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Original Article

Sex difference in skeletal muscle mass in relation to metabolic dysfunction-associated steatotic liver disease: a propensity score matching study

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ABSTRACT

Background: While low muscle mass is considered a risk factor for metabolic dysfunction-associated steatotic liver disease (MASLD), whether the relationship is independent of fat mass remains unclear.
Objectives: This study aims to clarify the association between the sex-specific height-adjusted low skeletal muscle mass index (LSMI) and MASLD.
Methods: Data from the 2008–2010 Korean National Health and Nutrition Examination Survey were analyzed. LSMI was defined using the 2019 Asian Working Group for Sarcopenia. The non-alcoholic fatty liver disease-liver fat score was used to assess MASLD. Gender-specific 1:1 propensity score matching (PSM) was performed to mitigate the confounding effects of anthropometric variables and lifestyles. Conditional logistic analysis was used on the dataset after PSM to estimate the odds ratio (OR) with a 95% confidence interval (CI).
Results: After PSM, the prevalence of MASLD was significantly higher in men with LSMI than in those without LSMI (37.4% vs. 29.6%). No significant difference was observed in the prevalence of MASLD between groups after PSM in women (20.4% vs. 20.3%). Conditional logistic analysis revealed that the odds of having MASLD were significantly higher in men with LSMI compared to those without LSMI (OR = 1.38, 95% CI: 1.09–1.75), while no significant association was found in women with LSMI (OR = 1.10, 95% CI: 0.87–1.40).
Conclusion: Height-adjusted LSMI is an independent factor associated with MASLD in the condition of the same level of fat mass in men. Further prospective studies in diverse populations are needed to confirm our findings.
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1. Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD), the recently changed nomenclature for non-alcoholic fatty liver disease (NAFLD) [1,2], has become the most common cause of chronic liver disease worldwide and is leading to an increasing chronic liver disease burden [3,4]. Recent studies have shown that MASLD is associated with sarcopenia, a major risk factor for falls, functional impairment, frailty, and mortality [5]. Sarcopenia is characterized by loss of strength and skeletal muscle mass, but it is usually defined by declines in appendicular muscle mass [6]. MASLD and sarcopenia share a common underlying mechanism characterized by systemic inflammation, obesity, physical inactivity, vitamin D deficiency, and adiponectin dysregulation [7]. Additionally, the loss of muscle mass can lead to insulin resistance, as skeletal muscle is the primary organ responsible for glucose disposal [8]. Therefore, considerable attention has been paid to the relationship between sarcopenia and MASLD [9–11]. Several epidemiologic studies have revealed that the prevalence of sarcopenia is higher in individuals with MASLD (~18–38%) and those with metabolic dysfunction-associated steatohepatitis (MASH) (~35%–63%) compared to healthy controls without MASLD (~8%–22%) [12–14].

Both low muscle mass and high fat mass are closely associated with MASLD, however, and this complicates the determination of which factor plays a more effective role in its development. Considering the current evidence on the relationship between MASLD and low skeletal muscle mass index (LSMI) with various definitions, it is expected that fat will contribute more to MASLD than muscle. For example, studies have consistently shown MASLD/MASH to be positively related to both body mass index (BMI)-adjusted and weight-adjusted LSMI [12,15,16]. On the other hand, other researchers have demonstrated an inverse relationship between height-adjusted LSMI and MASLD unless adjusted for weight or BMI [17–19]. These findings indicate that the effect of fat and/or bone,

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rather than muscle alone, may have a stronger correlation with MASLD. Furthermore, height-adjusted LSMI may not be a reliable predictor of MASLD given the uncertainty surrounding its actual association with the disease. Accordingly, we consider it necessary to conduct a more thorough investigation to determine whether muscle mass truly contributes to MASLD.

Therefore, an in-depth examination is necessary to determine whether LSMI has an independent association with MASLD while controlling for fat and bone mass. To this end, the current study aimed to examine the association between height-adjusted LSMI and MASLD using propensity score matching (PSM) to mitigate the confounding effects of fat and bone mass and other factors affecting muscle mass.

2. Methods

2.1. Study population

The current study follows a cross-sectional study design, analyzing data from the 2008–2010 Korean National Health and Nutrition Examination Survey (KNHANES). The KNHANES is a nationwide representative survey conducted by the Korea Disease Control and Prevention Agency to assess the health and nutritional status of Korean citizens.

