Menopause: The Journal of The North American Menopause Society
Vol. 29, No. 9, pp. 1040-1046
DOI: 10.1097/GME.0000000000002032

OPEN

ORIGINAL STUDY

Dynapenic-abdominal obesity as an independent risk factor for chronic kidney disease in postmenopausal women: a population-based cohort study

Youngju Choi, PhD,[1] Jinkyung Cho, PhD,[1,2] Jiyeon Kim, PhD,[1] Jun Hyun Bae, PhD,[1] Eun-Jeong Cho, MS,[1,3] Eunwook Chang, PhD,[1,4] Kyung-Lim Joa, MD, PhD,[1,5] Junghoon Kim, PhD,[6] Dong-Ho Park, PhD,[1,3,4] Ju-Hee Kang, MD, PhD,[1,3,7] and Hyo-Bum Kwak, PhD[1,3,4]

Abstract

Objective: Low muscle strength and obesity lead to a higher risk of chronic kidney disease (CKD). Perimenopause is associated with a natural decline in muscle strength and an increase in visceral adiposity. Dynapenic obesity, which is the coexistence of low muscle strength and obesity, is expected to synergistically increase the prevalence of CKD in postmenopausal women. The aim of this study was to determine combined associations of dynapenia and obesity with CKD in postmenopausal women.

Methods: This study used data from the Korean National Health and Nutrition Examination Survey, 2016 to 2019. The study included 4,525 postmenopausal women aged 42 to 80 years that were classified into four groups based on waist circumference (≥85 cm) and hand grip strength (<18 kg): normal, dynapenic, obese, or dynapenic-obese. According to the Kidney Disease: Improving Global Outcomes, we defined CKD as an estimated glomerular filtration rate <60 mL/min per 1.73 m^2. Complex sample logistic regression models were conducted to determine the relationships among coexistence of dynapenia, abdominal obesity, and the risk of CKD.

Results: Dynapenic-abdominal obese group displayed lower estimated glomerular filtration rate levels than other groups ($P < 0.05$ for all data). The prevalence rates of CKD were 15.5%, 7.8%, 6.2%, and 2.4% in the dynapenic-abdominal obese, dynapenic, abdominal obese, and normal groups, respectively ($P < 0.001$). Complex sample logistic regression analyses, after adjusting for age, height, health behaviors, and comorbidities, showed that the odds ratio for CKD with respect to dynapenic-abdominal obesity was 1.82 (95% confidence interval, 1.19-2.79) and to abdominal obesity was 1.54 (95% confidence interval, 1.07-2.22) than in the normal group.

Conclusions: This study demonstrated that dynapenic-abdominal obesity, as determined by low handgrip strength and high waist circumference values, was associated with increased risk of CKD in postmenopausal women.

Key Words: Estimated glomerular filtration rates – Handgrip strength – Sarcopenia – Waist circumference.

Sarcopenia, recently redefined as an age-related skeletal muscle disorder,[1] is now formally considered as a muscle disease (muscle failure) with the *International Classification of Diseases, Tenth Revision, Clinical Modification* diagnosis code,[2] and it is reportedly associated with physical disability and increased mortality risk.[3] Recently, low muscle strength has been highlighted as a primary indicator of sarcopenia by EWGSOP2 (European Working Group on Sarcopenia in Older People)[1]; the decrease in muscle strength is more rapid than the loss of muscle mass.[4,5] Loss of muscle strength is reported to be more strongly associated with detrimental health outcomes, including physical disability and mortality, than with loss of muscle mass.[6-8]

Recent data suggest that approximately 10% of the population worldwide has chronic kidney disease (CKD),[9] a noncommunicable

Received February 24, 2022; revised and accepted April 22, 2022.

From the [1]Institute of Sports and Arts Convergence (ISAC), Inha University, Incheon; [2]Korea Institute of Sports Science, Seoul; [3]Department of Biomedical Science, Program in Biomedical Science and Engineering, Inha University; [4]Department of Kinesiology, College of Arts & Sports, Inha University; [5]Department of Physical & Rehabilitation Medicine, College of Medicine, Inha University [6]Sports and Exercise Medicine Laboratory, Korea Maritime and Ocean University, Busan; and the [7]Department of Pharmacology, College of Medicine, Inha University, Incheon, Republic of Korea.

Funding/support: This work was supported by the Ministry of Education of the Republic of Korea and the National Research Foundation of Korea (NRF- 2019S1A5C2A03082727).

Financial disclosure/conflicts of interest: None reported.

Address correspondence to: Hyo-Bum Kwak, PhD, Department of Kinesiology, Department of Biomedical Science, Program in Biomedical Science & Engineering, Inha University, 100 Inha-ro, Michuhol-gu, Incheon 22212, Korea. E-mail: kwakhb@inha.ac.kr

disease that has contributed the most to global increases in morbidity and mortality in the past 20 years.[10] Age-related loss of muscle strength, referred to as dynapenia, has been reported to be associated with renal dysfunction, including CKD,[11-13] which is also associated with skeletal muscle impairment. It should be noted that muscle strength decreases with advancing age, and this decrease is more prevalent among older women than among older men.[4,14]

In women, estrogen deficit with menopause interacts with the aging process to accelerate the loss of muscle strength as well as muscle mass.[15-17] Furthermore, decreased estrogen level in postmenopausal women is associated with unfavorable changes in body composition, especially the redistribution of fat to the visceral area, which predisposes these women to abdominal obesity.[18,19] Similar to the loss of muscle strength, obesity is also associated with hemodynamic, structural, physiological, and pathological changes in the kidney,[20] leading to an increased risk of CKD progression.[21,22] Considering that poor muscle strength and obesity impose higher risk factors for CKD separately, the coexistence of both conditions (dynapenic-abdominal obesity) may increase the negative impact on renal function and enhance the progression of CKD, especially in postmenopausal women.

