ORIGINAL ARTICLE

The association between sarcopenia and decorin, an exercise-induced myokine, in patients with liver cirrhosis: a pilot study

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Abstract

Background Sarcopenia frequently occurs in patients with liver cirrhosis (LC). The skeletal muscles secrete myokines, including myostatin, irisin, and decorin, which regulate skeletal muscle mass. This study aimed to investigate the association between myokine levels and muscle mass and to identify independent factors for muscle mass in patients with LC.

Methods and Results Thirty-nine patients with LC were enrolled in this study (mean age, 75 years [41-84], female/male, 19/20) and were classified into muscle atrophy or non-atrophy groups according to the Japan Society of Hepatology guidelines. Serum levels of myostatin, irisin, and decorin were measured by ELISA/EIA. Independent factors associated with skeletal muscle index (SMI) were investigated. Profiles associated with non-atrophic muscle were determined by a decision-tree analysis. There were no significant differences in body mass index (BMI) or blood ammonia or myostatin levels between the muscle atrophy and non-atrophy groups. However, serum decorin and irisin levels were significantly higher in the non-atrophy group than the atrophy group (11,888±5,418 vs. 5,642±1,978 pg/mL, P=0.0394; 35.1±1.9 vs. 31.1±8.3 ng/mL, P=0.0109). BMI and serum decorin level were identified as independent factors associated with SMI (P=0.0121, P=0.0483). In the decision-tree analysis, serum decorin level was identified as the first divergence variable for non-atrophic muscle. Of the patients with ≥10,226.8 pg/mL of decorin, 75% were in the non-atrophy group.

Conclusions Serum decorin level was significantly associated with skeletal muscle mass and was an independent factor for skeletal muscle non-atrophy in patients with LC. Decorin may be an important myokine regulating sarcopenia in patients with LC

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Introduction

Sarcopenia is frequently seen in patients with liver cirrhosis (LC), regardless of its etiology [1, 2]. Sarcopenia is associated with a decline in the quality of life and physical inactivity in patients with LC [3]. Sarcopenia is also an independent risk factor for advanced hepatic fibrosis [4], hepatic encephalopathy, and covert hepatic encephalopathy in patients with LC [5]. Moreover, sarcopenia is associated with a poor prognosis in patients with LC [6, 7] and hepatocellular carcinoma (HCC) [8]. Thus, sarcopenia is an important pathological condition in patients with any stage of LC.

Recently, the skeletal muscles have become known as the largest endocrine organ. The skeletal muscles secrete cytokine, also called myokine, which regulates the metabolism as well as skeletal muscle mass [9]. There are various kinds of myokines, including myostatin [10]. Myostatin, one of the transforming growth factor (TGF)-β superfamily proteins, is a negative regulator of muscle protein synthesis, osteoblast differentiation [10], and muscle growth and inhibits proliferation and differentiation in myogenic cells from mesenchymal stromal cells [11]. Serum myostatin levels are reported to be elevated in patients with LC [1,12].

Irisin is also a myokine, which is released by the cleavage of the extracellular domain of the transmembrane receptor fibronectin type III domain-containing 5 protein in skeletal muscle cells [13]. Irisin affects white adipose cells and stimulates uncoupling protein 1 expression, inducing the browning of subcutaneous fat and thermogenesis [13]. In addition, irisin positively correlates with skeletal muscle mass [14] and causes muscle growth through down-regulation of myostatin and up-regulation of insulin-like growth factor-1 and peroxisome proliferator-activated receptor-γ coactivator-1α [15]. Moreover, secretory cathepsin B, a molecule regulating intracellular proteolysis, is reported to be a myokine that is increased in the gastrocnemius muscle by exercise in mice [16]. An increase in cathepsin B is consistent with muscle

regeneration after exercise-induced lysosomal activation [17]. Although cathepsin B is reported to be up-regulated in patients with LC [18], the association between cathepsin B and skeletal muscle mass remains unclear.

