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The Relationship Between Muscle Mass Assessed Using Different Formulas and Insulin Resistance

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BACKGROUND/AIMS
Obesity plays a critical role in the etiopathogenesis of insulin resistance, which is one of the risk factors for sarcopenia. We aimed to investigate the relationship between muscle mass assessed using different formulas and insulin resistance.

MATERIAL and METHODS
The patients aged between 18 and 65 years, who visited the obesity outpatient clinic between 2013-2015, were retrospectively evaluated. Based on the results of 75-g oral glucose tolerance test, patients whose fasting plasma glucose, HbAlc, and second-hour plasma glucose were within the normal limits were enrolled in the study. Appendicular lean mass (ALM) and total muscle mass were measured using bioimpedance analysis. Subsequently, the muscle mass ratio (MMR) was calculated as the percentage of total muscle mass divided by the body weight, and the skeletal muscle index (SMI) was calculated as the total muscle mass divided by the height^2.

RESULTS
Of the 284 participants, 159 (55.99%) were female. Although a positive correlation was observed for the homeostasis model assessment as an index of insulin resistance (HOMA-IR) level with body mass index (BMI), ALM/height^2, and fat percentage, a negative correlation was observed with MMR, ALM/body weight, and ALM/BMI in males (p<0.001, p=0.011, p=0.001, p=0.002, p=0.008, and p=0.004, respectively). In females, HOMA-IR was found to have a positive correlation with ALM and ALM/height2 (p=0.039 and p=0.035, respectively). When adjusted for fat percentage and BMI, no relationship was determined between HOMA-IR and relevant muscle measurements in both sexes (p>0.05 for females and males).

CONCLUSION
Although MMR and ALM/body weight were low in the participants with insulin resistance in both sexes, the difference was not statistically significant. ALM/height^2 that is used in the diagnosis of sarcopenia may not be appropriate for the assessment of muscle mass in insulin resistance.

Keywords: Sarcopenia, insulin resistance, skeletal muscle, obesity

INTRODUCTION

Insulin resistance is one of the most important causes of sarcopenia, which is defined as the age-related loss of muscle mass and muscle strength (1, 2). The muscle tissue is one of the main target organs for insulin hormone; thus, sarcopenia may contribute to the development of insulin resistance (3-5). The prevalence of obesity is growing worldwide, and it plays an important role in insulin resistance (1-5). Moreover, the assessment of muscle mass is difficult for obese participants because of the increased body mass index (BMI) and fat percentage (6). Although appendicular lean mass (ALM) can be used for diagnosing sarcopenia in normal-weight participants, it had been reported that ALM fails to detect the loss of muscle mass in overweight and obese participants (6). Another difficulty in assessing the muscle mass is the diversity of formulas used for the diagnosis of sarcopenia (1, 7). These formulas use ALM or total muscle mass, and either body weight or height included into some of these formulas (7). The present study aimed to evaluate the relationship between muscle mass assessed using different formulas and insulin resistance.

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MATERIAL and METHODS:

Study Population

The present study was derived from the data of the project "Evaluation of muscle mass in obesity, prediabetes and diabetes mellitus by different equations used for the diagnosis of sarcopenia". The medical files of the patients aged 18–65 years, who visited the obesity outpatient clinic of Kartal Dr. Lütfi Kırdar Training and Research Hospital between January 2013 and December 2015, were retrospectively evaluated. Subsequently, the participants receiving no antidiabetic agent who showed a fasting plasma glucose (FPG) level of <100 mg/dL or glycated hemoglobin (HbAlc) of <5.7% or second-hour plasma glucose level of <140 mg/dL on 75-g oral glucose tolerance test (OGTT) were enrolled into the study (8). The study was approved by the Ethics Committee of Kartal Dr. Lütfi Kırdar Training and Research Hospital (Approval No: 89513307/1009/537-118).