Fig. 1 presents a flowchart of the study population. Among the 29,235 participants who participated in the KNHANES from 2008 to 2010, we excluded participants with the following characteristics: (1) heavy alcohol drinker ($n = 1691$); (2) hepatitis B viral carrier ($n = 664$); (3) hepatitis C viral carrier ($n = 11$); (4) insufficient data to calculate NAFLD-liver fat score ($n = 16,251$); and (5) missing information pertaining to anthropometry, total energy intake, physical activity, or smoking status ($n = 6169$). From the remaining 7450 participants (men with LSMI [$n = 698$], men without LSMI [$n = 2092$], women with LSMI [$n = 1326$], women without LSMI [$n = 3334$]), we finally selected 3,098 participants (men with LSMI [n = 497], men without LSMI [$n = 497$], women with LSMI [$n = 1052$], women without LSMI [$n = 1052$]) after a 1:1 PSM analysis.

The study protocol conformed to the ethical guidelines of the 1964 Declaration of Helsinki and its later amendments. Informed consent was waived by the institutional review board (IRB) because of the retrospective study design. The study was approved by the IRB of Nowon Eulji Medical Center (IRB No. 2021-09-025).

2.2. Assessment of body composition

Dual-energy X-ray absorptiometry was used to measure the body composition of each participant (QDR 4500A; Hologic Inc., Bedford, MA, USA). Bone mineral content (g), fat mass (g), and lean body mass (g) were obtained from pre-defined anatomical areas including the head, arms, legs, trunk, pelvic region, and whole body. Skeletal muscle mass was calculated by subtracting bone mineral content (g) from lean body mass (g). Appendicular skeletal muscle mass was calculated as the summation of the skeletal muscle mass of both the upper and lower extremities. We defined the skeletal muscle mass index (SMI) as appendicular skeletal muscle mass (kg) divided by height squared (m^2). LSMI was defined as SMI < 7.0 in men and SMI < 5.4 in women using the cut-off points for LSMI defined by the 2019 Asian Working Group for Sarcopenia [20].

Height (cm) was measured to the nearest 0.001 m using a stadiometer on participants in a standing posture or supine position without shoes. Body weight (kg) was measured to the nearest 0.1 kg using a digital scale with participants in light clothing. BMI was calculated as body weight (kg) divided by height squared (m^2). Waist circumference (WC, cm) was measured in the horizontal plane, midway between the lowest rib and the iliac crest.

2.3. Assessment of MASLD

The NAFLD-liver fat score was used to assess MASLD [2]. The formula for NAFLD-liver fat score is as follows [21]:

NAFLD-liver fat score $= -2.89 + 1.18 \times$ metabolic syndrome (yes: 1, no: 0) $+ 0.45 \times$ type 2 diabetes mellitus (yes: 2, no: 0) $+ 0.15 \times$ insulin (μIU/mL) $+ 0.04 \times$ AST (U/L) $- 0.94 \times$ AST/ALT

where AST = serum aspartate transaminase and ALT = alanine transaminase. A person was considered to have MASLD if they had an NAFLD-liver fat score higher than -0.640 [21].

