

Effect of Sarcopenia and Body Shape on Cardiovascular Disease According to Obesity Phenotypes

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Background: This study aimed to assess the effects of sarcopenia and A Body Shape Index (ABSI) on cardiovascular disease (CVD) risk according to obesity phenotypes.

Methods: We used data from the National Health and Nutrition Examination Survey 1999 to 2012. A total of 25,270 adults were included and classified into the following groups: metabolically healthy normal weight (MHNW), metabolically healthy overweight/obese (MHO), metabolically unhealthy normal weight (MUNW), and metabolically unhealthy overweight/obese (MUO). Sarcopenia was defined as the appendicular skeletal mass index $<7 \text{ kg/m}^2$ in men and $<5.5 \text{ kg/m}^2$ in women. A multivariate logistic regression analysis was performed to evaluate the odds ratio (OR) of sarcopenia and ABSI for CVD events according to the obesity phenotype.

Results: The MHNW participants with sarcopenia had higher risk for CVD than those without sarcopenia (OR, 2.69; 95% confidence interval [CI], 1.56 to 4.64). In the analysis with MHNW participants without sarcopenia as a reference, the participants with sarcopenia showed a higher OR for CVD than those without sarcopenia in both MHO (OR in participants without sarcopenia, 3.31; 95% CI, 1.94 to 5.64) (OR in participants with sarcopenia, 8.59; 95% CI, 2.63 to 28.04) and MUO participants (OR in participants without sarcopenia, 5.11; 95% CI, 3.21 to 8.15) (OR in participants with sarcopenia, 8.12; 95% CI, 4.04 to 16.32). Participants within the second and third tertiles of ABSI had higher ORs for CVDs than the counterpart of obesity phenotypes within the first tertile.


Conclusion: These results suggest that clinical approaches that consider muscle and body shape are required.


Keywords: Body size; Obesity, metabolically benign; Sarcopenia

INTRODUCTION

Obesity remains a leading cause of type 2 diabetes mellitus (DM), cardiovascular diseases (CVDs), and stroke and has substantially increased the public health burden [1-4]. To evaluate obesity accurately, direct fat mass measurement should be performed with computed tomography, magnetic resonance

imaging, whole body dual-energy X-ray absorptiometry (DXA), or positron emission tomography-computed tomography [5]; however, direct measurements such as these are expensive and require modalities with limited availability in the clinical setting. Therefore, body mass index (BMI) has traditionally been used for the classification of obesity. However, one limitation of this method is that it cannot distinguish mus-

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cle from fat [6]. Recently, a number of studies found that low muscle mass; i.e., sarcopenia, was also associated with CVD [7]. Furthermore, epidemiologic studies suggested that a combination of sarcopenia and obesity has been associated with CVD and mortality [7].

Although obesity is usually associated with cardio-metabolic risk factors, not all obese individuals develop metabolic dysfunction. For example, some have a metabolically healthy overweight/obese (MHO) phenotype. While a recent meta-analysis of 19 studies showed that individuals with MHO were at a high risk of CVD, nine of studies did not produce statistically significant results [8] and the exact mechanism regarding this phenomenon remains unclear. Therefore, the inability of BMI to distinguish between fat and muscle may be one of the reasons results regarding the risk of CVD in individuals with MHO are heterogeneous. However, there have been no studies to assess the associations between muscle mass and CVD according to obesity phenotype.

Considering the limited availability of DXA in a clinical setting and the inability of BMI to estimate muscle mass, new obesity-related parameters that can distinguish between fat and muscle are needed. "A Body Shape Index" (ABSI) is a recently introduced parameter that reflects the body shape using waist circumference (WC), weight, and height [9]. Interestingly, ABSI was previously shown to have an inverse relationship with fat-free mass [10]; a modified ABSI also showed a positive association with the fat mass index as well as a negative association with the appendicular skeletal mass index (ASMI) [11]. Therefore, ABSI might supplement BMI by assessing muscle and fat mass.

In the present study, we assessed the effects of sarcopenia as defined by whole body DXA and body shape on CVD risk according to obesity phenotypes in a representative population in the United States.