Therefore, in this study, we aimed to examine the association between dynapenic-abdominal obesity and CKD among postmenopausal women, who are known to have decreased muscle strength and increased abdominal obesity, using data from a national representative sample of postmenopausal women.

METHODS

Data base and study population

This study used data from a nationwide population-based survey, the Korea National Health and Nutrition Examination Survey (KNHANES), conducted from 2016 to 2019. The database was developed through a series of nationwide cross-sectional, population-based surveys with nationally representative samples from the noninstitutionalized civilian population of South Korea, using a stratified and multistage probability cluster design.[23] This study included data from collecting information on health-related behaviors, anthropometric measures, and biochemical and clinical profiles with three component surveys: a health interview, health examination, and nutrition survey. The health interview and health examination were conducted by well-trained medical staff and interviewers at the mobile examination center. One week after the health interview and health examination surveys, nutrition survey was performed through home visits to the households of participants.

Data from the KNHANES 2016-2019 included 14,481 adult women (aged ≥19 years) and 6,782 postmenopausal women. Postmenopausal status is defined as the cessation of menstruation for ≥1 year and is reported on the questionnaire.[24] Of the 6,082 participants with natural menopausal status, we excluded participants who had missing data for important analytic variables including dynapenic-abdominal obesity (ie, handgrip strength and/or waist circumference [WC], n = 311), estimated glomerular filtration rate (eGFR; serum creatinine level, n = 129), and other covariates (health questionnaires and anthropometric variables, n = 360). We also excluded those with fasting blood samples of <8 hours (n = 264) and/or implausible energy intake (<500 or >4,000 kcal/d) (n = 493). Overall, 4,525 postmenopausal women were included in the analysis (Fig. 1). All participants provided written informed consent, and the KNHANES study was approved by the institutional review board of the Korea Centers for Disease Control and Prevention (approval nos. January 3, 2018-P-A and January 3, 2018-C-A).

Groups classification

The participants were divided into four groups (normal, dynapenic, abdominal obese, and dynapenic-abdominal obese) according to their WC and muscle strength (handgrip strength) values as per the following criteria: Dynapenia was defined as handgrip strength <18 kg in women, according to the criteria recommended by the Asian Working Group for Sarcopenia.[25] Abdominal obesity was defined as WC ≥85 cm in women according to the criteria of the Korean Society for the Study of Obesity.[26,27] Dynapenic-abdominal obesity was defined as a combination of dynapenia and abdominal obesity.

Clinical and biomedical measurements

Blood pressure (BP) was measured in triplicate using a mercury sphygmomanometer (Baumanometer Wall Unit 33, Baum, Copiague, NY) after resting in the sitting position for at least 5 minutes. The mean values of the second and third BP measurements were used for the analysis. Hypertension was defined as systolic/diastolic BP ≥140/90 mm Hg or the use of antihypertensive medication. Blood samples were obtained from each participant after fasting for at least 8 hours. The serum concentrations of cholesterol, triglycerides, creatinine, and fasting plasma glucose concentrations were determined using standard biochemical techniques. Diabetes mellitus was defined as fasting blood glucose ≥126 mg/dL, currently taking diabetes treatment (medication or injection), or a previous diagnosis by a physician. Dyslipidemia was defined as total cholesterol ≥240 mg/dL or the use of antihyperlipidemic medication.

Waist circumference and handgrip strength

Waist circumference was measured to the nearest 0.1 cm during exhalation at the midaxillary line on the horizontal plane midpoint between the inferior costal margin and the iliac crest using a measuring tape (SECA 200, SECA). Waist circumference was measured three times, and the mean value was used in the analysis. Handgrip strength was measured for each participant using a digital handgrip dynamometer (TKK 5401; Takei Scientific Instruments Co, Ltd, Tokyo, Japan).[28] In a standing position with the arms fully extended, participants were instructed to squeeze the dynamometer with the distal interphalangeal finger joints of the hand at 90° as firmly as they could for less than 3 seconds. Handgrip strength was measured three times each with the left and right hands with a resting interval of 1 minute between each measurement; the maximum value (of all six attempts) was used in the analysis.

Assessment of renal function and CKD definitions

The eGFR, an indicator of renal function,[29] was determined using the Chronic Kidney Disease Epidemiology Collaboration equation: for women with a serum creatinine level ≤0.7 mg/dL, eGFR (mL/min per 1.73 m^2) = 144 × (serum creatinine/0.7)$^{-0.329}$ × (0.993)^{Age}; for women with a serum creatinine level >0.7 mg/dL, eGFR = 144 × (serum creatinine/0.7)$^{-1.209}$ × (0.993)^{Age}.[30] Chronic

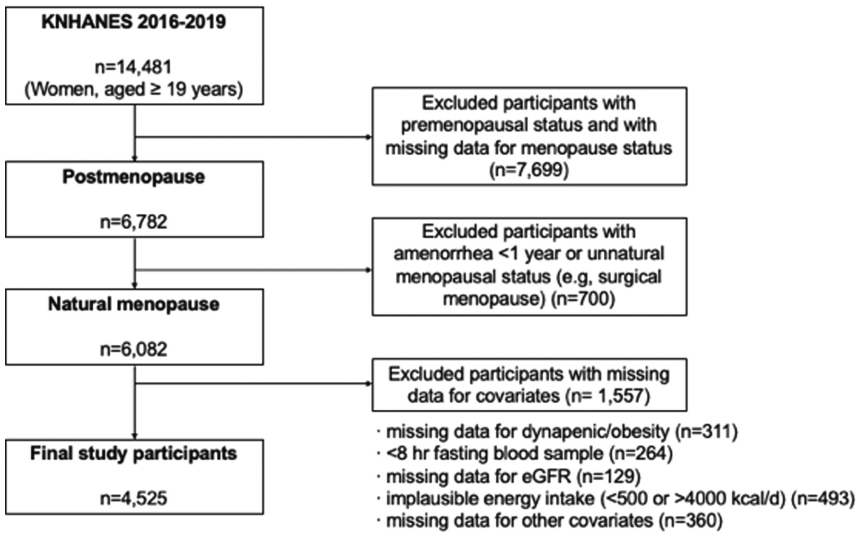

FIG. 1. Flowchart for inclusion and exclusion of study participants. KNHANES, Korean National Health and Nutrition Examination Survey.