Decorin, a recently described myokine, is known as a small leucine-rich proteoglycan. Decorin is an active component of the extracellular matrix and plays crucial roles in the modulation of the cell-matrix crosstalk [19]. Decorin is an anti-fibrotic molecule, which binds to active TGF-β1, leading to interference with its signaling and neutralizing its activity [19]. Decorin expression is known to be decreased in patients with fibroproliferative disease, including chronic obstructive pulmonary disease, focal segmental glomerulosclerosis, and systemic lupus erythematosus [20]. Decorin is also involved in the development of hepatic fibrosis [21]. Decorin protects against fibrogenesis and enhances the healing process by inhibiting TGF-β bioactivity [22] and inducing matrix metalloproteinase collagenase-1 expression [23]. In addition, decorin has been recently reported to promote muscle fiber hypertrophy by inhibiting myostatin, a negative regulator of muscle protein synthesis [24].

The aims of this study were to investigate an association between myokine and muscle mass and to identify independent factors for muscle mass in patients with LC. In addition, we investigated the factors associated with non-muscle atrophy in patients with LC.

Methods

Ethics

The study protocol conformed to the ethical guidelines of the Declaration of Helsinki as reflected in the prior approval given by the institutional review board of Kurume University. Informed consent for participation in the study was obtained from each patient. None of the patients were institutionalized.

Sample size

The sample size was estimated using the online sample size calculator at The University of California, San Francisco (UCSF) assuming 5% type 1 error, 20% type 2 error and a 0.5 correlation coefficient [25]. As a result, the sample size for correlation analysis was estimated 29 subjects.

Subjects

From March 2013 to June 2015, we enrolled 39 consecutive LC patients with hepatocellular carcinoma. Those patients met our inclusion and exclusion criteria. Inclusion criteria were patients who (1) were 20 years of age or more, (2) had a performance status of grade 0 to 2 as defined by the Eastern Cooperative Oncology Group, (3) had undergone biochemical examination and abdominal computed tomography (CT) scanning including the third lumbar (L3) vertebrae level before treatment for HCC. Exclusion criteria were patients with HCC (1) who were undergoing rehabilitation or participating in an exercise program, (2) had a performance status of grade 3 or more, (3) had refractory ascites, (4) had severe heart, pulmonary, renal, or brain failure, (5) had inflammatory diseases, (6) had other malignancies, or (7) had malabsorption.

In the analysis of differences in host factors, tumor factors, and myokines, subjects were classified into the muscle atrophy group (n=35) or the non-muscle atrophy group (n=4) according to The Japan Society of Hepatology guidelines for sarcopenia in liver disease [2].

Diagnosis of LC and HCC, and tumor node metastasis staging of HCC

LC was diagnosed based on AST to platelet ratio index > 1.0 [26]. Hepatocellular carcinoma was diagnosed by a tumor biopsy or a combination of tests for serum tumor makers such as α-fetoprotein and des-γ-carboxy prothrombin and imaging procedures such as ultrasonography, computed tomography, magnetic resonance imaging, and/or angiography. The clinical stage of HCC was evaluated by tumor node metastasis staging based on the Liver Cancer Study Group of Japan criteria [27].

Evaluation of skeletal muscle mass

Skeletal muscle mass was measured using diagnostic CT scans at L3 by measuring the abdominal skeletal muscles, as previously described [2]. The CT scans used for analysis were carried out as part of the HCC assessment. Skeletal muscle mass was evaluated by the skeletal muscle index (SMI), which was calculated by normalizing L3 skeletal muscle areas by the square of the height (m^2). Muscles in the L3 region encompass the psoas, erector spinae, quadratus lumborum, transversus abdominis, external and internal obliques, and rectus abdominis. The analysis was performed by using the diagnosis software ImageJ (U. S. National Institutes of Health, Bethesda, MA) [28].

Evaluation of visceral fat area (VFA)

VFA was measured as previously described [29]. Briefly, the VFA was measured by diagnostic CT scanning at the umbilical line. The CT scanning was performed for HCC evaluation. The VFA was measured by using the diagnostic software ImageJ [28] and was normalized by the square of the height (m^2).

