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Original Article

Evaluation of muscle mass in obesity, prediabetes and diabetes mellitus by different equations used for the measurement of muscle mass

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ABSTRACT

Objective: Insulin resistance is one of risk factors for sarcopenia and there is no specific equation for the measurement of muscle mass. The present study aimed to evaluate muscle mass in the patients with obesity, prediabetes (PDM) and type 2 diabetes mellitus (DM) by different equations for the measurement of muscle mass.

Methods: Obese patients aged 18–65 years old, who presented between 2013 and 2015 were reviewed and they were separated into three groups as obese, prediabetes (PDM) and diabetes mellitus (DM). Height, body weight, body mass index (BMI), sum of the appendicular lean masses (ALM) were measured in all participants. Body muscle mass ratio was calculated as the total muscle mass divided by the body weight, and skeletal muscle index was calculated as the total muscle mass divided by the square of the height. In addition, ALM/weight, ALM/height^2 and ALM/BMI ratios were also evaluated.

Results: A total of 1107 participants, of whom 666 (60.2%) were female, were enrolled into the study. Of the participants, 288 (%26.02) had obesity, 524 (%47.33) had PDM and 295 (26.65%) had DM. There was a significant difference in ALM/BMI ratio between the three groups for both genders ($p = 0.003$ for female and $p = 0.003$ for male). ALM/weight ratio and body muscle mass ratio were decreased between groups in female, whereas it was no difference in male ($p = 0.003$, $p < 0.001$ for females, respectively; $p = 0.802$, $p = 0.840$ for males, respectively).

Conclusions: ALM/BMI may be more accurate for the evaluation of muscle mass in middle-aged obese, PDM and DM subjects.

1. Introduction

The prevalence of obesity and type 2 diabetes mellitus (DM) is gradually increasing worldwide [1,2]. Nevertheless, obesity is one of the significant risk factors for the development of insulin resistance, which plays a role in the pathogenesis of prediabetes (PDM) and DM [3]. Muscle tissue is one of the main target organs for insulin hormone [2–4]. Insulin resistance is among the significant causes of age-related decrease in muscle mass, and low muscle mass may also improve insulin resistance and DM [2–4]. Sarcopenia, which is defined as aging-associated decrease in muscle mass and muscle strength, manifests with decrease in the total number of skeletal muscle fibers and increase in the intramuscular lipid content [5]. Earlier studies revealed significant relationship between sarcopenia and insulin resistance, PDM, DM and metabolic syndrome [2,4,6]. Myokines secreted by muscle tissue prevent insulin resistance, and deficiency of myokines in sarcopenia could play a role in development of insulin resistance [3]. Although there are numerous different methods used currently, bioimpedance analysis (BIA) is frequently preferred among these methods as it is cheap, easily applicable and contains no radioactivity [7]. Moreover, the diagnosis and assessment of sarcopenia become difficult because of different equations used for the measurement of muscle mass [8]. While some studies have used the sum of the muscle masses of the four limbs for the evaluation of muscle mass, some have used total muscle mass [8]. As the consequence, the diagnosis and the prevalence of sarcopenia cannot be assessed accurately [8]. Beside the absence of a consensus on how to make the measurement of muscle mass, there is also difficulty in assessing the muscle

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mass in obese subjects [5,9]. In the present study, it was aimed to evaluate the muscle mass in obese, prediabetes and type 2 diabetes mellitus patients by different equations used for the measurement of muscle mass.

2. Materials and methods

2.1. Participants

Medical records of the patients at the age of 18–65 years, who were presented to the Obesity Clinic of XXXX between 2013 and 2015 with BMI $\geq$ 30 kg/m^2 were retrospectively reviewed in the present study. The study participants were separated into three groups as obesity, PDM and DM according to the fasting plasma glucose (FPG), HbA1c, and 2nd hour plasma glucose on 75 gr oral glucose tolerance test (OGTT). Participants who have not been receiving any antidiabetic therapy (oral antidiabetic medications or insulin) and having FPG <100 mg/dL or HbA1c < 5.7% or 2ndhour plasma glucose<140 mg/dl on OGTT were assigned to the obesity group [1]. Patients who have not been receiving any antidiabetic therapy (oral antidiabetic medications or insulin) and having FPG of 100–125 mg/dL or HbA1c of 5.7–6.4% or 2ndhour plasma glucose of140–199 mg/dl on 75 gr OGTT were assigned to the PDM group [1]. In addition, patients with FPG $\geq$ 126 mg/dl or HbA1c $\geq$ 6.5% or 2ndhour plasma glucose $\geq$ 200 mg/dl on 75 gr OGTT or receiving any antidiabetic therapy (oral antidiabetic medications or insulin) were assigned to the DM group [1]. The study was approved by the Ethics Committee of XXX (Date of Approval: 29 Jan 2016. Approval Number: 89513307/1009/537–118). Informed consent is not necessary due to the retrospective nature of this study.