METHODS

Study population

We used data from the National Health and Nutrition Examination Survey (NHANES) collected between 1999 and 2012. This survey covers a representative sample from the United States and has been performed biannually by the National Center for Health Statistics since 1999 using questionnaire-based personal interviews, physical examinations, and laboratory tests. Among a population of 71,916, those 20 years of age

or younger as well as those who lacked questionnaire-based data on CVD events; weight, height, and blood pressure (BP) measurements; and/or laboratory data including fasting glucose, triglycerides, and high-density lipoprotein were excluded. Ultimately, 25,270 adults were included in this study (Supplementary Fig. 1). Whole body DXA data were available between 1999 and 2005; therefore, 11,317 participants were included in the subgroup analysis for body composition.

Measurements

WC was measured by placing a flexible tape around the uppermost lateral border of the ilium. BMI was defined as the weight (kg) divided by the square of the height (m). BP was measured three times after a minimum of 5 minutes of rest while the participant was in a sitting position, and the mean value of the three measurements was used in our analysis. Fasting blood glucose and lipid levels were measured using the enzymatic method. More detailed sample collection and test methods are described in the NHANES Laboratory Procedures Manual [12].

Definition of the obesity phenotypes and CVD

In the present study, overweight/obesity was defined as a BMI above 25 kg/m² based on the World Health Organization criteria [13]. Owing to lack of a standard definition for metabolically healthy status, the revised National Cholesterol Education Program-Adult Treatment Panel III criteria (NCEP-ATP III criteria) for metabolic syndrome, which are the most commonly used criteria in previous studies [14-17], were also used. Metabolic abnormality was defined as having two or more metabolic risk factors according to the revised NCEP-ATP III criteria, including impaired fasting glucose (i.e., a fasting glucose level >100 mg/dL or a diagnosis of DM), high BP (hypertensive BP >130 mm Hg and/or diastolic BP >85 mm Hg, or a diagnosis of hypertension), triglyceride level \geq 150 mg/dL, and a high-density lipoprotein cholesterol level <40 mg/dL in men and <50 mg/dL in women. Owing to the collinearity between BMI and WC, the central obesity criterion was not used. Based on these aforementioned criteria, the participants were classified into the following groups: metabolically healthy normal weight (MHNW), MHO, metabolically unhealthy normal weight (MUNW) and metabolically unhealthy overweight/obese (MUO). We identified the existence of a CVD event if 1 or more of the following structured questions were answered in the affirmative:

1. Has a doctor ever told you that you have congestive heart

failure?

2. Has a doctor ever told you that you have coronary heart disease?
3. Has a doctor ever told you that you had a heart attack (or myocardial infarction)?
4. Has a doctor ever told you that you have angina pectoris?
5. Has a doctor ever told you that you have cerebrovascular disease?

Measurement of body composition and ABSI

Among the 25,270 study participants, 11,317 underwent a whole body DXA using a QDR 4500A fan beam X-ray bone densitometer (Hologic Inc., Marlborough, MA, USA). The total and regional body compositions as measured using the DXA scans were analyzed using the Hologic Discovery software version 12.1 (Hologic Inc.). The appendicular skeletal mass was defined as the sum of the total lean mass excluding bone mineral contents from the limbs, and the ASMI was defined as the appendicular skeletal mass divided by the square of the height (m). Sarcopenia was defined as an ASMI $<7 \text{ kg/m}^2$ in men and $<5.5 \text{ kg/m}^2$ in women based on the revised European consensus on the definition and diagnosis of sarcopenia [18]. ABSI was calculated using the following equation: $\text{ABSI} = \text{WC} / (\text{BMI}^{2/3} \times \text{height}^{1/2})$ [9].