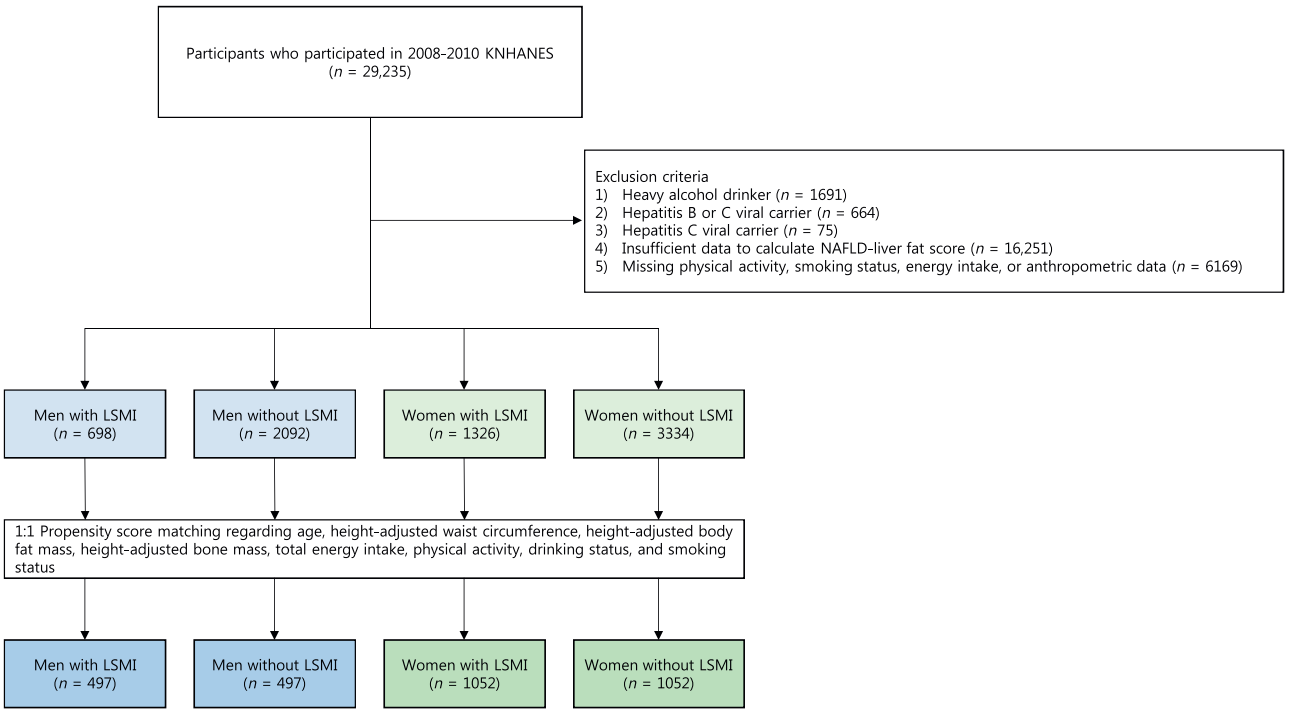

Fig. 1. Flowchart of study population.

2.4. Covariates

Systolic and diastolic blood pressure were measured with participants in a sitting position after at least five minutes of resting, followed by calculating the mean blood pressure (MBP). Smoking status was categorized as "current smoker," "intermittent smoker," "former smoker," and "never smoker." A heavy alcohol drinker was defined as a person who consumed ≥30 g of alcohol per day in case of men and ≥20 g per day in case of women. Except for heavy alcohol drinkers, participants were divided into categories of either "current drinker" or "non-drinker." A regular exerciser was defined as a person who engaged in 20 min of vigorous exercise at least three days per week or 30 min of moderate exercise at least five days per week. Total energy intake (kcal/day) was calculated using a food frequency questionnaire. After at least eight hours of fasting, concentrations of fasting plasma glucose as well as serum aspartate transaminase, alanine transaminase, insulin, total cholesterol, triglyceride, and high-density lipoprotein cholesterol were measured.

2.5. Statistical analysis

All statistical analyses were performed separately for men and women. Data for clinical characteristics of the participants were presented as mean ± standard deviation for continuous variables and number (percentage, %) for categorical variables. For data before PSM, Student's t-test was performed for continuous variables, and a chi-squared test was performed for categorical variables.

We utilized PSM to estimate the average marginal effect of LSMI on MASLD among those who received the intervention, adjusting for confounding by including covariates. PSM, defined as the probability of treatment assignment conditional on observed covariates [22], was implemented using gender-specific 1:1 nearest neighbor matching to mitigate confounding effects of anthropometric variables including height-adjusted WC, total fat mass, and total bone mass as well as age, total energy intake, physical activity, current drinking status, and smoking status. This approach employed the R package "MatchIt" [23]. After adjusting the caliper to 0.1, we conducted a round of 1:1 matching without replacement, which achieved adequate balance, as evidenced in Fig. 2. All standardized mean differences for the covariates, as well as for squares and two-way interactions between covariates, were below 0.1 and 0.15, respectively, confirming that an adequate balance was successfully attained. The matched clinical characteristics of the gender-specific groups with or without LSMI were compared using the linear mixed model for the continuous variables and the generalized estimating equations for categorical data. We performed both conditional logistic analysis on the dataset after PSM and conventional logistic analysis on the dataset before PSM to estimate the odds ratio (OR) with a 95% confidence interval (CI) for MASLD in a gender-specific group with LSMI compared to a group without LSMI.

All statistical analyses were performed using SAS statistical software (version 9.4; SAS Institute Inc., Cary, NC, USA) and R (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria). The significance level was set at $p < 0.05$.

3. Results

3.1. Clinical characteristics of participants before and after PSM

Table 1 presents the clinical characteristics of the gender-specific groups with or without LSMI. Before PSM, men with LSMI had a higher mean age and lower mean total energy intake, height-adjusted fat mass, height-adjusted bone mass, and height-adjusted WC than men without LSMI, and there was a lower proportion of regular exercisers, current drinkers, and never-smokers. Women with LSMI had a lower mean age, height-adjusted fat mass, height-adjusted bone mass, and height-adjusted WC than women without LSMI, and there was a lower proportion of regular exercisers and never-smokers. After PSM, no significant difference was observed in the matched variables between the groups with and without LSMI in both men and women. Regarding the unmatched variables, the groups with LSMI had lower mean BMI and MBP values than the groups without LSMI in both men and women. The proportion of patients with type 2 diabetes mellitus was higher in men with LSMI than in men without LSMI.

