–3.67)</td>
<td></td>
<td></td>
<td></td>
<td>3.25 (2.34–4.52)</td>
<td></td>
<td></td>
<td></td>
<td>1.99 (1.42–2.79)</td>
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</tr>
</tbody>
</table>

BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; MetS, metabolic syndrome; WC, waist circumference.

For BMI and sex-specific WC: Model 1: unadjusted. Model 2: age, sex, smoking, alcohol, income, cerebrovascular disease, heart failure, diabetes mellitus (DM), dyslipidemia, systolic blood pressure (SBP), estimated glomerular filtration rate (eGFR). Model 3: model 2 + waist circumference.

Figure 1. The Kaplan-Meier survival curve indicating renal disease progression-free survival. (A) Body mass index category, (B) sex-specific waist circumference quartile, and (C) metabolic syndrome.
Figure 2. The risk of renal disease progression related to metabolic syndrome in different subgroups. CI, confidence interval; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HR, hazard ratio; HTN, hypertension.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>HR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.15 [1.00–1.31]</td>
</tr>
<tr>
<td>Female</td>
<td>1.46 [1.28–1.68]</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>&lt;75</td>
<td>1.31 [1.17–1.46]</td>
</tr>
<tr>
<td>≥75</td>
<td>1.08 [0.91–1.28]</td>
</tr>
<tr>
<td>DM</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.20 [1.06–1.36]</td>
</tr>
<tr>
<td>Yes</td>
<td>1.29 [1.11–1.50]</td>
</tr>
<tr>
<td>HTN</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.28 [1.04–1.58]</td>
</tr>
<tr>
<td>Yes</td>
<td>1.23 [1.11–1.37]</td>
</tr>
<tr>
<td>eGFR</td>
<td></td>
</tr>
<tr>
<td>≥60</td>
<td>1.23 [1.11–1.36]</td>
</tr>
<tr>
<td>&lt;60</td>
<td>1.50 [1.16–1.93]</td>
</tr>
</tbody>
</table>

The risk of renal disease progression related to metabolic syndrome in different subgroups. CI, confidence interval; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HR, hazard ratio; HTN, hypertension.

In this study, subcutaneous adipose tissue, visceral abdominal fat (VAT), intermuscular fat area, BMI, and WC were all significantly associated with kidney function decline. Although VAT, BMI, and WC were associated with incident CKD, only VAT was a significant risk factor for incident CKD when other covariates were adjusted [21]. More recently, Esmeijer et al. [22] assessed the association between obesity assessed by BMI or WC and the rate of kidney function decline in 2,410 older post-myocardial infarction patients in the Alpha and Omega Trial, aged 60–80 years. They found that obese men and women showed, on average, 30% and 45% faster annual kidney function decline, respectively, than individuals of normal weight [22]. However, one study by Kramer et al. [23] showed contrasting results. This study examined the associations between obesity, as measured by BMI or WC, and the development of ESRD from 26,960 participants in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort study. In this study, obesity was not a predictor of ESRD after adjustment for other obesity parameters or obesity-related comorbidities [23]. The patient’s hard outcome ESRD might be the reason for no association. One limitation of this study was that the study population was not entirely elderly, although the mean baseline age of REGARDS participants was 64.8 ± 9.4 years, with 45.1% aged 65 years or older. In addition to these conflicting results, all of these studies were performed in Western population (three in the United States and one in the Netherlands), and there are few studies in the Asian population.

Oh et al. [24] followed 454 Korean adults in the Hallym Aging Study (HAS) for 6 years. They found that increased WC and waist-to-hip ratio, but not BMI, were associated with renal function decline [24]. The mean age of study participants was 67.4 ± 8.4 years, but 30% of HAS participants were aged 65–64 years old, and the small number of participants was also a limitation. A more recent and larger study by Jung et al. [25] analyzed 6,538 Koreans from the general population with normal kidney function from the Korean Genome and Epidemiology Study Database. During the 12-year follow-up, obese people had an increased risk of incident CKD, and this association was significant only in 60- to 69-year-old individuals, but not in younger individuals. However, in the subgroup analysis of our study, the BMI-defined obesity-induced renal outcome did not increase when baseline eGFR was equal to 60 mL/min/1.73 m² or over. This discrepancy might be due to dif-
ferences in the characteristics of enrolled patients. Unlike
previous studies, our study included patients with DM, hypertension, kidney disease patients, and patients over 70
years old.

Differentiating true CKD from natural aging of the kidney
is not easy in elderly individuals with a mild decrease in
eGFR and no evidence of kidney damage. There is a con-
cern for over-diagnosis of CKD in the elderly with an eGFR
just below 60 mL/min/1.73 m² and a suggestion for the use
of an age-specific CKD definition [26]. Accordingly, our
stricter definition of renal outcome in our study has more
clinical implications.

On the other hand, as in our study, metabolic syndrome
was consistently shown to be a risk factor for CKD develop-
ment or renal function decline in the elderly [27,28].