Statistical analysis

The NHANES is a complex sample survey representing the United States population; the sample analysis was conducted using weighted values. Continuous variables are shown as mean values and 95% confidence intervals (CIs), while categorical variables are shown as the prevalence and percentage according to each obesity phenotype. Each variable was compared using 1-way analysis of variance and Pearson's chi-square test. We implemented Pearson's correlation coefficient to verify the correlation of ABSI with ASMI, BMI, and WC. A receiver operating characteristic (ROC) curve was used to analyze the correlation between ABSI and sarcopenia according to obesity phenotypes. A multivariate logistic regression analysis was performed to evaluate the odds ratio (OR) for CVD events according to the obesity phenotype. To determine the effects of muscle mass, groups were divided according to the presence of sarcopenia, and each group's OR for a CVD event was examined. Moreover, ABSI was divided into three categories, and the ORs for CVD events were calculated. Furthermore, changes in the ORs for CVD events in each obesity phenotype as a

function of changes in ABSI were analyzed using the restricted cubic spline plots with 3 knots. The analysis was performed using R version 3.1.0 (R Foundation for Statistical Computing, Vienna, Austria; www.r-project.org) and IBM SPSS Statistics version 24.0 (IBM Co., Armonk, NY, USA). A $P < 0.05$ indicated statistical significance.

Ethics statement

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Institutional Review Board of Hallym University Kangnam Sacred Heart Hospital (IRB No. HKS 2017-07-007). All the NHANES protocols were approved by the Research Ethics Review Board of the National Center for Health Statistics, US Centers for Disease Control and Prevention (NCHS IRB/ERB protocol numbers: 1999–2004, Protocol #98-12; 2005–2010, Protocol #2005-06; and 2011–2012, Protocol #2011-17). All participants volunteered and provided written informed consent prior to their enrollment. All participants' records were anonymized before being accessed by the authors, and all methods were performed in accordance with approved guidelines and regulations.

RESULTS

Baseline characteristics

The baseline characteristics of the participants according to their obesity phenotypes are summarized in Table 1. Of the 25,270 participants assessed in this study, 5,176 had MHNW, 6,688 were MHO, 2,671 were MUNW, and 10,735 were MUO. Compared to metabolically healthy participants, those metabolically unhealthy participants were more likely to be men and of older age; they also had higher BP, poorer lipid and glucose profiles, and a higher prevalence of CVD. Metabolically unhealthy participants had higher ABSIs than metabolically healthy counterparts. DXA data were available for 11,317 of the 25,270 subjects; participants who were obese had significantly higher ASMIs than those who were not. Moreover, participants with normal weight showed a higher prevalence of sarcopenia than obese participants did.

Association between obesity phenotypes and the risk of CVD events

A total of 2,637 CVD events were reported. In the multivariate logistic regression model with adjustment for age, sex, ethnicity and smoking status, participants with MHO were at a moder-