2.2. Study measurements

The height, body weight, lean masses of the arms and legs, and total fat mass were evaluated in all participants by JAWON Medical GAIA 359 PLUS (Korea, 2011) after 12-h fasting period. Subsequently, total muscle mass was calculated by the equation $[(\text{height}^2(\text{cm}) \div \text{BIAresistance} \times 0.401) + (\text{gender} \times 3.825) + (\text{age} \times -0.071) + 5.102]$ [7], and skeletal muscle index and body muscle mass ratio were assessed. The equations used for the evaluation of fat and muscle masses are summarized in Table 1 [8,10]. In addition, HOMA-IR was calculated to estimate the insulin resistance using the equation FPG (mg/dL) x fasting insulin (uIU/mL)/405 [11].

2.3. Exclusion criteria

Type 1 diabetes mellitus, hyperthyroidism, chronic renal failure, chronic liver failure, Cushing syndrome, history of past malignancy, documented skeletal muscle system disease, limbs amputated for any reason, and pregnant women were excluded. Moreover, subjects over the age of 65 years were also excluded as they might have reduced muscle mass due to aging.

2.4. Statistical analysis

Statistical analysis of data were performed using SPSS 22 program. Descriptive statistical analysis of data was presented as frequency, percentage, mean ± standard deviation and median (minimum – maximum). Student t-test and one-way ANOVA test were performed for continuous variables with normal distribution and Mann Whitney U test, Kruskal Wallis test and Spearman correlation test were used for continuous variables with abnormal distribution. A p-value less than 0.05 was considered significant.

3. Results

A total of 1107 participants, of whom 666 (60.2%) were female, were enrolled into the study. Of the participants, 288 (26.02%) had obesity, 524 (47.33%) had PDM and 295 (26.65%) had DM. While the mean age of females in both obese and DM groups were significantly higher than males, there was no difference in the PDM group ($p = 0.001$ for obesity group, $p < 0.001$ for DM group, and $p = 0.338$ for PDM group, respectively). The median HOMA-IR of males were higher than females in the PDM and DM groups, however there was no difference in the obese group ($p = 0.053$ for obesity group, $p < 0.001$ for PDM group and, $p = 0.002$ for DM, respectively). Besides, the mean BMI of females were significantly higher than males in all groups ($p = 0.042$ for obesity group, $p = 0.006$ for PDM group and, $p = 0.002$ for DM, respectively). Age, BIA measurements and HOMA-IR of females and males according to their groups are demonstrated in Table 2.

Considering the BIA measurements in females, only BMI was significantly difference between obese and PDM patients ($p = 0.006$). BMI and body fat percentage in DM females were higher than PDM females, but ALM/weight, body muscle mass ratio and ALM/BMI in DM females were lower than PDM females ($p = 0.002$, $p < 0.001$, $p = 0.004$, $p < 0.001$ and $p = 0.003$, respectively). Moreover, BMI, ALM/height^2 and body fat percentage in the DM group were higher than the obesity group, while ALM/weight, body muscle mass ratio and ALM/BMI in the DM group were lower than the obesity group ($p < 0.001$, $p = 0.003$, $p < 0.001$, $p = 0.003$, $p < 0.001$ and $p = 0.003$, respectively). .

With regard to the BIA measurements in males, ALM/BMI in the obese group was higher than the PDM group and, skeletal muscle index in the PDM group was higher than the obesity group ($p = 0.020$ and $p = 0.025$, respectively). There was no significant difference between PDM and DM males in terms of BMI and skeletal muscle index ($p = 0.212$ and $p = 0.191$). Although ALM/BMI in the PDM males was higher than the DM males, it was not statistically significant ($p = 0.170$). However, BMI and skeletal muscle index in the DM males were higher than the obese males, ALM/BMI in the DM males were lower than the obese males ($p = 0.008$, $p = 0.002$ and $p = 0.001$, respectively).