kidney disease was defined as an eGFR less than 60 mL/min per 1.73 m^2 (<50% of normal renal function), according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria.[31]

Health-related behaviors

The participants were categorized as "nonsmoker or former smoker" or "current smoker," based on their smoking habit. Alcohol consumption was defined as drinking at least one glass of alcohol every month over the previous year. Strength exercise habit was defined as performing any kind of strength exercise, including push-ups, sit-ups, weightlifting, and pull-ups, twice or more per week in the most recent week.

Statistical analysis

We used a complex survey design with two-stage stratified, random, and cluster sampling. Participant characteristics were expressed as weighted mean and SE for continuous variables and as weighted percentages (%) for categorical variables.

To evaluate the combined effects of dynapenia and abdominal obesity on CKD, we created four groups as combined categorical variables: nondynapenic and nonabdominal obese (reference; ie, normal), dynapenic and nonabdominal obese (ie, dynapenia alone), nondynapenia and abdominal obese (ie, abdominal obesity alone), and dynapenic and abdominal obese (ie, dynapenic-abdominal obesity). The statistical significance of dynapenia and abdominal obesity status was determined using Rao-Scott χ^2 tests with a residual analysis for categorical variables and complex sample linear regression followed by Bonferroni post hoc test for continuous variables. Complex sample logistic regression models, which provided the odds ratios (ORs) and 95% confidence intervals (CIs), were used to predict the risk of CKD from dynapenia and/or abdominal obesity. To assess the effects of potential confounding factors, three sequential logistic regressions were developed: model 1 was adjusted for demographic factors (age and height); model 2 was adjusted for health-related behaviors (smoking, alcohol consumption, energy/protein intake, and resistance exercise) in addition to the model 1 covariates. Also, model 3 was additionally adjusted for comorbidities (hypertension, diabetes, and dyslipidemia), which is a common traditional risk factor for CKD.[32,33] All statistical analyses were performed using IBM SPSS Statistics 26.0 (IBM Inc, Chicago, IL), and statistical significance was defined as $P < 0.05$.

RESULTS

Demographic and clinical characteristics of the participants

The characteristics of the participants are presented in Table 1. The mean age of the participants was 63.9 (SE, 0.2) years, and the mean menopausal age was 50.1 (0.1). The mean eGFR level was 87.4 (0.3), and the prevalence of CKD (as defined by eGFR <60 mL/min per 1.73 m^2) was 5.0% in the total population. Overall, 920 participants (19.1%) had diabetes mellitus, 2,148 participants (48.1%) had dyslipidemia, and 2,730 participants (57.3%) had hypertension.

Among 4,525 postmenopausal women, 466 participants (9.4%) had dynapenia (as defined by handgrip strength <18 kg), 1,337 participants (29.0%) had abdominal obesity (WC ≥85 cm), and 387 (7.6%) had dynapenic-abdominal obesity. There were significant differences in the age, menopause age, body composition, handgrip strength, blood biochemical factors, BP, and nutrient status (all $P < 0.001$ by complex sample linear regression). Specifically, complex sample linear regression followed by Bonferroni post hoc test showed that postmenopausal women with dynapenic-abdominal obesity were significantly older and have lower high-density lipoprotein cholesterol and eGFR levels than in the other groups (all $P < 0.05$). The Rao-Scott χ^2 test showed that there were significant differences in the frequencies of alcohol consumption, resistance exercise habit, and prevalence of diabetes mellitus, dyslipidemia, and hypertension ($P < 0.001$ for all data). In addition, residual analysis showed that the proportion of postmenopausal women with dynapenic-abdominal obesity reporting "alcohol consumption <1 glass per year" and "regular resistance exercise <2 times per week" was significant (adjusted residual = 2.5 and 2.8, respectively). The dynapenic-abdominal obesity group also showed significant contribution of diabetes mellitus (36.1%), dyslipidemia

TABLE 1. *Demographic characteristics of the participants according to presence of abdominal obesity and dynapenia among postmenopausal women*