Table 1. Characteristics of the participants according to obesity phenotype

Variable	Metabolically healthy		Metabolically unhealthy		P value
	Normal weight (MHNW) (n=5,176)	Overweight/obesity (MHO) (n=6,688)	Normal weight (MUNW) (n=2,671)	Overweight/obesity (MUO) (n=10,735)	
Age, yr	38.2 (37.6–38.8)	40.9 (40.4–41.5)	54.7 (53.8–55.5)	51.7 (51.3–52.2)	<0.001
Men, %	39.6 (38.0–41.2)	47.6 (46.3–49.0)	48.1 (45.8–50.3)	54.1 (53.0–55.2)	<0.001
Ethnicity/Race, %					<0.001
Mexican American	6.2 (5.4–7.2)	9.2 (7.7–10.9)	4.6 (3.8–5.5)	8.2 (6.7–9.8)	
Other Hispanic	4.3 (3.3–5.4)	6.1 (4.8–7.7)	4.4 (3.2–6.1)	5.4 (4.3–6.9)	
Non-Hispanic White	73.9 (71.7–75.9)	67.6 (64.7–70.3)	73.4 (70.3–76.3)	71.9 (69.1–74.6)	
Non-Hispanic Black	8.4 (7.4–9.6)	13.2 (11.6–15)	7.5 (6.4–8.9)	10.2 (8.9–11.7)	
Other race	7.2 (6.2–8.3)	4 (3.3–4.8)	10 (8.3–12.1)	4.3 (3.6–5.1)	
CVD events ^a , %	2.3 (1.8–2.9)	4 (3.5–4.6)	12.3 (10.9–13.9)	12.5 (11.7–13.4)	
Smoking, %	45.4 (43.3–47.6)	43.8 (42.1–45.7)	55.5 (53–58.1)	51.3 (49.9–52.7)	
BMI, kg/m ²	22 (22–22.1)	30.2 (30–30.3)	22.6 (22.5–22.7)	32 (31.8–32.1)	<0.001
Waist circumference, cm	80.7 (80.4–81)	100.3 (99.9–100.8)	85.5 (85.1–85.9)	107.3 (106.8–107.7)	<0.001
ABSI	0.0791 (0.0789–0.0793)	0.0798 (0.0796–0.0800)	0.0826 (0.0823–0.0828)	0.0823 (0.0821–0.0824)	<0.001
ASMI [†] , kg/m ²	6.55 (6.49–6.62)	8.16 (8.10–8.22)	6.45 (6.37–6.54)	8.30 (8.24–8.36)	<0.001
Sarcopenia, %	27.0 (24.4–29.8)	1.4 (1.0–1.9)	38.8 (35.9–41.8)	2.1 (1.7–2.7)	<0.001
Systolic BP, mm Hg	112 (111.5–112.5)	115.6 (115.2–116)	131 (129.8–132.2)	129.1 (128.5–129.6)	<0.001
Diastolic BP, mm Hg	67.9 (67.5–68.4)	69.7 (69.3–70.1)	72.5 (71.8–73.2)	73.9 (73.5–74.4)	<0.001
FBG level, mg/dL	90.8 (90.4–91.2)	93.5 (93–94.1)	105.9 (104.4–107.5)	114.1 (112.8–115.4)	<0.001
HbA1c, %	5.2 (5.2–5.2)	5.3 (5.3–5.3)	5.6 (5.6–5.7)	5.9 (5.8–5.9)	<0.001
Total cholesterol, mg/dL	185.7 (184.3–187.2)	193.4 (192.2–194.6)	209.2 (206.9–211.4)	208.5 (207.1–209.8)	<0.001
HDL-C, mg/dL	61.4 (60.8–62)	54.9 (54.4–55.3)	56.4 (55.3–57.5)	46.5 (46.1–46.9)	<0.001
TG, mg/dL	89.5 (86.7–92.3)	107.9 (105.4–110.5)	141.8 (131.7–151.8)	183.3 (177.6–189.1)	<0.001
Metabolic state, %					
High BP	5.2 (4.5–6)	6.8 (6–7.7)	59.8 (57.2–62.4)	51.4 (49.9–52.8)	<0.001
Hyperglycemia	4.1 (3.5–4.7)	5.9 (5.2–6.6)	44.4 (41.7–47.1)	55.6 (54–57.2)	<0.001
Low HDL-C level	9.3 (8.2–10.4)	13.1 (12–14.2)	34 (31.4–36.8)	52.5 (51.2–53.9)	<0.001
High TG level	37.5 (35.9–39.2)	48.3 (46.5–50)	91.9 (90.4–93.2)	91.8 (91–92.5)	<0.001

Values are presented as mean (95% confidence interval).

MHNW, metabolically healthy normal weight; MHO, metabolically healthy overweight/obese; MUNW, metabolically unhealthy normal weight; MUO, metabolically unhealthy overweight/obese; CVD, cardiovascular disease; BMI, body mass index; ABSI, A Body Shape Index; ASMI, appendicular skeletal mass index; BP, blood pressure; FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride.

^aParticipants who had either angina pectoris, coronary heart disease, myocardial infarction, congestive heart failure, or cerebrovascular disease.

ate risk of developing CVD when compared with MHNW participants (OR, 1.543; 95% CI, 1.158 to 2.056), whereas participants with metabolic abnormalities were at high risk regardless of obesity status (OR in MUNW, 2.026; 95% CI, 1.539 to 2.667) (OR in MUO, 2.725; 95% CI, 2.186 to 3.398) (Table 2).

Correlation of ABSI with ASMI and other obesity-related parameters

ABSI showed a moderate negative correlation with ASMI as well as a strong positive correlation with WC, regardless of obesity phenotype (Table 3). In contrast to ABSI, WC and BMI

Table 2. Weighted odds ratios for cardiovascular disease events according to obesity phenotypes

Variable	OR (95% CI)	P value
MHNNW	1 (reference)	
MHO	1.543 (1.158–2.056)	0.003
MUNNW	2.026 (1.539–2.667)	<0.001
MUO	2.725 (2.186–3.398)	<0.001

Adjusted for age, sex, ethnicity, and smoking.