3.2. Relationship between gender-specific LSMI and MASLD before and after PSM

Fig. 3A illustrates the prevalence of MASLD among gender-specific groups, comparing individuals with and without LSMI prior to PSM. In women, prior to PSM, the prevalence of MASLD was significantly higher in those with LSMI compared to those without (19.2% vs. 7.6%, $p < 0.001$). Conversely, in men, there was no significant difference in the prevalence of MASLD between those with and without LSMI before PSM (35.2% vs. 34.4%, $p = 0.691$). Fig. 3B presents the data following the PSM. After adjusting for confounding variables, the prevalence of MASLD in men with LSMI increased significantly compared to those without LSMI (37.4% vs. 29.6%, $p = 0.009$). However, in women, the prevalence of MASLD remained statistically similar between those with and without LSMI after PSM (20.4% vs. 20.3%, $p = 0.957$).

Table 2 shows the results of the logistic regression for MASLD of the gender-specific groups with and without LSMI before and after PSM. Before PSM, a simple logistic regression analysis revealed that the OR (95% CI) for MASLD for women with LSMI compared to those without

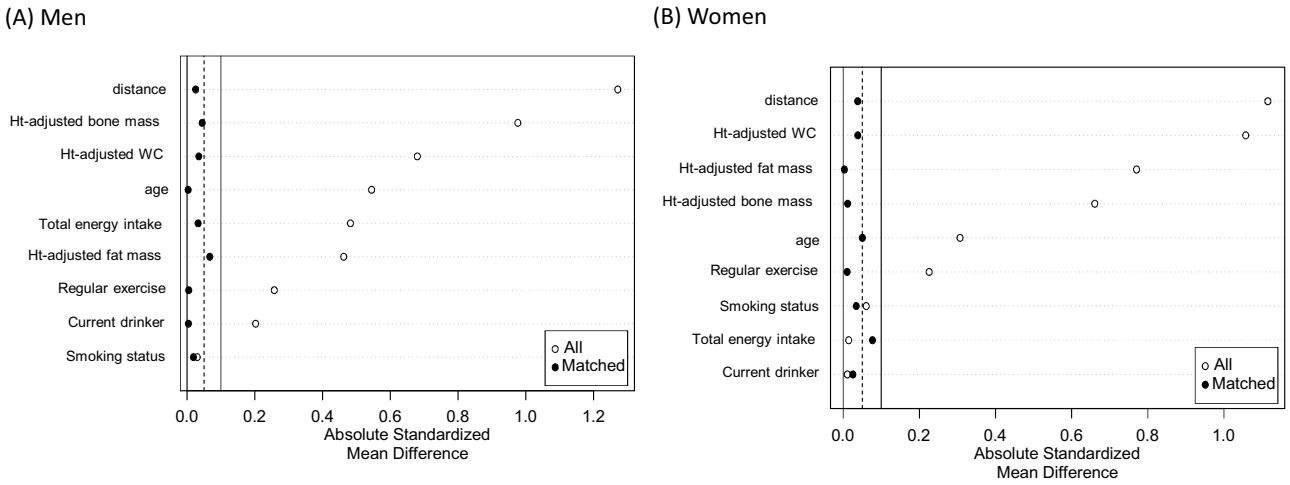

Fig. 2. Love plot of balance following propensity-score matching.

Table 1
Clinical characteristics of gender-specific groups with or without LSMI before and after propensity score matching.

