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Association of Myosteatosis with Nonalcoholic Fatty Liver Disease, Severity, and Liver Fibrosis Using Visual Muscular Quality Map in Computed Tomography (*Diabetes Metab J* 2023;47:104-17)

Eun Roh

Department of Internal Medicine, Hallym University College of Medicine, Chuncheon, Korea

Nonalcoholic fatty liver disease (NAFLD) has become a predominant chronic liver disease worldwide. NAFLD is characterized by ectopic fat accumulation in the liver without secondary causes of hepatic steatosis, such as excessive alcohol consumption, medications, or viral infection. The rapidly increasing prevalence of NAFLD is accompanied by global increase of obesity rates and population aging. The NAFLD spectrum consists of isolated fatty liver (NAFLD), non-alcoholic steatohepatitis accompanied by chronic inflammation and cell damage, and fibrosis. Since the underlying pathophysiology involves insulin resistance and chronic inflammation, NAFLD is closely related to obesity, type 2 diabetes mellitus, and dyslipidemia. Liver fibrosis predicts increased liver-related mortality as well as increased cardiovascular mortality.

Sarcopenia has also emerged as a global health problem due to aging of the world population. Sarcopenia and obesity have a synergistic impact on increased risk of functional decline, cardiometabolic diseases, and mortality [1]. Growing evidence suggests that sarcopenia, the progressive loss of muscle mass and strength, is independently associated with development of NAFLD [2]. Conversely, a recent study reported NAFLD as an independent risk factor for development of sarcopenia, both low muscle mass and low muscle strength, in the elderly [3]. A vicious cycle between NAFLD and sarcopenia has been proposed with common underlying mechanisms including aging, diet, physical inactivity, hormonal change, insulin resistance, inflammation, and vitamin D deficiency. In addition, several hepatokines have been proposed to be involved in muscle homeostasis either through direct effects or through promotion of insulin resistance.

Although the original definition of sarcopenia was based only on detection of low muscle mass, low muscle strength is better than lower muscle mass in predicting unhealthy outcomes. In 2019, the updated European Working Group on Sarcopenia in Older People 2 (EWGSOP2) sarcopenia definition emphasized low muscle strength over the role of low muscle mass as a principal determinant of sarcopenia to facilitate prompt identification in practice [4]. Confirmation of sarcopenia diagnosis is based on low muscle quantity and quality [4]. Muscle quality describes micro- and macroscopic changes in muscle architecture and composition. Fat infiltration into muscle, so called myosteatosis, is associated with low muscle strength and physical disability and is an important contributing factor to poor muscle quality [5,6]. While myosteatosis is essentially a histological diagnosis, the muscle biopsy is invasive and not practical. Skeletal muscle attenuation as measured by computed tomography (CT) had good correlation with muscle lipid content compared to muscle biopsy or MR spec-

Corresponding author: Eun Roh https://orcid.org/0000-0001-8413-5006
Department of Internal Medicine, Hallym University College of Medicine,
1 Hallimdaehak-gil, Chuncheon 24252, Korea
E-mail: roheun@gmail.com

troscopy findings [7]. Low-attenuation muscle indicates a large proportion of myosteatosis and is associated with poor muscle quality.

As most studies have used muscle mass instead of muscle quality to define sarcopenia [2], the association between sarcopenia and NAFLD should be reexamined after integrating the concept of muscle quality. In this article entitled, "Association of myosteatosis with nonalcoholic fatty liver disease, severity, and liver fibrosis using visual muscular quality map in computed tomography," Kim et al. [8] suggested that a large proportion of good muscle quality was associated with lower risks of NAFLD and fibrosis. This cross-sectional study included 13,452 subjects who underwent abdominal CT scans during routine health check-ups. Total abdominal muscle area (TAMA) was measured at the L3 level and was segmented into skeletal muscle area (SMA) and intramuscular adipose tissue. Intramuscular adipose tissue represents the fat tissue between muscle groups and muscle fibers. SMA was further classified into normal attenuation muscle area (NAMA) and low attenuation muscle area (LAMA). Indicators of myosteatosis include SMA/body mass index (BMI), NAMA/BMI, NAMA/TAMA, and LAMA/BMI. NAFLD and its severity were assessed by ultrasonography, and the severity of liver fibrosis was measured by calculating NAFLD fibrosis score (NFS) and fibrosis-4 (FIB-4) index scores. The odds ratio (OR) for NAFLD increased with decreasing quartiles of SMA/BMI, NAMA/BMI, and NAMA/TAMA in each sex (P for trend <0.001 for all). The ORs of moderate/severe NAFLD were significantly higher in the lowest quartile than in the highest quartile for SMA/BMI, NAMA/BMI, and NAMA/TAMA in men. Moreover, the ORs of intermediate/high liver fibrosis scores as assessed by NFS and FIB-4 scores increased linearly with decreasing quartile for SMA/BMI, NAMA/BMI, and NAMA/TAMA in each sex (P for trend <0.001 for all).

Myosteatosis results from ectopic fat accumulation in skeletal muscle when available lipids exceed the disposal capacity of adipose tissue. Since intramyocellular fat serves as an energy source to promote muscle contraction, it is not necessarily abnormal. Extramyocellular fat accumulation is mostly pathologic and involves either intramuscular (between muscle fibers) or intermuscular (between muscle bundles) accumulation. Since myosteatosis increases with age and increase in visceral adipose tissue, it is characteristically associated with insulin resistance and liver steatosis [9]. Kim et al. [8] supported a significant association between poor muscle quality as measured by CT and the risk of NAFLD and liver fibrosis. Consistently, a recent analysis of UK Biobank data revealed that participants with NAFLD combined with adverse muscle composition, defined as the presence of both low muscle volume (<25th percentile of the population) and high muscle fat infiltration (>75th percentile of the population), exhibited higher prevalence of metabolic comorbidities and functional impairment compared to 'normal muscle composition,' 'only low muscle volume,' and 'only high muscle fat' groups [10]. Therefore, the risk of functional disability due to low muscle mass in NAFLD is exacerbated by myosteatosis. People with previous abdominal CT scans can benefit from measurement of muscle area and quality to evaluate the risk of NAFLD and fibrosis. Further studies to identify optimal cut-offs for muscle fat are necessary to enable detection of poor muscle quality in clinical practice.

CONFLICTS OF INTEREST

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

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