OR, odds ratio; CI, confidence interval; MHNNW, metabolically healthy normal weight; MHO, metabolically healthy overweight/obese; MUNNW, metabolically unhealthy normal weight; MUO, metabolically unhealthy overweight/obese.

Table 3. Correlation between ABSI and ASMI, BMI, and waist circumference

Group	Correlation coefficients		
	ASMI	BMI	Waist circumference
MHNNW			
Men	–0.586 ^b	0.039	0.695 ^b
Women	–0.332 ^b	–0.039 ^a	0.660 ^b
MHO			
Men	–0.400 ^b	0.082 ^b	0.552 ^b
Women	–0.285 ^b	–0.132 ^b	0.403 ^b
MUNNW			
Men	–0.596 ^b	0.036	0.711 ^b
Women	–0.283 ^b	–0.043	0.694 ^b
MUO			
Men	–0.433 ^b	–0.024	0.399 ^b
Women	–0.351 ^b	–0.249 ^b	0.251 ^b

ABSI, A Body Shape Index; ASMI, appendicular skeletal mass index; BMI, body mass index; MHNNW, metabolically healthy normal weight; MHO, metabolically healthy overweight/obese; MUNNW, metabolically unhealthy normal weight; MUO, metabolically unhealthy overweight/obese.

^a $P < 0.05$, ^b $P < 0.001$.

both showed a strong positive correlation with ASMI (overall correlation coefficient for WC, 0.631, $P < 0.001$; overall correlation coefficient for BMI, 0.655, $P < 0.001$). The area under the ROC curve (AUC) for ABSI showed significant accuracy for identifying sarcopenia (Table 4).

Effect of sarcopenia and ABSI on the risk of CVDs according to obesity phenotypes

The multivariate logistic regression analysis showed that the

Table 4. Area under the receiver operating characteristics curve of ABSI for sarcopenia

Group	Men		Women	
	AUC (95% CI)	P value	AUC (95% CI)	P value
MHNNW	0.755 (0.722–0.787)	0.017	0.677 (0.646–0.708)	0.016
MHO	0.884 (0.802–0.966)	0.042	0.722 (0.644–0.800)	0.040
MUNNW	0.776 (0.737–0.815)	0.020	0.635 (0.589–0.681)	0.023
MUO	0.854 (0.818–0.889)	0.018	0.672 (0.613–0.732)	0.030

ABSI, A Body Shape Index; AUC, area under curve; CI, confidence interval; MHNNW, metabolically healthy normal weight; MHO, metabolically healthy overweight/obese; MUNNW, metabolically unhealthy normal weight; MUO, metabolically unhealthy overweight/obese.

participants with sarcopenia had higher risk for CVD than those without sarcopenia in the group with MHNNW (OR, 2.69; 95% CI, 1.56 to 4.64). The obese participants with sarcopenia showed a significantly higher ORs of CVD than those without sarcopenia in both the metabolically healthy and unhealthy groups (Fig. 1). Fig. 1A shows each OR according to obesity phenotype and sarcopenia status compared to MHNNW participants without sarcopenia as a reference. The information in Fig. 1B is based on MHNNW participants with sarcopenia as a reference. MHO participants had a significantly higher risk for CVD than did MHNNW participants without sarcopenia (OR in MHO without sarcopenia, 3.31; 95% CI, 1.94 to 5.64) (OR in MHO with sarcopenia, 8.59; 95% CI, 2.63 to 28.04) (Fig. 1A). However, MHO participants did not have a significantly higher risk for CVD compared to the MHNNW participants with sarcopenia (OR in MHO without sarcopenia, 1.23; 95% CI, 0.77 to 1.96) (OR in MHO with sarcopenia, 3.19; 95% CI, 0.99 to 10.23) (Fig. 1B).