	Men						Women					
	Before propensity score matching			After propensity score matching			Before propensity score matching			After propensity score matching		
	Without LSMI	With LSMI	*p*	Without LSMI	With LSMI	*p*	Without LSMI	With LSMI	*p*	Without LSMI	With LSMI	*p*
Variables	(n = 2092)	(n = 698)		(n = 497)	(n = 497)		(n = 3334)	(n = 1326)		(n = 1052)	(n = 1052)	
Matched variables												
Age (years)	47.3 ± 15.6	56.8 ± 17.3	< 0.001	54.0 ± 16.3	54.1 ± 17.2	0.959	49.9 ± 15.3	44.9 ± 16.5	< 0.001	47.1 ± 16.7	46.2 ± 16.1	0.247
Regular exerciser, n (%)	621 (29.7%)	136 (19.5%)	< 0.001	104 (20.9%)	103 (20.7%)	1	824 (24.7%)	217 (16.4%)	< 0.001	185 (17.6%)	189 (18.0%)	0.864
Current drinker, n (%)	1509 (72.1%)	435 (62.3%)	< 0.001	327 (65.8%)	326 (65.6%)	1	1237 (37.1%)	499 (37.6%)	0.761	391 (37.2%)	378 (35.9%)	0.587
Smoking status, n (%)			0.048			0.458			0.016			0.095
Never smoker	515 (24.6%)	165 (23.6%)		107 (21.5%)	117 (23.5%)		3080 (92.4%)	1194 (90.0%)		968 (92.0%)	948 (90.1%)	
Formal smoker	304 (14.5%)	132 (18.9%)		98 (19.7%)	99 (19.9%)		36 (1.1%)	28 (2.1%)		11 (1.0%)	22 (2.1%)	
Intermittent smoker	527 (25.2%)	160 (22.9%)		130 (26.2%)	109 (21.9%)		84 (2.5%)	41 (3.1%)		24 (2.3%)	36 (3.4%)	
Current smoker	746 (35.7%)	241 (34.5%)		162 (32.6%)	172 (34.6%)		134 (4.0%)	63 (4.8%)		49 (4.7%)	46 (4.4%)	
Total energy intake kcal/day	2301.9 ± 879.9	1972.2 ± 683.9	< 0.001	2046.9 ± 701.5	2069.3 ± 689.9	0.612	1638.7 ± 622.9	1648.2 ± 652.2	0.653	1610.0 ± 572.2	1660.2 ± 664.8	0.064
Height-adjusted total fat mass, g/m^2	5242.1 ± 1748.0	4465.0 ± 1681.4	< 0.001	4838.4 ± 1646.9	4725.5 ± 1636.3	0.278	7844.5 ± 2174.9	6485.6 ± 1764.0	< 0.001	6754.7 ± 1908.0	6749.4 ± 1758.7	0.947
Height-adjusted Total bone mass g/m^2	688.5 ± 80.8	603.9 ± 86.7	< 0.001	633.4 ± 69.7	629.5 ± 82.4	0.425	574.1 ± 85.0	524.6 ± 74.9	< 0.001	533.9 ± 76.8	534.7 ± 73.8	0.792
Height-adjusted WC m/m^2	0.5 ± 0.1	0.5 ± 0.1	< 0.001	0.5 ± 0.0	0.5 ± 0.1	0.548	0.5 ± 0.1	0.5 ± 0.1	< 0.001	0.5 ± 0.1	0.5 ± 0.1	0.363
Unmatched variables												
BMI, kg/m^2	24.8 ± 2.7	21.1 ± 2.3	< 0.001	23.4 ± 2.3	21.6 ± 2.1	< 0.001	24.4 ± 3.2	20.6 ± 2.2	< 0.001	22.5 ± 2.5	21.0 ± 2.1	< 0.001
MBP, mmHg	94.5 ± 11.1	93.1 ± 11.2	0.005	94.4 ± 10.8	93.0 ± 10.9	0.037	90.0 ± 12.3	85.9 ± 11.5	< 0.001	87.9 ± 12.2	86.7 ± 11.7	0.018
FPG, mg/dL	100.0 ± 22.5	99.9 ± 22.6	0.914	99.8 ± 23.4	101.7 ± 25.1	0.218	97.4 ± 21.6	92.4 ± 18.1	< 0.001	93.4 ± 18.8	93.2 ± 18.6	0.813
Insulin, μIU/mL	10.4 ± 5.9	10.5 ± 6.0	0.974	10.4 ± 5.9	10.6 ± 6.3	0.478	10.4 ± 5.3	10.0 ± 5.2	0.037	10.0 ± 5.3	9.9 ± 4.9	0.797
Triglyceride, mg/dL	158.8 ± 123.6	138.9 ± 112.6	< 0.001	141.5 ± 102.5	147.4 ± 121.5	0.409	121.9 ± 82.6	98.6 ± 62.2	< 0.001	108.3 ± 73.8	102.4 ± 65.1	0.051
HDL cholesterol, mg/dL	44.2 ± 9.8	46.4 ± 11.0	< 0.001	45.4 ± 10.2	45.8 ± 10.7	0.539	49.2 ± 10.7	52.4 ± 10.9	< 0.001	51.5 ± 11.0	51.8 ± 11.0	0.488
Percentage of protein intake to total energy intake, %	14.6 ± 4.0	14.0 ± 3.9	0.001	14.1 ± 3.6	14.3 ± 4.0	0.442	14.0 ± 3.9	14.2 ± 3.8	0.050	14.2 ± 4.0	14.1 ± 3.8	0.822
DM, n (%)	234 (11.2%)	103 (14.8%)	0.015	52 (10.5%)	81 (16.3%)	0.009	332 (10.0%)	73 (5.5%)	< 0.001	49 (4.7%)	64 (6.1%)	0.176

Abbreviations: WC, waist circumference; BMI, body mass index; MBP, mean blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; DM, diabetes mellitus.

