Low skeletal muscle mass is associated with non-alcoholic fatty liver disease in Korean adults: the Fifth Korea National Health and Nutrition Examination Survey

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BACKGROUND: Sarcopenia and non-alcoholic fatty liver disease (NAFLD) share similar pathophysiological mechanisms, and the relationship between sarcopenia and NAFLD has been recently investigated. The study investigated whether low skeletal muscle mass is differentially associated with NAFLD by gender in Korean adults.

METHODS: We conducted a cross-sectional analysis of the data from the Fifth Korea National Health and Nutrition Examination Survey. The skeletal muscle index (SMI) was obtained by the appendicular skeletal muscle mass divided by the weight. NAFLD was defined as a fatty liver index (FLI) ≥60 in the absence of other chronic liver disease.

RESULTS: Among the included subjects, 18.3% (SE: 1.4%) in men and 7.0% (SE: 0.7%) in women were classified as having FLI-defined NAFLD. Most of the risk factors for FLI-defined NAFLD showed a significant negative correlation with the SMI in both genders. Multiple logistic regression analysis showed that low SMI was associated with FLI-defined NAFLD, independent of other metabolic and lifestyle parameters in both genders [males: odds ratio (OR)=1.35; 95% confidence interval (CI): 1.17-1.54; females: OR=1.36; 95% CI: 1.18-1.55]. The magnitude of the association between FLI-defined NAFLD and low SMI was higher in middle aged to elderly males (OR=1.50; 95% CI: 1.22-1.84) than in males less than 45 years of age (OR=1.25; 95% CI: 1.02-1.52) and in premenopausal females (OR=1.50; 95% CI: 1.12-2.03) than in postmenopausal females (OR=1.36; 95% CI: 1.20-1.54).

CONCLUSIONS: Low SMI is associated with the risk of FLI-defined NAFLD independent of other well-known metabolic risk factors in both genders. This association may differ according to age group or menopausal status. Further studies are warranted to confirm this relationship.

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KEY WORDS: Korea National Health and Nutrition Examination Survey; non-alcoholic fatty liver disease; sarcopenia; skeletal muscle

Introduction

Sarcopenia, defined as a loss of muscle mass and strength, was originally regarded as an age-related change.[1] Growing evidence demonstrates that chronic inflammation plays an important role in the development and progression of sarcopenia.[2, 3] Moreover, insulin resistance may accelerate muscle protein loss, and thereby decrease muscle mass and strength.[4, 5] In contrast, sarcopenia may promote insulin resistance because skeletal muscle is a primary insulin-responsive target tissue.[6] Several reports[7-9] have revealed that low skeletal

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muscle mass is associated with metabolic syndrome or type 2 diabetes.

Non-alcoholic fatty liver disease (NAFLD), which is characterized by abnormal fat accumulation in the liver, is the most prevalent chronic liver disease in Western countries;[10] its prevalence is also increasing rapidly in Asian countries, including Korea.[11] Insulin resistance plays a key role in the development of NAFLD, and studies[12, 13] have revealed a close relationship between NAFLD and each component of metabolic syndrome. Therefore, NAFLD is regarded as the hepatic manifestation of metabolic syndrome.[14] Moreover, NAFLD is associated with chronic oxidative stress and inflammation of the liver secondary to hepatic triglyceride accumulation.[15]

Accordingly, NAFLD and sarcopenia share similar pathophysiological mechanisms of insulin resistance and chronic inflammation. Two recent studies investigated the association between sarcopenia and NAFLD.[16, 17] However, neither studies analyzed the gender-specific impact of sarcopenia on the development of NAFLD despite the fact that gender and age differentially influence muscle mass.[18]

The aim of the present study was to investigate whether low skeletal muscle mass is differentially associated with NAFLD by gender, independent of other metabolic factors, in a representative Korean adult population based on the data from the Fifth Korea National Health and Nutrition Examination Survey (KNHANES V), conducted from 2010 to 2011.

Methods

Study population

This study used the data from the KNHANES V, conducted from 2010 to 2011. The KNHANES is a series of nationally representative, cross-sectional surveys administered since 1998. It uses a complex, stratified, multistage, probability sampling design to assess the health and nutritional status of the non-institutionalized civilian Korean population.[19, 20] The survey was approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention. All participants provided written informed consent. Moreover, we used de-identified data in the study.

A total of 6093 subjects aged ≥19 years participated in the health examination, which included whole-body dual-energy X-ray absorptiometry (DXA) and interview. Subjects were excluded for the following reasons: a history of malignancy (n=83), a physician's diagnosis of chronic hepatitis or cirrhosis (n=35), chronic renal failure (n=289), pregnancy (n=24), excessive alcohol use (>20 g/day in male subjects, >10 g/day in female subjects) (n=991), and absence of data (n=932). These exclusion criteria eliminated many participants. However, this conservative approach was important to minimize potential bias due to inclusion of chronic liver disease other than NAFLD or other factors influencing skeletal muscle mass. After exclusion of ineligible subjects, 3739 subjects (1184 males and 2555 females) were included in the analysis.

Dual-energy X-ray absorptiometry

In the KNHANES V, a whole-body DXA scan (Discovery-W; Hologic, Waltham, MA, USA) was indicated for each participant aged ≥10 years to measure the whole-body skeletal muscle and fat mass. The appendicular skeletal muscle (ASM), defined as the sum of the lean soft tissue masses of the arms and legs,[21] has been known to correlate with total body skeletal muscle.[22] The skeletal muscle index [SMI (%)=ASM (kg)/weight (kg)×100] was calculated as described by Janssen et al.[23]

Surrogate measure of fatty liver

To identify fatty liver, the fatty liver index (FLI) was calculated according to an algorithm based on triglycerides, body mass index (BMI), gamma-glutamyl transferase (GGT), and waist circumference:[24]

$$FLI=e^{0.953\times Ln(triglycerides)+0.139\times BMI+0.718\times Ln(GGT)+0.053\times waist\ circumference\ -\ 15.745}/(1+e^{0.953\times Ln(triglycerides)+0.139\times BMI+0.718\times Ln(GGT)+0.053\times waist\ circumference\ -\ 15.745})\times 100$$

The FLI score ranges from 0 to 100. It has been validated against fatty liver diagnosed by ultrasonography with a proven accuracy of 0.84 [95% confidence interval (CI): 0.81-0.87].[24] When the FLI is ≥60, the likelihood of having fatty liver disease is >78%.[25] In this study, subjects were classified as having NAFLD if the FLI was ≥60 in the absence of other causes of chronic liver disease (history of hepatitis or cirrhosis, hepatitis B surface antigen negative, excessive alcohol consumption, as defined above).

Anthropometric and laboratory measurements

Height (m) and weight (kg) were measured with the subject wearing light clothing and barefoot. Height was measured using a stadiometer (Seca 225; Seca, Hamburg, Germany), and weight was measured using an electronic scale (GL-6000-20; Caskorea, Seoul, Korea). BMI was calculated as weight (kg)/height^2 (m^2). Waist circumference (cm) was measured at the midpoint between the costal margin and the iliac crest at the end of a normal expiration. Blood pressure (BP) was measured three times using a mercury sphygmomanometer (Baumanometer; Baum, Copiague, NY, USA) on the right arm after a