The multivariate logistic regression analysis showed that MHO participants who were within the second and third tertiles of ABSI had significantly higher ORs for CVDs, while those who were within the first tertile of ABSI had only a slightly higher risk for CVD, compared to the MHNNW participants who were within the first ABSI tertile (Fig. 1C). However, MHO participants did not have a significantly higher risk of CVD compared to the MHNNW participants within the third ABSI tertile (OR in MHO participants within the first tertile, 0.86; 95% CI, 0.56 to 1.32) (OR in MHO participants within the second tertile, 1.04; 95% CI, 0.71 to 1.54) (OR in MHO participants within the third tertile, 1.34; 95% CI, 0.98 to 1.84) (Fig. 1D). On restricted cubic spline regression analysis, ORs for CVD increased by ABSI in each obesity phenotype (Fig. 2).

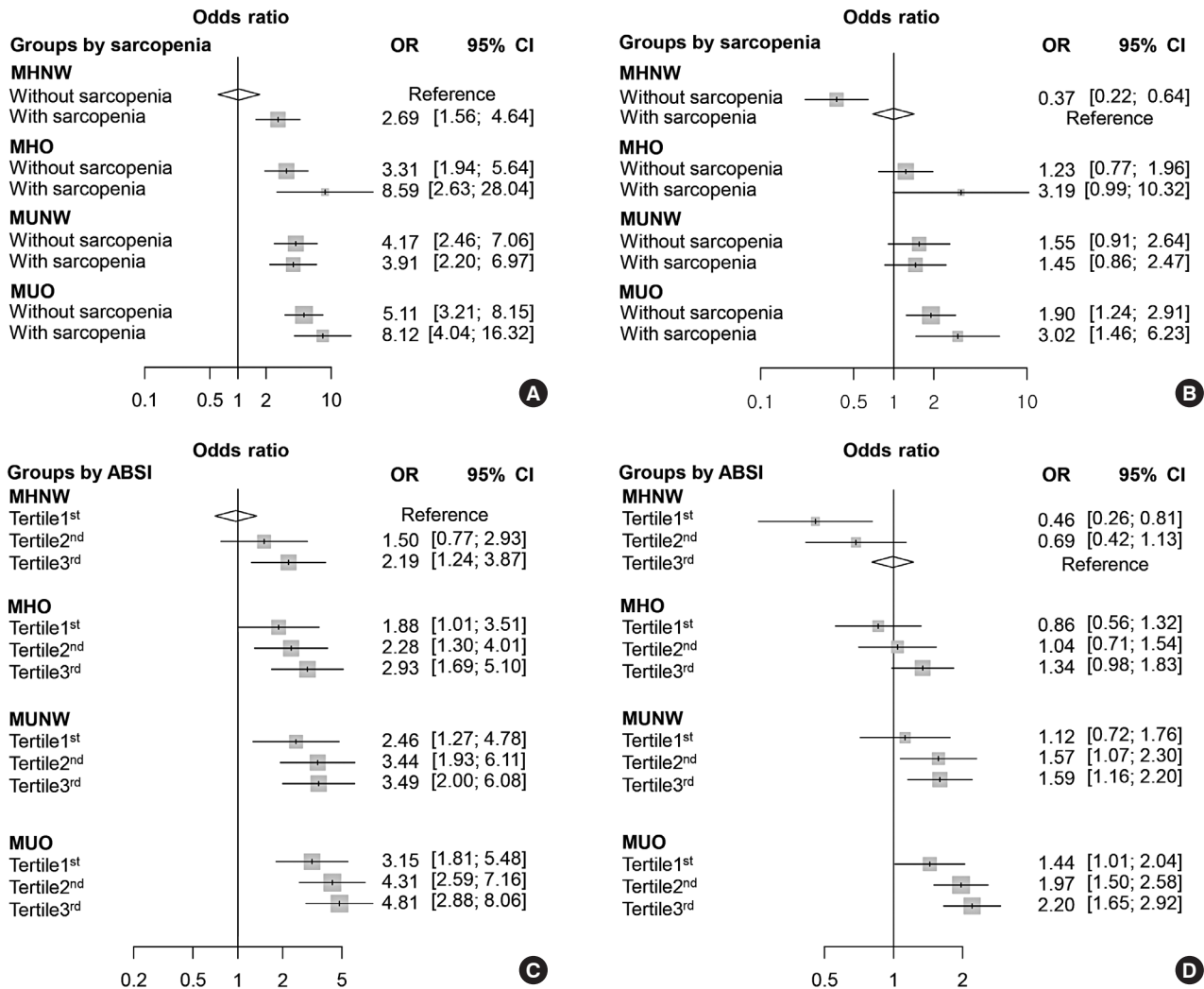


Fig. 1. Weighted odds ratio (OR) (95% confidence interval [CI]) for cardiovascular events in terms of (A, B) obesity phenotype and sarcopenia, or (C, D) tertiles of A Body Shape Index (ABSI). (A) Compared to metabolically healthy normal weight (MHNW) without sarcopenia, (B) compared to MHNW with sarcopenia, (C) compared to MHNW with the first ABSI tertile, and (D) compared to MHNW with the third ABSI tertile. Values were adjusted for age, sex, ethnicity, and smoking status. MHO, metabolically healthy overweight/obese; MUNW, metabolically healthy normal weight; MUO, metabolically unhealthy overweight/obese.

DISCUSSION