In summary of previous results, BMI or WC is a predictor
of renal function decline in the Western population. How-
ever, in the Asian population, only a few studies exist, and
evidence supporting the role of obesity as a risk factor for
renal function decline is still lacking. In this context, our
study has the advantage of being large, nationally represen-
tative, and using a harder clinical outcome of deterioration
in kidney function, including progression to ESRD in the
elderly. In addition, in order to prevent or slow the decline
of renal function in the elderly, it is suggested that the crite-
rion for diagnosis and treatment of obesity should be based
on metabolic syndrome and related abnormalities rather
than simply on BMI or WC.

There are several possible explanations as to why only
metabolic syndrome, and not BMI or WC, was associated
with renal function decline in the elderly. First, BMI and
WC might not be good markers of adiposity in the elderly.
The relationship between body fat percent and BMI is
age-dependent, and the accuracy of BMI in diagnosing
obesity is diminished in the elderly; therefore, BMI might
be a suboptimal marker of adiposity in the elderly [29].
Although WC is better than BMI at predicting prognosis in
the elderly [30], its pattern and implications in the elderly
are different from those seen in the young, and cut-off
values for defining obesity are controversial [31]. Second,
Asians have different patterns of BMI and body composi-
tion from those of Caucasians. In general, Asians have low-
er BMI than Caucasians, but Asians have higher body fat
percentages compared to Caucasians with the same BMI
[32]. This might affect the clinical implications of BMI or
WC in Asians and Caucasians and might have caused the
different results seen in our study but not in Western stud-
ies. Third, our findings might be explained as a spectrum
of the obesity paradox. The obesity paradox is an observa-
tion that all-cause or cardiovascular mortality is lower in
patients with elevated BMI than in those with normal BMI,
particularly in the elderly or patients with chronic illness.
Potential biases such as survival effect, unmeasured con-
founders, and reverse causation and potential beneficial
effects of obesity such as energy reserves and prevention
of malnutrition are the suggested mechanisms underlying
the obesity paradox [33]. Fourth, metabolic syndrome is
consistently associated with poor renal and cardiovascular
outcomes and high mortality in the elderly [27,28,34]. Un-
like anthropometry, predicting renal function decline with
metabolic syndrome was more prominent in the elderly in
a study [28]. Metabolic syndrome is a complex of cardio-
vascular risk factors associated with visceral adiposity [35],
and visceral fat is an important risk factor for incident CKD
[20]. In the same manner, among the components of the
metabolic syndrome in the elderly, except for overweight,
elevated glucose, high triglyceride, high blood pressure,
and low HDL cholesterol were consistently associated with
cardiovascular, and all-cause mortality [33,34]. In addition,
glomerular hyperfiltration is an important mechanism of
renal function deterioration due to obesity, which is related
to renin-angiotensin system activation by adipose tissue,
especially visceral adipose tissue, increased inflammation,
and endothelial cell injury [12,35,36]. Previous studies
have shown that renal damage due to glomerular hyper-
filtration is not only related to obesity, but also to DM, and
hypertension, and in this respect, abnormalities belonging
to the metabolic syndrome are related to glomerular hy-
pofiltration [37–39]. Our results suggest that correction of
metabolic abnormalities, rather than weight reduction for
obesity management, is a more reasonable approach for
the elderly in terms of preserving renal function.

Our study has several limitations. First, our study is ob-
servational in nature, so it does not provide causality and
cannot exclude the possibility of residual confounding.
However, large-scale long-term randomized controlled tri-
als to confirm the effect of weight control are not feasible.
Second, renal function was assessed only once at baseline
and follow-up. There are possibilities of transient change
of renal function or acute kidney injury at check-ups. How-
ever, a large sample size would reduce any bias associated with the occurrence of these events. Third, we used the MDRD equation to calculate eGFR. The MDRD equation is known to underestimate GFR when renal function is preserved [40] and to be less accurate than the Chronic Kidney Disease Epidemiology Collaboration equation [16]. However, the method for determining creatinine concentration was not standardized using or traceable to isotope dilution mass spectrometry. Despite these limitations, the strengths of this study include the large sample size, nationally representative data, harder patient outcomes, and confirmation of synergistic effects of metabolic components.

In conclusion, this study showed that the presence of metabolic syndrome or metabolic abnormalities, rather than high BMI or WC, is significantly associated with an increased risk of renal function decline in the elderly general population. This suggests that we should concentrate more on improving metabolic abnormalities rather than weight reduction for obesity management in preserving the renal function of the elderly.

Additional information

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Conflicts of interest

All authors have no conflicts of interest to declare.

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Data sharing statement

The data presented in this study are available upon reasonable request from the corresponding author.

Authors’ contributions

Conceptualization, Visualization: JY
Data curation, Formal analysis: HSL, CYL
Investigation: HK, SC, SHK, JHC, KKY, WYP, IOS, BCY, GJK, JWY, WMH, SHS, SJS, YAH, EB, YYH
Project administration: SHK, JHC, KKY, WYP, IOS, BCY, GJK, JWY, WMH, SHS, SJS, YAH, EB, YYH
Resources: SC
Supervision: HK, YYH
Validation: YYH
Writing—original draft: JY, YYH
Writing—review & editing: HK, SC, SHK, JHC, KKY, WYP, IOS, BCY, GJK, JWY, WMH, SHS, SJS, YAH, EB, YYH
All authors read and approved the final manuscript.
Yang, et al. Obesity impact on renal function in Korean elderly

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