Methods Used in the Study

All participants underwent height, body weight, BMI, ALM, and impedance and fat percentage measurements using JAWON Medical GAIA 359 PLUS (Jawon Medical, Seoul,Korea, 2011) bioimpedance analysis (BIA) device. All metal accessories of participants were removed, and BIA measurements were evaluated in a standing position after the 12-hour fasting period. Thereafter, total muscle mass was calculated using the formula [(height^2 (cm)/BIA resistance×0.401)+(gender×3.825)+(age×-0.071)]+5.102, where height is reported in centimeters; and gender is equal to 1 for men and 0 for women (9). The muscle mass ratio (MMR) was assessed as the percentage of total muscle mass divided by the body weight, whereas the skeletal muscle index (SMI) was assessed as the total muscle mass divided by the square of the height in meters (7, 10). In addition, the FPG level was measured by the hexokinase method (Abbott Diagnostics, USA), and fasting insulin level was measured by chemiluminescence immunoassay (Cabase e411/Modular E170, USA) after the 12-hour fasting period; subsequently, homeostasis model assessment as an index of insulin resistance (HOMA-IR) was calculated using the formula FPG (mg/dL)×fasting insulin (μU/mL)/405 (11). A HOMA-IR level of ≥2.7 was considered as the cut-off value for insulin resistance, whereas <2.7 was considered normal (11). ALM was derived as the sum of the fat-free soft tissues of the arms and the legs.

Study Exclusion Criteria

Participants who have been receiving any insulin-sensitizing drugs, who had a history of chronic kidney disease, chronic liver disease, hyperthyroidism, and documented neuromuscular disease, and pregnant women were excluded. Moreover, participants aged ≥65 years were also not included in the study because aging is a risk factor for sarcopenia.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) 22.0 (IBM, SPSS Corp.; Armonk, NY, USA) programs. Descriptive statistics were presented as frequency, percentage, mean ± standard deviation, and median (minimum–maximum) values. Continuous variables showing normal distribution were analyzed by Student t test, whereas continuous variables not showing normal distribution were analyzed by Mann-Whitney U test. In addition, Spearman's correlation test was used to assess the relationship between continuous variables. A p-value of <0.05 was considered significant for all statistics.

RESULTS

Of the 284 study participants in total, 159 (55.9%) were females, the mean age was 36.16±11.5 years, and the mean BMI was 36.98±5.19kg/m^2. Regarding the sexes, the mean age was 33.20±10.31 years in males and 38.49±11.93 years in females; the mean BMI was 36.43±4.94 kg/m^2 in males and 37.42±5.36 kg/m^2 in females (p<0.001 and p=0.108, respectively). Median HOMA-IR was 3.88 (1.19–16.52) in males and 3.71 (0.93–13.27) in females (p=0.038). The distribution of BIA measurements of the participants is summarized in Table 1.

The mean age was 32.85±10.2 and 34.64±10.83 years in males with and without insulin resistance, whereas the mean age was 36.41±11.65 and 43.93±11.03 years in females with and without insulin resistance (p=0.460 for males and p<0.001 for females). The mean BMI was 36.96±5.18 kg/m^2 and 34.30±3.02 kg/m^2 in males with and without insulin resistance, respectively (p=0.015). Regarding females, the mean BMI was 37.93±5.47 kg/m^2 in those with insulin resistance and 36.07±4.85 kg/m^2 in those without insulin resistance (p=0.040). Table 2 summarizes the distribution of insulin resistance, HOMA-IR levels, and BIA measurements among sexes.

Although there was a negative correlation between HOMA-IR level and age in females, no significant relationship was de-

TABLE 1. Distribution of bioimpedance analysis measurements

	Females		Males	
	n (%)	Mean±SD	n (%)	Mean±SD
Total muscle mass (kg)	159 (55.99)	28.69±4.97	125 (44.01)	43.34±5.75
SMI (kg/m^2)	159 (55.99)	11.49±1.80	125 (44.01)	14.06±1.68
MMR (%)	159 (55.99)	30.88±3.71	125 (44.01)	38.91±4.28
ALM (kg)	159 (55.99)	25.59±4.27	125 (44.01)	35.86±6.16
ALM/BMI	159 (55.99)	0.686±0.077	125 (44.01)	0.990±0.151
ALM/height^2 (kg/m^2)	159 (55.99)	10.25±1.51	125 (44.01)	11.62±1.79
ALM/body weight (%)	159 (55.99)	27.46±1.96	125 (44.01)	32.03±3.75
Fat percentage (%)	159 (55.99)	40.75±3.51	125 (44.01)	31.89±5.24