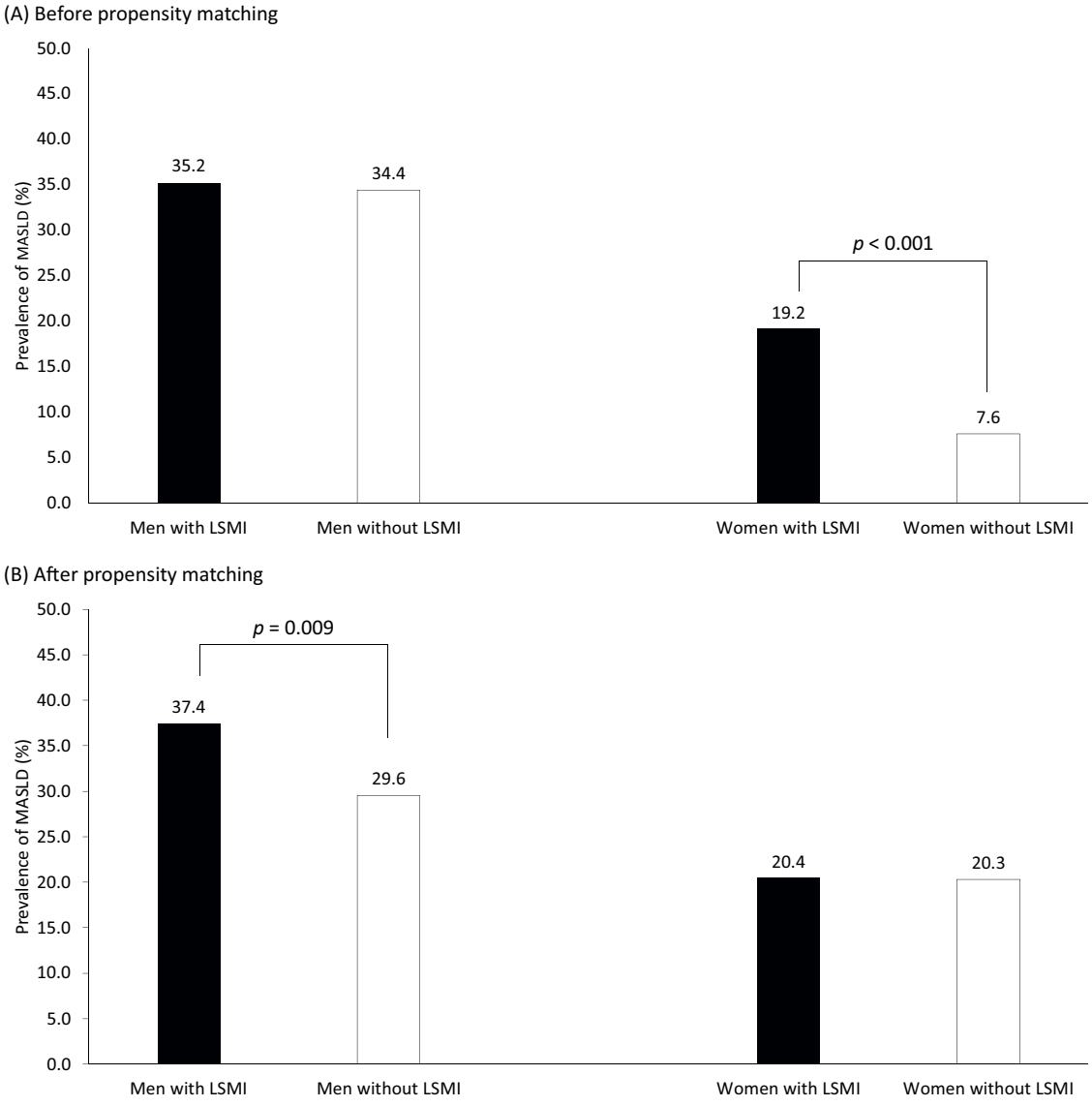

Fig. 3. Prevalence of MASLD among the gender-specific groups with or without LSMI before and after propensity score matching.

Table 2
Logistic regression models for MASLD according to the gender-specific groups with LSMI and without LSMI.

	Men			Women		
	Without LSMI OR	With LSMI OR (95% CI)	*p*	Without LSMI OR	With LSMI OR (95% CI)	*p*
Before propensity score matching*						
Crude model	1 (reference)	1.04 (0.87–1.24)	0.691	1 (reference)	0.52 (0.45–0.61)	<0.001
Adjusted Model 1	1 (reference)	1.30 (1.03–1.64)	0.031	1 (reference)	0.98 (0.81–1.18)	0.804
Adjusted Model 2	1 (reference)	1.36 (1.02–1.82)	0.036	1 (reference)	1.10 (0.88–1.38)	0.404
After propensity score matching**						
Crude model	1 (reference)	1.49 (1.13−1.98)	0.005	1 (reference)	1.04 (0.84−1.30)	0.721
Adjusted model†	1 (reference)	1.38 (1.09−1.75)	0.008	1 (reference)	1.10 (0.87−1.40)	0.423

Abbreviations: LSMI, low skeletal muscle index; MASLD, metabolic dysfunction-associated steatotic liver disease; OR, odds ratio; CI, confidence interval; BMI, body mass index; MBP, mean blood pressure; DM, diabetes mellitus.