The present study showed that sarcopenia was associated with a high risk of CVD in MHNW participants. We also observed that sarcopenia increased the risk of CVD even in obese participants regardless of metabolic abnormalities. Our large-scale data also revealed that ABSI is associated with sarcopenia and CVD risk according to obesity phenotypes.

Notably, our results in MHNW participants with sarcopenia illustrated the need for taking into account muscle mass mea-

surements when defining normal weight with BMI. Numerous epidemiological studies have found that sarcopenia is associated with insulin resistance [19], type 2 DM [20], increased risk of CVD-related mortality, and all-cause mortality [21-23]. Our results were therefore consistent with those of previous studies. In addition, many studies showed that a combination of sarcopenia and obesity was more likely associated with metabolic disorders and morbidity [24-28]. A recent meta-analysis found that sarcopenic obesity increased the risk of all-cause mortality by 21% [29]. Our results found that obese patients with sarco-

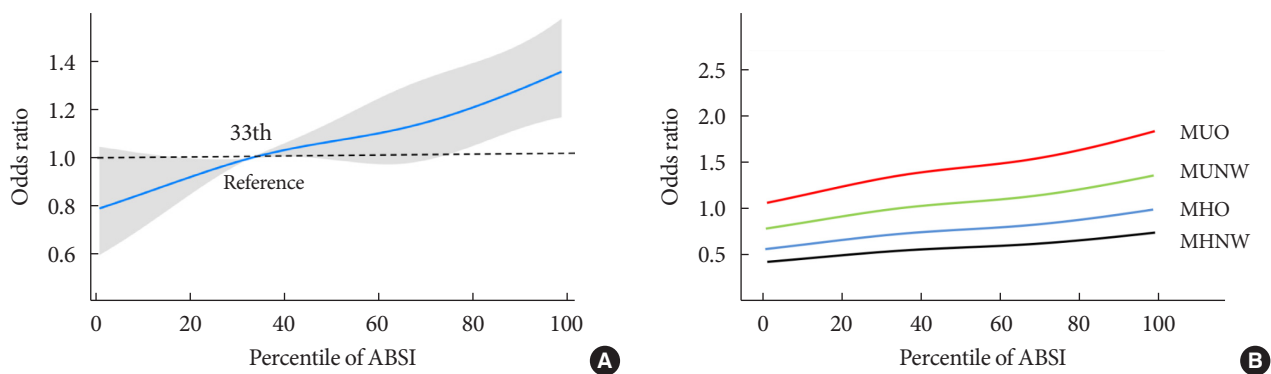


Fig. 2. Relationship between continuous A Body Shape Index (ABSI) and the odds ratios for cardiovascular events according to obesity phenotypes. (A) Total population, and (B) obesity phenotype subgroups. Values were adjusted for age, sex, ethnicity, and smoking status. MUO, metabolically unhealthy overweight/obese; MUNW, metabolically unhealthy normal weight; MHO, metabolically healthy overweight/obese; MHNW, metabolically healthy normal weight.

penia had a higher risk of CVD than those without sarcopenia in both the metabolically healthy and unhealthy group.