ALM: Appendicular lean mass, BMI: body mass index, MMR: Muscle mass ratio, SMI: Skeletal muscle index

TABLE 2. Insulin resistance and bioimpedance analysis measurements according to the sexes

	Females (n=159)			Males (n=125)		
	Insulin resistance			Insulin resistance		
	No (n=44)	Yes (n=115)	p	No (n=25)	Yes (n=100)	p
Total muscle mass (kg)	27.62±4.19	29.09±5.20	0.069	42.95±4.13	43.43±6.10	0.637
SMI (kg/m^2)	11.16±1.42	11.62±1.91	0.104	13.77±1.36	14.13±1.75	0.270
MMR (%)	31.19±3.67	30.76±3.73	0.513	40.40±4.74	38.54±4.11	0.081
ALM (kg)	24.40±3.41	26.05±4.48	0.014	34.72±3.86	36.15±6.59	0.164
ALM/BMI	0.681±0.084	0.688±0.074	0.630	1.014±0.097	0.984±0.161	0.246
ALM/height^2 (kg/m^2)	9.86±1.12	10.40±1.62	0.020	11.09±0.91	11.75±1.93	0.016
ALM/body weight (%)	27.48±1.99	27.46±1.96	0.938	32.45±2.26	31.93±4.04	0.394
Fat percentage (%)	40.43±3.61	40.86±3.48	0.500	30.56±4.10	32.22±5.45	0.099

ALM: Appendicular lean mass, BMI: body mass index, MMR: Muscle mass ratio, SMI: Skeletal muscle index, Student t test
Data are presented as mean±standard deviation.

termined in males (r=-0.274, p<0.001 for females, and r=-0.017, p=0.850, for males, respectively). Considering the relationship of BIA measurements and HOMA-IR, there was a positive correlation for HOMA-IR level with BMI, ALM/height^2, and fat percentage in males, whereas there was a negative correlation with MMR, ALM/body weight, and ALM/BMI ratio (r=0.359, p<0.001; r=0.225, p=0.011; r=0.286, p=0.001; r=-0.274, p=0.002; r=-0.236, p=0.008, and r=-0.255, p=0.004, respectively). In females, there was a positive correlation between HOMA-IR value and ALM and ALM/height^2 ratios (r=0.167, p=0.039 and r=0.167, p=0.035, respectively). When HOMA-IR level and relevant muscle measurements were re-evaluated after adjusting for fat percentage and BMI, no relationship was determined between HOMA-IR and any of the relevant muscle measurements in any of the sexes (p>0.05 for females and males).

DISCUSSION

We aimed to evaluate the relationship between the muscle mass assessed by using different formulas and insulin resistance. As a result, insulin resistance was found to be associated with high BMI and ALM/height^2 ratio. Moreover, insulin resistance was found to be also associated with low MMR and high SMI in both sexes although no statistical significance was determined. As a result, HOMA-IR was positively associated with high BMI and ALM/height^2 ratio, and negatively associated with low MMR and high SMI in both sexes although no statistical significance was determined.

Because the muscle tissue is one of the main target organs for insulin, the relationship between sarcopenia and insulin resistance is increasingly gaining importance (5). Although some studies reveal that insulin resistance increases the risk of sarcopenia, some studies have reported that sarcopenia leads to insulin resistance (1-4). Studies assessing the muscle mass using MMR demonstrated the relationship between sarcopenia and insulin resistance (1, 4, 5). Although the studies assessing the muscle mass by using MMR demonstrated a negative correlation between muscle mass and insulin resistance, a study determined that the correlation is weakened when adjusted for fat mass (1,5). In addition, there are studies demonstrating a negative correlation between insulin resistance and SMI and lean mass. Every 1 kg/m^2 increase in SMI is associated with a 4% decrease in HOMA-IR level (5, 12). In the present study, although MMR decreased in both males and females having insulin resistance, no statistical significance was determined. There was no relationship between HOMA-IR levels and MMR in females, whereas a negative correlation was determined in males; however, the relationship between HOMA-IR level and MMR was not determined in either sex when adjusted for fat percentage and BMI. The present study reports increased SMI in both sexes having insulin resistance but found no statistical significance or relationship between HOMA-IR level and SMI. These outcomes of the present study were different from those reported in literature, which may be due to the higher mean BMI values than those in other studies in the literature. The evaluation of muscle mass becomes more difficult in obese subjects due to an increased fat percentage, and sarcopenia can be underestimated in obese participants (6).