Table 1
The equations used for the evaluation of fat and muscle masses.

BMI (kg/m^2)	Body weight/height^2
Fat percentage (%)	(Fat mass/body weight) x 100
ALM (kg)	Sum of the appendicular lean masses of the four limbs
ALM/height^2 (kg/m^2)	ALM/height^2
ALM/weight (%)	(ALM/weight) x100
Skeletal muscle index (kg/m^2)	Total muscle mass/height^2
Body muscle mass ratio (%)	(Total muscle mass/body weight) x 100
ALM/BMI ratio	ALM/BMI

ALM, Appendicular lean mass; BMI, Body mass index.

Table 2
Age, BIA measurements and HOMA-IR of females and males according to their groups.

	Females (n = 666)				Males (n = 441)			
	Obesity group (n = 160)	PDM group (n = 330)	DM group (n = 176)	p	Obesity group (n = 128)	PDM group (n = 194)	DM group (n = 119)	p
Age (year)	38.32 ± 12.30	42.05 ± 12.11	55.79 ± 9.03	<0.001[a]	33.63 ± 10.70	40.97 ± 13.11	49.82 ± 11.4	<0.001[a]
BMI (kg/m2)	37.66 ± 5.20	39.07 ± 5.54	40.72 ± 5.72	<0.001[a]	36.67 ± 4.79	37.65 ± 5.69	38.51 ± 6.00	0.034[a]
Body fat percentage (%)	40.88 ± 3.44	41.36 ± 3.40	42.70 ± 3.66	<0.001[a]	32.04 ± 5.23	32.42 ± 5.60	32.71 ± 6.03	0.646[a]
ALM/height^2 (kg/m^2)	10.35 ± 1.59	10.66 ± 1.66	10.86 ± 1.51	0.014[a]	11.69 ± 1.75	11.92 ± 1.66	12.18 ± 1.89	0.087[a]
ALM/weight (%)	27.58 ± 2.82	27.34 ± 2.20	26.78 ± 2.02	0.004[a]	32.01 ± 3.74	31.83 ± 2.81	31.76 ± 2.60	0.802[a]
ALM/BMI	0.68 ± 0.09	0.68 ± 0.07	0.66 ± 0.07	0.003[a]	0.98 ± 0.15	0.95 ± 0.13	0.93 ± 0.11	0.003[a]
Total muscle mass (kg)	28.85 ± 4.89	29.47 ± 4.18	28.92 ± 4.42	0.238[a]	43.51 ± 5.78	43.46 ± 6.32	43.50 ± 6.55	0.997[a]
Skeletal muscle index (kg/m^2)	11.56 ± 1.77	11.81 ± 1.45	11.74 ± 1.64	0.280[a]	14.12 ± 1.64	14.56 ± 1.80	14.86 ± 2.05	0.006[a]
Body muscle mass ratio (%)	30.86 ± 3.70	30.45 ± 3.23	29.06 ± 3.43	<0.001[a]	38.78 ± 4.18	39.10 ± 4.88	38.96 ± 4.70	0.840[a]
HOMA-IR	3.77 (0.93–13.27)	4.73 (0.78–22.77)	5.10 (0.07 –269.63)	<0.001[b]	3.89 (1.19–16.52)	5.42 (0.46–35.38)	7.19 (1.51–63.95)	<0.001[b]

ALM, Appendicular lean mass; DM group, type 2 diabetes mellitus group; PDM group, prediabetes group; BMI, body mass index.
Data are presented as mean ± standard deviation and median (minimum-maximum).
[a] One-way ANOVA test.
[b] Kruskal Wallis test.

After adjusting age and BMI, no relation was determined between HOMA-IR and muscle-related formulas for each group in the both genders ($p > 0.05$).

4. Discussion

The present study shown that ALM/BMI and ALM/weight ratios were difference between obesity, PDM and DM groups in both genders. However, that difference in ALM/BMI ratio was significant in both genders, the difference in ALM/weight ratio was significant in only females. ALM/BMI ratio in the DM group was lower than obesity and PDM groups in females. In addition, ALM/BMI ratio in the obesity group was higher than PDM and DM groups in males.