* OR and 95% CI were calculated using multiple logistic regression analysis; Model 1: adjusted for height-adjusted waist circumference, height-adjusted total fat mass, height-adjusted total bone mass, age, total energy intake, physical activity, current drinking status, and smoking status; Model 2: adjusted for variables used in Model 1 plus BMI, MBP, and DM.

** OR and 95% CI were calculated using multiple conditional logistic regression analysis; †adjusted for BMI, MBP, and DM.

LSMI was 0.52 (0.45–0.61), while no significant association was found in men. In adjusted models 1 and 2, the relationship became insignificant in women while it became significant in men (Adjusted model 1: OR = 1.30, 95% CI: 1.03–1.64, p = 0.031; Adjusted model 2: OR = 1.36, 95% CI: 1.02–1.82, p = 0.036). After PSM, a simple conditional logistic regression analysis showed that the odds of having MASLD were 1.49 times higher in

men with LSMI than in those without LSMI (OR = 1.49, 95% CI: 1.13–1.98, p = 0.005), while no significant association was found in women. After adjusting for BMI, MBP, and type 2 diabetes mellitus, the adjusted OR (95% CI) for MASLD of the group with LSMI compared to the group without LSMI was 1.38 (1.09–1.75) in men (p = 0.008). No significant relationship was observed in the adjusted model in women.

4. Discussion

Numerous studies have demonstrated that low skeletal mass increases the risk of MASLD. In a recent meta-analysis, the sarcopenia group showed a 1.33-fold higher risk of MASLD and a 2.4-fold higher risk of MASH compared to the control group [24]. Among the 19 articles included in the meta-analysis, studies that utilized weight-adjusted or BMI-adjusted LSMI consistently reported an increased risk of MASLD or advanced fibrosis associated with sarcopenia. Conversely, the study by Zhai et al., which compared the risk of MASLD using height-adjusted LSMI, reported contrary results with an OR for MASLD of 0.47 (95% CI: 0.31–0.74) [25]. Similarly, in a study conducted with a Western population, MASLD was found to be significantly and positively associated with sarcopenia as defined by weight-adjusted LSMI but inversely associated when using height-adjusted LSMI [19]. The divergence in results across studies, depending on the definition of LSMI, can potentially be attributed to the confounding influences of fat. Additionally, findings from a longitudinal study [26], which reported that fat mass at baseline exerts a higher influence on the development of MASLD than muscle mass, further support this assumption.

To the best of our knowledge, this is the first study to examine the relationship between height-adjusted LSMI and MASLD by setting the same conditions for fat, bone mass, and other factors affecting muscle mass. Our study findings indicated that, independent of fat mass, the odds of having MASLD were 1.38 times higher in men with LSMI compared to those without LSMI after PSM, while no significant association was found in women. This suggests that a decrease in skeletal muscle mass alone can increase the risk of MASLD in men. The prevalence of MASLD in LSMI was higher in men than women; however, it was lower than that in the Chinese population (50% in men and 39.6% in women) [27]. Considering that the previous study on Chinese participants defined sarcopenia by measuring not only muscle mass but also muscle strength, we can say that they observed a more rigorous association between sarcopenia and MASLD compared to our study. However, there are limitations due to the small sample size (12 men with sarcopenia and 48 women with sarcopenia), indicating the need for future large-scale studies applying a rigorous definition of sarcopenia.

Skeletal muscle, a target organ for insulin, plays an essential role in glucose metabolism and regulating fat accumulation in the liver [28]. Decreased skeletal muscle induces insulin resistance, which, in turn, can exacerbate MASLD. Furthermore, dysregulated mTORC1 signaling in skeletal muscle, driven by chronic hyperinsulinemia, leads to increased protein breakdown and further muscle mass [29]. Myokines secreted from skeletal muscle play important roles in the sarcopenia–MASLD relationship by counteracting the pro-inflammatory and metabolic effects of adipocytes derived from fat tissue [30–32].