Variables	Overall (n = 4,525)	Normal (n = 2,335)	Dynapenic (n = 466)	Abdominal obese (n = 1,337)	Dynapenic-abdominal obese (n = 387)	*P*
Age, y	63.9 ± 0.2	61.0 ± 0.2	70.1 ± 0.6[a]	65.0 ± 0.3[a,b]	72.4 ± 0.5[a,b,c]	<0.001[d]
Menopause age, y	50.1 ± 0.1	50.2 ± 0.1	49.1 ± 0.3[a]	50.2 ± 0.1[b]	49.8 ± 0.3	<0.001[d]
Height, cm	154.8 ± 0.1	155.7 ± 0.1	150.4 ± 0.4[a]	155.4 ± 0.2[b]	151.5 ± 0.3[a,c]	<0.001[d]
Weight, kg	57.6 ± 0.1	54.3 ± 0.1	49.8 ± 0.4[a]	65.5 ± 0.2[a,b]	60.8 ± 0.4[a,b,c]	<0.001[d]
Body mass index, kg/m^2	24.0 ± 0.1	22.4 ± 0.1	22.0 ± 0.1[a]	27.1 ± 0.1[a,b]	26.5 ± 0.2[a,b,c]	<0.001[d]
Waist circumference, cm	82.3 ± 0.2	76.9 ± 0.1	76.6 ± 0.3	91.7 ± 0.2[a,b]	91.2 ± 0.3[a,b]	<0.001[d]
Waist circumference <85 cm, n (%)	2,801 (63.4)	2,335 (100.0)	466 (100.0)	0 (0.0)	0 (0.0)	
Waist circumference ≥85 cm, n (%)	1,724 (36.6)	0 (0)	0 (0.0)	1,337 (100.0)	387(100.0)	
HGS, kg	22.3 ± 0.1	23.8 ± 0.1	15.1 ± 0.1[a]	23.8 ± 0.1[b]	15.0 ± 0.1[a,c]	<0.001[d]
Normal muscle strength (HGS ≥18), n (%)	3,672 (83.0)	2,335 (100)	0 (0.0)	1,337 (100.0)	0 (0.0)	
Low muscle strength (HGS <18), n (%)	853 (17.0)	0 (0)	466 (100.0)	0 (0.0)	387(100.0)	
Total cholesterol, mg/dL	199.4 ± 0.7	203.8 ± 1.0	194.2 ± 2.2[a]	196.3 ± 1.4[a]	186.5 ± 2.3[a,c]	<0.001[d]
Triglyceride, mg/dL	127.2 ± 1.4	115.9 ± 1.6	119.2 ± 3.6	145.5 ± 3.1[a,b]	147.0 ± 4.6[a,b]	<0.001[d]
Triglyceride/HDL cholesterol	2.71 ± 0.04	2.36 ± 0.46	2.57 ± 0.10	3.23 ± 0.10[a,b]	3.42 ± 0.13[a,b]	<0.001[d]
HDL cholesterol,[f] mg/dL	53.0 ± 0.2	55.3 ± 0.3	52.0 ± 0.7[a]	50.5 ± 0.4[a]	47.5 ± 0.7[a,b,c]	<0.001[d]
Fasting glucose, mg/dL	103.1 ± 0.4	98.9 ± 0.4	101.0 ± 1.2	110.0 ± 1.0[a,b]	109.5 ± 1.2[a,b]	<0.001[d]
Serum creatinine, mg/dL	0.727 ± 0.004	0.713 ± 0.005	0.733 ± 0.018	0.737 ± 0.009[a]	0.786 ± 0.017[a,c]	<0.001[d]
CRP,[e] mg/dL	0.12 ± 0.00	0.10 ± 0.01	0.14 ± 0.01[a]	0.14 ± 0.01[a]	0.16 ± 0.01[a]	<0.001[d]
Systolic blood pressure, mm Hg	124.6 ± 0.4	121.6 ± 0.5	127.8 ± 1.1[a]	127.5 ± 0.6[a]	131.2 ± 1.1[a,c]	<0.001[d]
Diastolic blood pressure, mm Hg	75.0 ± 0.2	75.2 ± 0.2	72.0 ± 0.5[a]	76.1 ± 0.3[a,b]	73.0 ± 0.6[a,c]	<0.001[d]
Caloric intake, kcal/d	1,553.2 ± 10.2	1,595.1 ± 13.7	1,397.8 ± 27.4[a]	1,569.8 ± 19.7[b]	1,383.5 ± 29.0[a,c]	<0.001[d]
Protein intake, g/d	53.8 ± 0.5	56.6 ± 0.6	45.3 ± 1.2[a]	53.8 ± 0.9[a,b]	44.0 ± 1.2[a,c]	<0.001[d]
Fat intake, g/d	29.6 ± 0.4	32.0 ± 0.5	24.0 ± 1.0[a]	29.0 ± 0.7[a,b]	21.9 ± 1.2[a,c]	<0.001[d]
eGFR, mL/min per 1.73 m^2[b]						<0.001[g]
Normal renal function (eGFR ≥60), n (%)	4,265 (95.0)	**2,266 (97.6)**[h]	**428 (92.2)**	**1,247 (93.8)**	**324 (84.5)**	
Decreased renal function (eGFR <60), n (%)	260 (5.0)	**69 (2.4)**	**38 (7.8)**[h]	**90 (6.2)**[h]	**63 (15.5)**[h]	
Health-related behaviors						
Alcohol consumption, n (%)						<0.001[g]
No	3,338 (72.1)	**1,646 (68.9)**	**383 (82.4)**[h]	991 (72.9)	**318 (78.7)**[h]	
Yes	1,187 (27.9)	**689 (31.1)**[h]	**83 (17.6)**	346 (27.1)	**69 (21.3)**	
Current smoker, n (%)						0.890
No	4,385 (96.4)	2,260 (96.1)	456 (96.6)	1,293 (96.7)	376 (96.7)	
Yes	140 (3.6)	75 (3.9)	10 (3.4)	44 (3.3)	11 (3.3)	
Regular resistance exercise, n (%)						<0.001[g]
No	3,935 (86.0)	**1,933 (81.9)**	**437 (93.5)**[h]	**1,202 (89.6)**[h]	**363 (91.4)**[h]	
Yes	590 (14.0)	**402 (18.1)**[h]	**29 (6.5)**	**135 (10.4)**	**24 (8.6)**	
Comorbidities						
Diabetes mellitus, n (%)						<0.001[g]
No	3,605 (80.9)	**2,048 (88.6)**[h]	378 (80.8)	**935 (71.2)**	**244 (63.9)**	
Yes	920 (19.1)	**287 (11.4)**	88 (19.2)	**402 (28.8)**[h]	**143 (36.1)**[h]	
Dyslipidemia, n (%)						<0.001[g]
No	2,377 (51.9)	**1,354 (57.5)**[h]	**288 (60.9)**[h]	**581 (41.7)**	**163 (39.3)**	
Yes	2,148 (48.1)	**990 (42.5)**	**178 (39.1)**	**756 (58.3)**[h]	**224 (60.7)**[h]	
Hypertension, n (%)						<0.001[g]
No	1,795 (42.7)	**1,153 (52.2)**[h]	187 (41.2)	**379 (9.1)**	**76 (20.1)**	
Yes	2,730 (57.3)	**1,182 (47.8)**	279 (58.8)	**958 (68.7)**[h]	**311 (79.9)**[h]	