Another formula used to evaluate muscle mass is the ALM/body weight or ALM/height^2 (7). A negative correlation was determined between ALM/body weight, which is used to diagnose sarcopenia, and HOMA-IR level (2, 13, 14). Nevertheless, one of the earlier studies determined the positive correlation between ALM/body weight and HOMA-IR level; however, a significant correlation was found only in males when adjusted for fat mass (1). It was found that the ALM/body weight ratio is significantly low in nonalcoholic steatohepatitis (NAHS), which is thought to be associated with insulin resistance (15). In another study, the HOMA-IR level was found higher in participants with sarcopenia vs. participants without when muscle mass is assessed using ALM/body weight ratio (3). Since ALM/height^2 showed high correlation with BMI, it was considered as a limited measure in defining sarcopenia in obese participants with sarcopenia (14). Moreover, in a population-based study conducted in elderly, although there was a positive correlation of HOMA-IR levels with ALM/height^2, significantly negative correlation was determined with ALM/body weight (2). A study reported that ALM/height^2 ratio remains inadequate in diagnosing sarcopenia in the participants with insulin resistance and that ALM/body weight would be more appropriate because ALM/height^2 is affected by fat mass (1). In the present study,

we found significantly increased ALM/height^2 ratio for the participants having insulin resistance. In addition, although there was a negative correlation between HOMA-IR level and ALM/body weight and BMI only in males, no significant relationship was observed when adjusted for fat percentage and BMI. Comparing with literature, the difference of the present study may be because the study population comprised young and middle-aged participants. Sarcopenia is generally considered as a geriatric health problem, and earlier studies in the literature have usually been conducted with elderly participants (3). On the other hand, lean mass begins to decrease from the age of 45 years, whereas a decrease in the ratio of lean mass to body weight begins from the third decade, therefore sarcopenia in the young population may occur (3).The etiology of sarcopenia shows variation among age groups (3, 4). Sarcopenia in elderly participants occurs due to inadequate muscle mass in youth period and the loss of muscle mass reaching to the maximum level depending on aging (3, 4). Another possible reason for this is the fact that ALM fails to detect the loss of muscle mass when used in overweight and obese participants although it is suitable for the diagnosis of sarcopenia in normal-weight participants (6).

In the earlier studies, although relevant muscle measurements determined to be high in males, BMI and fat percentage were observed to be higher in females (1, 2, 16). Similarly, in the present study as well, all the relevant muscle measurements were significantly higher in males; however, the fat percentage was higher in females.

One of the limitations of the present study is the use of HOMA-IR level for the assessment of insulin resistance. The HOMA-IR level is an easily applicable method in assessing insulin resistance and is frequently used, particularly in the epidemiological studies; however, the hyperinsulinemic-euglycemic clamp is the gold standard in making the diagnosis (17). Another limitation is that the participants were not evaluated for metabolic syndromes that are associated with low muscle mass and sarcopenia, independent of insulin resistance (3, 13).

In conclusion, insulin resistance is increasingly gaining importance with growing prevalence of obesity. The relationship between insulin resistance and muscle mass is not definite yet and becomes more difficult to assess in obese participants due to the limitations in assessing the muscle mass. The present study revealed a significant increase in ALM/height^2 ratio in those with insulin resistance. Nevertheless, although there was a decrease in MMR and ALM/body weight in the participants having insulin resistance in both sexes, there was no statistical significance. The results of the present study suggest that ALM/height^2 used in the diagnosis of sarcopenia may not be appropriate for the assessment of muscle mass in a participant with insulin resistance. Further research is needed to develop new formulas for the evaluation of muscle mass in patients with insulin resistance.

Ethics Committee Approval: Ethics committee approval was received for this study from Kartal Dr Lütfi Kırdar Training and Research Hospital. (Approval Date: 29.01.2016, Approval Number: 89513307/1009/537-118).

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

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