This study showed gender differences in the association between MASLD and LSMI. These findings suggest that men may be more susceptible to the negative effects of muscle loss on metabolic health. One possible explanation for this gender-based difference in the risk of MASLD according to the height-adjusted LSMI status is the hormonal differences between men and women, as testosterone is an important hormone for muscle growth [33]. Testosterone has important metabolic effects, including increasing insulin sensitivity and reducing fat accumulation in the liver [34,35]. Therefore, when men experience muscle loss, they may be more vulnerable to metabolic dysfunction than women. Additionally, a prior study indicated that MASLD is more prevalent in men, potentially due to a protection effect of estrogen against MASLD [36]. Menopause and oophorectomy in young women with endometrial cancer elevate the risk of MASLD and liver fibrosis due to prolonged periods of estrogen deficiency.

Another reason could be the difference in body composition between men and women. A recent cross-sectional analysis compared the relationship between skeletal muscle mass and its distribution with the risk of metabolic dysfunction-associated fatty liver disease (MAFLD) as well as the influence of gender on this association [37]. In the study, adequate appendicular skeletal muscle mass reduced the risk of MAFLD in both sexes, whereas adequate trunk skeletal muscle mass increased the risk of fibrosis in women. A possible mechanism is that the trunk skeletal muscle, being surrounded by visceral and subcutaneous adipose tissues, is more susceptible to myosteatosis, which could contribute to the progression of liver fibrosis [38]. Similarly, in another study evaluating sex-specific differences in the impact of fat distribution on MASLD and liver fibrosis, the effects of android fat deposition on fibrosis were observed only in women [39]. In our study, prior to adjusting for fat mass or performing PSM, we observed a higher prevalence of MASLD in women with LSMI. However, after adjusting for fat mass or conducting PSM, the difference in MASLD risk disappeared. This aligns with previous studies suggesting that fat mass and fat deposition may have a higher impact on MASLD in women than in men.

In addition, LSMI, type 2 diabetes mellitus, and MASLD are interconnected through a common pathophysiological pathway, primarily insulin resistance. Insulin resistance in skeletal muscles impairs glucose uptake, which, in turn, increases insulin levels and enhances lipolysis. This leads to an increased flux of free fatty acids to the liver, exacerbating hepatic fat accumulation and thus promoting the progression of MASLD. In the current study, men with LSMI exhibited a higher prevalence of type 2 diabetes mellitus compared to those without LSMI, suggesting that the effect of LSMI on insulin resistance may be more pronounced in men than in women. Therefore, our findings highlight the need for clinical strategies focusing on improving muscle mass and function, which could potentially mitigate the risks associated with diabetes mellitus and MASLD in men with LSMI.

Although the present study reveals important findings, it has several limitations. First, because of the cross-sectional study design, we could not establish a causal relationship between height-adjusted LSMI and MASLD. Future prospective studies are necessary to determine this longitudinal association. Second, the study participants were limited to Korean adults, which may limit the generalizability of the findings to other populations. Third, MASLD was defined using the NAFLD-liver fat score rather than liver imaging or histological analysis, which could potentially have affected the accuracy of our results. Fourth, we were unable to examine the effect of muscle strength and physical performance on MASLD owing to the lack of data in the KNHANES. Finally, PSM adjusts solely for observed variables, which means there is a possibility of hidden bias. Despite these limitations, this study is significant in that it used PSM to control for potential confounding variables and reduce the impact of selection bias. In addition, through a gender-specific analysis, this study explored the potential gender-based difference in the association between LSMI and MASLD. Finally, using a large sample, the study has established the statistical power to detect a meaningful association between LSMI and MASLD even after controlling for multiple potential confounding variables.

5. Conclusions

In conclusion, height-adjusted LSMI appears to be associated with MASLD in the condition of the same level of fat mass, only in men. This finding suggests the potential value of targeting muscle mass to prevent and manage MASLD, particularly in men. Our results also indicate that body composition assessments in relation to MASLD risk might require gender-specific approaches. However, further prospective studies featuring diverse populations are needed to validate these preliminary

findings. In addition, future research should also consider the potential role of hormones in the relationship between muscle mass and MASLD.

Availability of data and materials

Data analyzed in this study were obtained from the Korean National Health and Nutritional Survey and are available in the following website: https://knhanes.kdca.go.kr/knhanes/main.do

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Author contributions

DHS, YJK, and JHL: study concept and design, acquisition, analysis, and interpretation of data, drafting the manuscript; YJK and JHL: study concept and design, interpretation of data, supervision, revising the manuscript; DHS, YJK, and JHL: approval of the final manuscript.

Ethics approval and consent to participate

The study protocol conformed to the ethical guidelines of the 1964 Declaration of Helsinki and its later amendments. Informed consent was waived by the IRB because of the retrospective study design. The study was approved by the IRB of Nowon Eulji Medical Center (IRB No. 2021-09-025).

Consent for publication

Not applicable.

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