Data presented as weighted mean ± SE or weighted percentages.
CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; HGS, handgrip strength.
[a]$P < 0.05$ versus normal.
[b]$P < 0.05$ versus dynapenic.
[c]$P < 0.05$ versus abdominal-obese.
[d]Calculated using complex sample linear regression followed by Bonferroni post hoc test.
[e]CRP: n = 3,226.
[f]High-density lipoprotein cholesterol: n = 4,523.
[g]Calculated using Rao-Scott χ^2 test, supplemented by a residual analysis. Bold font indicates significant contribution to the Rao-Scott χ^2 test result at absolute adjusted residual >2.0.
[h]Adjusted residual >2.0.

(60.7%), and hypertension (79.9%) (adjusted residual = 6.7, 4.6, and 10.3, respectively).

Prevalence of CKD according to dynapenia and abdominal obesity

The combined influence of dynapenia and abdominal obesity on eGFR levels (Fig. 2A) and prevalence of CKD (Fig. 2B) is shown in Figure 2. The eGFR levels (mL/min per 1.73 m^2) were 78.2 (1.2), 83.9 (0.9), 85.9 (0.5), and 90.1 (0.3) in the dynapenic-abdominal obese, dynapenic, abdominal obese, and normal groups, respectively. Complex sample linear regression showed that the eGFR levels were significantly associated with presence of dynapenia and abdominal obesity ($P < 0.001$). Dynapenic and abdominal obese groups presented lower eGFR levels than normal group ($P < 0.05$ for both

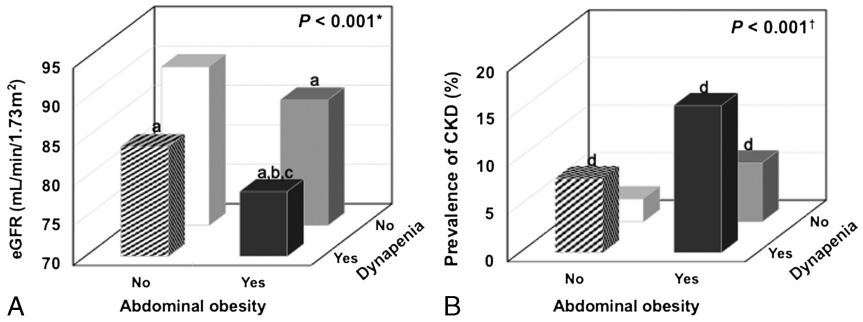

FIG. 2. Estimated glomerular filtration rate (eGFR) levels (**A**) and prevalence of chronic kidney disease (CKD) (**B**) among dynapenic-abdominal obese, dynapenic nonabdominal obese, nondynapenic abdominal obese, nondynapenic and nonobese (normal) groups. *P* values were evaluated by complex samples regression models for eGFR levels and Rao-Scott χ^2 tests for prevalence of CKD (%). *Calculated using complex sample linear regression followed by Bonferroni post hoc test. [a]$P < 0.05$ versus normal; [b]$P < 0.05$ versus dynapenic; [c]$P < 0.05$ versus abdominal-obese. [†]Calculated using Rao-Scott χ^2 test supplemented by a residual analysis. [d]Adjusted residual >2.0. The Rao-Scott χ^2 test showed that the prevalence of CKD was significantly associated with the presence of dynapenia and abdominal obesity ($P < 0.001$). Residual analysis showed that the prevalence of CKD was significantly low in the normal group (adjusted residual = −18.0), whereas the prevalence of CKD was significantly high in dynapenic, abdominal obese, and dynapenic-abdominal obese groups (adjusted residual = 4.2, 5.5, and 7.9, respectively).

data). Of note, dynapenic-abdominal obese group displayed lower eGFR levels than other groups ($P < 0.05$ for all data). In contrast, the prevalence rates of CKD were 15.5%, 7.8%, 6.2%, and 2.4% in the dynapenic-abdominal obese, dynapenic, abdominal obese, and normal groups, respectively. The Rao-Scott χ^2 test showed that the prevalence of CKD was significantly associated with presence of dynapenia and abdominal obesity ($P < 0.001$). In addition, residual analysis showed that the prevalence of CKD was significantly low in the normal group (adjusted residual = −18.0), whereas the prevalence of CKD was significantly high in dynapenic, abdominal obese, and dynapenic-abdominal obese groups (adjusted residual = 4.2, 5.5, and 7.9, respectively).

Odds ratio of CKD according to dynapenia and abdominal obesity

Complex sample logistic regression analyses were conducted to investigate the association between the coexistence of dynapenia and abdominal obesity and the risk of CKD (Table 2). Compared with the normal group, the unadjusted ORs of CKD in the dynapenic, abdominal obese, and dynapenic-abdominal obese groups were 3.47 (95% CI, 2.22-5.42), 2.70 (95% CI, 1.90-3.85), and 7.49 (95% CI, 4.89-11.49), respectively. The OR for CKD was attenuated but remained significant in abdominal obese and dynapenic-abdominal obese groups after adjusting for confounding variables including age, height, current smoking, alcohol consumption, energy/protein intake, resistance exercise, and comorbidities in model 3; the risk of CKD was nearly 1.5-fold higher in the abdominal obese group (OR, 1.54; 95% CI, 1.07-2.22; model 3) and 1.8-fold higher in the dynapenic-abdominal obese group (OR, 1.82; 95% CI, 1.19-2.79; model 3) than in the normal group. However, there was no statistically significant association between dynapenia and CKD after adjusting for confounding variables (OR, 1.05; 95% CI, 0.65-1.67; model 3).