Numerous different equations are used to evaluate the muscle mass [8,10]. Decrease in ALM/BMI ratio, which is an index developed recently, begins as of the third decade and thereby it is considered that it can be used for the measurement of muscle mass at early ages [10]. Recently studies found that obesity needs to be taken into account while evaluating the muscle mass and that ALM/BMI ratio would be more beneficial for the assessment of muscle mass particularly in obese patients [10,12]. In the present study, decreased ALM/BMI ratio was determined between the groups for both genders. Decrease in ALM/BMI ratio was determined between obesity and PDM and between obesity and DM groups in male participants, whereas it was determined between PDM and DM and between obesity and DM groups in female participants. The difference between genders in terms of decreased ALM/BMI ratio might have resulted from higher insulin resistance in males than females in the PDM and DM groups. A population-based study was reported that differences between genders need to be taken into consideration while evaluating the muscle mass [12]. Although males have higher muscle mass, they are subject to more progressive muscle loss with aging [13,14]. However, DM is a more critical risk factor for decrease in muscle mass in females [5,13].

ALM/height^2 ratio, which is another equations used for the evaluation of muscle mass, in diagnosing sarcopenia in obese subjects has limitations as it shows strong correlation with BMI and that using ALM/weight ratio would be more appropriate [4]. Decrease in muscle mass and muscle strength begins as of 35 years of age; muscle mass decreases and fat mass increases with aging even body weight remains constant [4,8]. Although a decrease was determined in ALM/weight ratio as of the third decade in both genders, ALM/height^2 ratio increased in females but decreased in males [10]. Age alone is a risk for not only decreased muscle mass, but also for insulin resistance [6]. In the present study, although decrease in ALM/weight and increase in ALM/height^2 were observed between the groups for both genders, these changes were found to be statistically significant only for females. This might have resulted from higher mean age of the females in all groups.

Body muscle mass ratio is another equations used for the evaluation of muscle mass [2]. Earlier studies determined higher frequency of sarcopenia using body muscle mass ratio in the subjects with DM and metabolic syndrome [5,13]. In addition, the prevalence of sarcopenia determined by body muscle mass ratio was found to be higher in obese versus. non-obese subjects in a population-based study [6]. In the present study, while body muscle mass ratio was significantly decreased between the groups for females, such a relationship not demonstrated for males. One of the important reasons for this difference may be higher BMI and body fat percentage in females than males in all groups. Higher mean age in females than males in all groups may be another reason.

There are the studies showing that the relationship between insulin resistance and muscle loss [2–6]. However, no correlation was found between HOMA-IR and muscle-related formulas after adjusting age and BMI in present study. The reason for this result may be the use of HOMA-IR in the assessment of insulin resistance. Although the HOMA-IR level is an easily applicable and frequently used method in assessing insulin resistance, the hyperinsulinemic-euglycemic clamp is the gold standard in making the diagnosis [15].

One of the present study limitations is the fact that there were both participants receiving oral antidiabetic and insulin therapy in the DM group. It is propounded that exogenous insulin hormone enhances protein synthetic activity in the muscle tissue and suppresses degradation of muscle protein [16]. Another limitation of study include undocumented duration of insulin resistance. Additionally, insulin is secreted pulsatile in healthy individuals and, HOMA-IR has limitation used to measure for insulin resistance [17]. A limitation of the present study is muscle strength, which is important in the diagnosis of sarcopenia, was not measured.

5. Conclusion

Insulin resistance, which is one of the causes of muscle loss, is common among obese subjects, and decreased muscle mass can be dissembled in obese subjects [3,6,14]. It was determined that obese subjects with high fat mass and low muscle mass can have sarcopenia even though the measurements do not prove [18]. Although

progressive muscle loss with aging is a major health problem in the elderly population, the percentage of total lean body mass to body weight begins to reduce from the third decade, and consequently, sarcopenia may develop in young and middle-aged population [3,8]. In addition, there is no formula agreed for the evaluation of muscle mass, especially in young and middle-aged person [8]. In the present study, decreased ALM/BMI ratio was demonstrated between the groups for both genders, whereas decrease in ALM/weight ratio was demonstrated in only female patients. Moreover, increased ALM/height^2 ratio was determined in females and increased skeletal muscle index was determined in males. It was concluded that, ALM/BMI ratio may be more appropriate formula than other formulas for the evaluation of muscle mass in middle-aged obese, PDM and DM patients in the clinical practice.

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Conflicts of interest

All authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.05.007.

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