In the case of MHO phenotypes, several large-scale population-based studies have found an association between MHO and CVD risk [8], whereas several observational studies showed that MHO did not increase the risk of coronary atherosclerosis [30] or heart failure [31]. Our data suggested that if one study had an MHNW group with a high prevalence of sarcopenia as a control, their MHO phenotypes were not likely associated with an increased risk of CVD. Our data also revealed that if a study had an MHNW group with a low prevalence of sarcopenia as a control, their MHO phenotypes showed a remarkably higher risk for CVD. Therefore, the heterogeneity of information regarding prognoses in the various obesity studies could, at least in part, be due to overlooking the muscle mass measurement in their cohorts.

Our result also revealed that ABSI was positively correlated with WC but inversely correlated with the ASMI and had moderate accuracy for identifying sarcopenia. This result is consistent with recent studies which found an association between ABSI and sarcopenic obesity [10,11,32,33]. Considering limited availability of DXA in a clinical setting and the inability of BMI for estimating muscle mass, ABSI (which is easily obtained from the weight, height, and WC) is a useful alternative for identifying individuals who are at risk of sarcopenic obesity.

Several studies have examined the ABSI value as a predictor of CVD and mortality [9,34–36]. Moreover, a recent meta-analysis of 38 studies found that ABSI outperformed BMI and WC as a reliable predictor of all-cause mortality [37]. However, there is insufficient data on the association between ABSI and

CVD according to obesity phenotypes. Only one study showed that a high level of modified ABSI increased the risk of CVD across obesity phenotypes using a Korean representative sample [38]. These data are consistent with our study using the United States representative sample. Considering the association between ABSI and sarcopenic obesity, the heterogeneity of CVD risk by ABSI in each obesity phenotype might reflect the influence of muscle loss on CVD.

There were limitations to our study. First, the fact that it was cross-sectional indicates that additional prospective studies are necessary to clarify the relationship between each obesity phenotype and CVD events. Second, fatal CVD events may have been missed given that we did not assess mortality data. However, our study is the first study to investigate the association between sarcopenia and CVD events according to obesity phenotypes in the recent national representative sample. Our findings might provide one explanation for the heterogeneous results produced by previous studies with respect to the risk of developing CVD in obese individuals [8,39,40].

In conclusion, obese participants with sarcopenia had a higher risk of CVD than those without sarcopenia, regardless of metabolic abnormalities. We also showed that sarcopenia increased the risk of CVD even in healthy participants and these results persisted in ABSI. These results suggest that clinical approaches that consider muscle mass are required. However, since whole body DXA cannot be applicable to measure muscle mass in most clinical setting, ABSI is a useful alternative for identifying obese individuals who are at risk of sarcopenia and CVD. However, additional prospective studies must be conducted to determine the effect of muscle mass and ABSI

on CVD according to the obesity phenotype.

SUPPLEMENTARY MATERIALS

Supplementary materials related to this article can be found online at <https://doi.org/10.4093/dmj.2019.0223>.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Conception or design: S.M., J.G.K.

Acquisition, analysis, or interpretation of data: W.C., S.M., O.H.R.

Drafting the work or revising: H.W.C., W.C., S.M., M.K.K., J.G.K.

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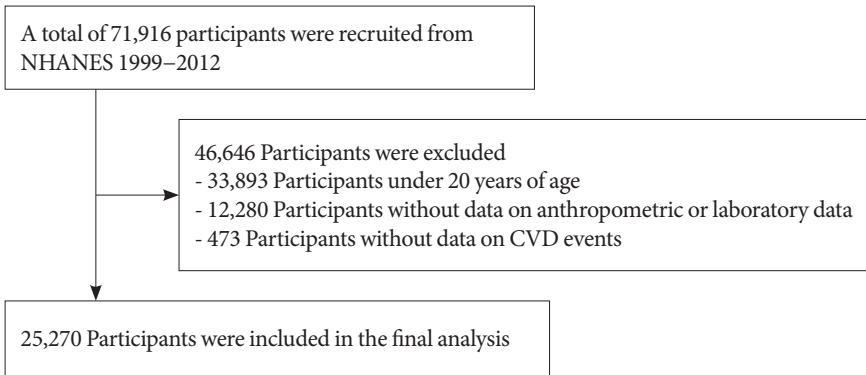
None

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Supplementary Fig. 1. Flowchart showing the selection process for the study's population. NHANES, National Health and Nutrition Examination Survey; CVD, cardiovascular disease.