DISCUSSION

In this study, we examined the association between the coexistence of low muscle strength and abdominal obesity, a condition referred to as dynapenic-abdominal obesity, and the incidence of CKD in a representative sample of Korean postmenopausal women. We found that the dynapenic-abdominal obese group displayed significantly lower eGFR levels compared with normal, dynapenic, abdominal-obese groups in postmenopausal women. Moreover, the dynapenic-abdominal obese group was independently associated with a higher risk of CKD, even after adjusting for confounding variables including age, height, health behaviors (current smoking status, alcohol consumption, energy/protein intake, and resistance exercise), and comorbidities (hypertension, diabetes, and dyslipidemia).

Menopause is associated with a natural decline in estrogen levels, which is related to an increase in visceral adipose tissue[34,35] and

TABLE 2. *Odds ratios for CKD by obesity and dynapenic categories (n = 4,525)*

		CKD (+)		
	Normal (n = 2,335)	Dynapenic (n = 466)	Abdominal obese (n = 1,337)	Dynapenic-abdominal obese (n = 387)
No. of CKD	69	38	90	63
Unadjusted	1 (Reference)	**3.47 (2.22-5.42)**	**2.70 (1.90-3.85)**	**7.49 (4.89-11.49)**
Model 1	1 (Reference)	1.02 (0.64-1.63)	**1.62 (1.13-2.33)**	**1.93 (1.26-2.95)**
Model 2	1 (Reference)	1.03 (0.65-1.65)	**1.62 (1.13-2.33)**	**1.95 (1.27-2.99)**
Model 3	1 (Reference)	1.05 (0.65-1.67)	**1.54 (1.07-2.22)**	**1.82 (1.19-2.79)**

Values presented as odds ratio (95% confidence interval). Model 1: adjusted for age and height. Model 2: adjusted for age, height, current smoking, alcohol consumption, energy/protein intake, and resistance exercise. Model 3: adjusted for age, height, current smoking, alcohol consumption, energy/protein intake, resistance exercise, and comorbidities (hypertension, diabetes, and dyslipidemia). Bold indicates statistical significance at $P < 0.05$ compared with reference (normal group).
CKD, chronic kidney disease.

a decrease in skeletal muscle mass and strength.[15,16] Indeed, postmenopausal women show higher visceral adipose tissue than premenopausal women,[34] leading to abdominal obesity. Population-based studies have shown that WC, not body mass index (BMI), is a better predictor of CKD.[36,37] These studies suggest that abdominal adiposity measured with WC may be valuable as a component of obesity to predict decline in renal function and CKD risk, especially in postmenopausal women. Furthermore, recent evidence by EWGSOPS2 adopted low muscle strength, not low muscle mass, as a principal determinant of sarcopenia, because muscle strength is considered to be a better predictor of adverse health outcomes.[6-8] Sarcopenia, as defined by muscle mass (ie, appendicular skeletal muscle mass/body weight), was not associated with CKD in women, but there was a significant association between sarcopenia and CKD in men.[38] A recent study by Hong et al[39] using KNHANES data reported an independent association between sarcopenic obesity and renal dysfunction in postmenopausal women; however, their study failed to find any relationship between sarcopenia or obesity alone and the risk of CKD. Such discrepancies may be due to the use of different criteria for the definition of sarcopenic obesity (ie, muscle mass and BMI). The major strength of our study is that we adopted handgrip strength and WC, which would be suitable to define dynapenic-abdominal obesity for predicting CKD in postmenopausal women. Furthermore, our results revealed that low muscle strength, increased WC, and the combined effects of dynapenic-abdominal obesity have independent risks for increased CKD. Our results provide compelling evidence that muscle strength coupled with WC could be a superior predictor of an increase in CKD risk in postmenopausal women.

To date, the underlying mechanisms of the association between dynapenic obesity and CKD in postmenopausal women remain unclear. It has been suggested that individuals with obesity[40] or low muscle strength[41] seem to have elevated levels of inflammatory markers. Interestingly, Schrager et al[42] reported that low handgrip strength and high WC seem to have higher C-reactive protein, interleukin-6, and interleukin-1 levels. Specifically, their study pointed out that abdominal obesity (as defined by WC) promotes more inflammation than general obesity (as defined by BMI) and that abdominal obesity contributes negatively to muscle strength, ultimately leading to dynapenic-abdominal obesity. Systemic inflammation results in increased insulin resistance, which in turn amplifies inflammation. Systemic inflammation and insulin resistance have been suggested to contribute synergistically to impairment of renal function.[43,44] Here, we found that C-reactive protein levels in postmenopausal women with dynapenic-abdominal obesity were the highest among the four groups. Furthermore, we clearly showed that the triglyceride/high-density lipoprotein cholesterol ratio, a surrogate marker of insulin resistance,[45] was highest in postmenopausal women with dynapenic-abdominal obesity compared with the other groups. Therefore, inflammation and insulin resistance induced by dynapenic-abdominal obesity may be partly responsible for renal dysfunction, leading to an increased risk for CKD.

In addition to dynapenic-abdominal obesity-induced inflammation and insulin resistance, mitochondrial dysfunction is considered a key factor in the development of CKD.[46,47] It has been reported that mitochondrial dysfunction in the kidney, including impaired mitochondrial dynamics with increased mitochondrial fragmentation,[48] reduced efficiency of mitochondrial biogenesis with down-regulation of peroxisome proliferator-activated receptor-gamma coactivator-1 alpha,[49] and excessive mitochondrial oxidative stress[50] are associated with the development and progression of various kidney diseases, ultimately leading to CKD. In a recent study by Andres-Hernando et al,[51] the authors demonstrated that obese mice with sarcopenia markedly accelerated the progression of CKD and that the decrease in renal function was associated with more severe mitochondrial dysfunction, as indicated by mitochondrial numbers, expression of mitochondrial proteins, and intracellular levels of adenosine triphosphate. Thus, mitochondrial dysfunction induced by dynapenic-abdominal obesity can partially explain the increased risk of CKD in postmenopausal women. Further studies are needed to clarify the mechanisms (ie, inflammation, insulin resistance, mitochondrial dysfunction, etc) underlying the impact of dynapenic-abdominal obesity on prevalence of CKD in postmenopausal women.

Our study has limitations that should be noted. First, we could not determine the exact cause-and-effect relationships for dynapenic-abdominal obesity and CKD because this study used a cross-sectional design. Second, although most previous studies have used the term "sarcopenic obesity" based on low muscle mass and BMI, emerging evidence has highlighted that low muscle strength and abdominal obesity are determinant factors for predicting CKD. Here, we used a definition of dynapenic-abdominal obesity, including handgrip strength and WC because these criteria serve as predictors superior to sarcopenic obesity (as defined by muscle mass and BMI) for CKD in postmenopausal women. Third, we could not rule out selection bias because of exclusion of individuals with missing or implausible data.

CONCLUSIONS

This study is the first to demonstrate the association of dynapenic-abdominal obesity, as determined by poor muscle strength and abdominal obesity, with CKD in postmenopausal women. Although these findings were limited to low handgrip strength and high WC, the hallmarks of sarcopenia obesity, we believe that low muscle strength and abdominal obesity were associated with an increased risk of CKD in postmenopausal women. Larger longitudinal studies are needed to corroborate our findings on the impact of dynapenic-abdominal obesity on CKD in postmenopausal women.

REFERENCES

1. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019;48:16-31.
2. Cao L, Morley JE. Sarcopenia is recognized as an independent condition by an *International Classification of Disease, Tenth Revision, Clinical Modification* (*ICD-10-CM*) code. *J Am Med Dir Assoc* 2016;17:675-677.
3. Arango-Lopera VE, Arroyo P, Gutierrez-Robledo LM, Perez-Zepeda MU, Cesari M. Mortality as an adverse outcome of sarcopenia. *J Nutr Health Aging* 2013;17:259-262.
4. Hughes VA, Frontera WR, Wood M, et al. Longitudinal muscle strength changes in older adults: influence of muscle mass, physical activity, and health. *J Gerontol A Biol Sci Med Sci* 2001;56:B209-B217.

5. Frontera WR, Hughes VA, Fielding RA, Fiatarone MA, Evans WJ, Roubenoff R. Aging of skeletal muscle: a 12-yr longitudinal study. *J Appl Physiol (1985)* 2000;88:1321-1326.
6. Newman AB, Kupelian V, Visser M, et al. Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. *J Gerontol A Biol Sci Med Sci* 2006;61:72-77.
7. Manini TM, Visser M, Won-Park S, et al. Knee extension strength cutpoints for maintaining mobility. *J Am Geriatr Soc* 2007;55:451-457.
8. Menant JC, Weber F, Lo J, et al. Strength measures are better than muscle mass measures in predicting health-related outcomes in older people: time to abandon the term sarcopenia? *Osteoporos Int* 2017;28:59-70.
9. World Kidney Day. Chronic kidney disease. Available at: http://www.worldkidneyday.org/faqs/chronic-kidney-disease. Accessed April 29, 2021.
10. Carney EF. Epidemiology: Global Burden of Disease Study 2013 reports that disability caused by CKD is increasing worldwide. *Nat Rev Nephrol* 2015;11:446.
11. Chang YT, Wu HL, Guo HR, et al. Handgrip strength is an independent predictor of renal outcomes in patients with chronic kidney diseases. *Nephrol Dial Transplant* 2011;26:3588-3595.
12. Hanatani S, Izumiya Y, Onoue Y, et al. Non-invasive testing for sarcopenia predicts future cardiovascular events in patients with chronic kidney disease. *Int J Cardiol* 2018;268:216-221.
13. Vogt BP, Borges MCC, Goés CR, Caramori JCT. Handgrip strength is an independent predictor of all-cause mortality in maintenance dialysis patients. *Clin Nutr* 2016;35:1429-1433.
14. Frontera WR, Hughes VA, Lutz KJ, Evans WJ. A cross-sectional study of muscle strength and mass in 45- to 78-yr-old men and women. *J Appl Physiol (1985)* 1991;71:644-650.
15. Cheng MH, Wang SJ, Yang FY, Wang PH, Fuh JL. Menopause and physical performance—a community-based cross-sectional study. *Menopause* 2009;16:892-896.
16. Rolland YM, Perry HM 3rd, Patrick P, Banks WA, Morley JE. Loss of appendicular muscle mass and loss of muscle strength in young postmenopausal women. *J Gerontol A Biol Sci Med Sci* 2007;62:330-335.
17. Cho EJ, Choi Y, Jung SJ, Kwak HB. Role of exercise in estrogen deficiency–induced sarcopenia. *J Exerc Rehabil* 2022;18:2-9.
18. Toth MJ, Tchernof A, Sites CK, Poehlman ET. Effect of menopausal status on body composition and abdominal fat distribution. *Int J Obes Relat Metab Disord* 2000;24:226-231.
19. Toth MJ, Tchernof A, Sites CK, Poehlman ET. Menopause-related changes in body fat distribution. *Ann N Y Acad Sci* 2000;904:502-506.
20. Kopple JD, Feroze U. The effect of obesity on chronic kidney disease. *J Ren Nutr* 2011;21:66-71.
21. Kramer H, Luke A, Bidani A, Cao G, Cooper R, McGee D. Obesity and prevalent and incident CKD: the Hypertension Detection and Follow-up Program. *Am J Kidney Dis* 2005;46:587-594.
22. Yun HR, Kim H, Park JT, et al. Obesity, metabolic abnormality, and progression of CKD. *Am J Kidney Dis* 2018;72:400-410.
23. Kweon S, Kim Y, Jang MJ, et al. Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). *Int J Epidemiol* 2014;43:69-77.
24. Harlow SD, Gass M, Hall JE, et al. Executive summary of the Stages of Reproductive Aging Workshop +10: addressing the unfinished agenda of staging reproductive aging. *J Clin Endocrinol Metab* 2012;97:1159-1168.
25. Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc* 2014;15:95-101.
26. Lee SY, Park HS, Kim DJ, et al. Appropriate waist circumference cutoff points for central obesity in Korean adults. *Diabetes Res Clin Pract* 2007;75:72-80.
27. Kim MK, Lee WY, Kang JH, et al. 2014 Clinical practice guidelines for overweight and obesity in Korea. *Endocrinol Metab (Seoul)* 2014;29:405-409.
28. Roberts HC, Denison HJ, Martin HJ, et al A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. *Age Ageing* 2011;40:423-429.
29. Lopez-Giacoman S, Madero M. Biomarkers in chronic kidney disease, from kidney function to kidney damage. *World J Nephrol* 2015;4:57-73.
30. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;150:604-612.
31. Levey AS, Eckardt KU, Tsukamoto Y, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2005;67:2089-2100.
32. Muntner P, Coresh J, Smith JC, Eckfeldt J, Klag MJ. Plasma lipids and risk of developing renal dysfunction: the atherosclerosis risk in communities study. *Kidney Int* 2000;58:293-301.
33. Haroun MK, Jaar BG, Hoffman SC, Comstock GW, Klag MJ, Coresh J. Risk factors for chronic kidney disease: a prospective study of 23,534 men and women in Washington County, Maryland. *J Am Soc Nephrol* 2003;14:2934-2941.
34. Abildgaard J, Danielsen ER, Dorph E, et al. Ectopic lipid deposition is associated with insulin resistance in postmenopausal women. *J Clin Endocr Metab* 2018;103:3394-3404.
35. Lovejoy JC, Champagne CM, de Jonge L, Xie H, Smith SR. Increased visceral fat and decreased energy expenditure during the menopausal transition. *Int J Obes (Lond)* 2008;32:949-958.
36. Oh H, Quan SA, Jeong JY, Jang SN, Lee JE, Kim DH. Waist circumference, not body mass index, is associated with renal function decline in korean population: Hallym Aging Study. *PLoS One* 2013;8:e59071.
37. Noori N, Hosseinpanah F, Nasiri AA, Azizi F. Comparison of overall obesity and abdominal adiposity in predicting chronic kidney disease incidence among adults. *J Ren Nutr* 2009;19:228-237.
38. Moon SJ, Kim TH, Yoon SY, Chung JH, Hwang HJ. Relationship between stage of chronic kidney disease and sarcopenia in Korean aged 40 years and older using the Korea National Health and Nutrition Examination Surveys (KNHANES IV-2, 3, and V-1, 2), 2008–2011. *PLoS One* 2015;10:e0130740.
39. Hong C, Baek JY, Lee JW, et al. Relationship between decreased estimated glomerular filtration rate and sarcopenic obesity among postmenopausal women: Korea National Health and Nutrition Examination Survey (2008–2011). *Korean J Fam Med* 2020;41:332-338.
40. Panagiotakos DB, Pitsavos C, Yannakoulia M, Chrysohoou C, Stefanadis C. The implication of obesity and central fat on markers of chronic inflammation: the ATTICA study. *Atherosclerosis* 2005;183:308-315.
41. Hamer M, Molloy GJ. Association of C-reactive protein and muscle strength in the English Longitudinal Study of Ageing. *Age (Dordr)* 2009;31:171-177.
42. Schrager MA, Metter EJ, Simonsick E, et al. Sarcopenic obesity and inflammation in the InCHIANTI study. *J Appl Physiol (1985)* 2007;102:919-925.
43. Hiramoto JS, Katz R, Peralta CA, et al. Inflammation and coagulation markers and kidney function decline: the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Kidney Dis* 2012;60:225-232.
44. Cheng HT, Huang JW, Chiang CK, Yen CJ, Hung KY, Wu KD. Metabolic syndrome and insulin resistance as risk factors for development of chronic kidney disease and rapid decline in renal function in elderly. *J Clin Endocrinol Metab* 2012;97:1268-1276.
45. McLaughlin T, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G. Use of metabolic markers to identify overweight individuals who are insulin resistant. *Ann Intern Med* 2003;139:802-809.
46. Galvan DL, Green NH, Danesh FR. The hallmarks of mitochondrial dysfunction in chronic kidney disease. *Kidney Int* 2017;92:1051-1057.
47. Che R, Yuan Y, Huang S, Zhang A. Mitochondrial dysfunction in the pathophysiology of renal diseases. *Am J Physiol Renal Physiol* 2014;306:F367-F378.
48. Brooks C, Wei Q, Cho SG, Dong Z. Regulation of mitochondrial dynamics in acute kidney injury in cell culture and rodent models. *J Clin Invest* 2009;119:1275-1285.
49. Deane CS, Willis CRG, Phillips BE, et al. Transcriptomic meta-analysis of disuse muscle atrophy vs. resistance exercise-induced hypertrophy in young and older humans. *J Cachexia Sarcopenia Muscle* 2021;12:629-645.
50. Dieter BP, Alicic RZ, Meek RL, Anderberg RJ, Cooney SK, Tuttle KR. Novel therapies for diabetic kidney disease: storied past and forward paths. *Diabetes Spectr* 2015;28:167-174.
51. Andres-Hernando A, Lanaspa MA, Kuwabara M, et al. Obesity causes renal mitochondrial dysfunction and energy imbalance and accelerates chronic kidney disease in mice. *Am J Physiol Renal Physiol* 2019;317:F941-F948.