Laboratory determinations

The following biochemical examination levels were measured using standard clinical methods: red blood cell count, hemoglobin, white blood cell count , platelet count, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, γ- glutamyltransferase (GGT), total protein, albumin, total bilirubin, total cholesterol, blood urea nitrogen, creatinine, estimated glomerular filtration rate (eGFR), creatine kinase, hemoglobin A1c, ammonia, alpha-fetoprotein (AFP), and des-γ-carboxy prothrombin. AST to platelet ratio index (APRI) was calculated by the following equation: serum AST level (U/L)/upper limit of normal AST (33 U/L) × 100/platelet count ($\times 10^6$/mL). Patients with APRI values above 1.0 were diagnosed with LC as previously described [30].

Measurement of myokine

Serum levels of myostatin, irisin, decorin, and cathepsin B were measured by using a Myostatin Quantikine ELISA Kit (DGDF80 R&D; Systems, Inc., Minneapolis, MN, USA), an Irisin ELISA Kit (EK-067-16; Phoenix Pharmaceuticals, Inc., Burlingame, CA, USA), a Human Decorin ELISA Kit (ab99998; Abcam plc., Cambridge, UK), and a Human Cathepsin B ELISA Kit (ab119584; Abcam plc., Cambridge, UK) according to the manufacturers' instructions.

Statistical analysis

Data are expressed as the median (interquartile range), range, or number. Correlation analysis between SMI and host factors, tumor factors, and myokine levels was performed by a simple linear regression analysis. Differences in host factors, tumor factors, and myokine levels between the muscle atrophy and non-atrophy groups were analyzed with the Wilcoxson rank sum test. The least square analysis was applied to identify any independent factor variables associated with SMI. Profiles associated with muscle non-atrophy were evaluated by a decision-tree analysis. The level of statistical significance was set at $P<0.05$.

Results

Patient characteristics

The patients' characteristics are summarized in Table 1. The median age was 75 years old, and the ratio of women to men was 19:20. The median performance status was 0. Muscle atrophy was seen in 89.7% (35/39) of enrolled patients. The median serum levels of ALT, albumin, prothrombin activity, total bilirubin, and Child-Pugh score, and eGFR values were 33.0 IU/L, 3.37 g/dL, 73.0%, 1.08 mg/dL, 6 points, and 81.8 mL/min/1.73m^2, respectively (Table 1). The median serum levels of cathepsin B, irisin, myostatin, and decorin were 91.1 ng/mL, 29.6 ng/mL, 1,769.25 pg/mL, and 5,025.2 pg/mL, respectively (Table 1).

Correlation analysis between SMI and host factors, tumor factors, and myokine levels

SMI was not significantly correlated with age, serum levels of ALT, albumin, total bilirubin, Child-Pugh score, or eGFR (Table 2). There was a significant positive correlation between SMI and body mass index (BMI), GGT, and blood ammonia levels. Meanwhile, a significant negative correlation was seen between SMI and serum AFP level (Table 2). Serum cathepsin B, myostatin, and irisin levels were not correlated with SMI; however, a significant positive correlation was seen between SMI and serum decorin level (Table 2).

Difference in host factors, tumor factors, and myokine levels between the muscle atrophy and non-atrophy groups

There was no significant difference between the atrophy and non- atrophy groups in BMI, serum GGT, AFP, or blood ammonia levels (Figure 1A, B, C, and D). No significant difference between the atrophy and non- atrophy groups was also seen in serum myostatin or cathepsin B levels (Figure 1E and F). However, serum irisin and decorin levels were significantly higher in the muscle non-atrophy group than in the atrophy group (Figure 1G and H).

The least square analysis for SMI

We evaluated the factors associated with SMI by the least square method and found that BMI, but not age or Child-Pugh score, was an independent factor associated with SMI (Table 3). Serum cathepsin B, myostatin, and irisin levels were not associated with SMI. However, serum decorin level was an independent factor associated with SMI (Table 3).

Decision-tree analysis for muscle non-atrophy

We also performed a decision tree analysis to identify the profiles associated with the non-muscle atrophy group. Non-muscle atrophy was seen in 10.3% of enrolled patients. Serum decorin levels were identified as the first divergence variable. Non-atrophy was seen in 2.8% of patients with serum decorin levels of <10,226.8 pg/mL. Meanwhile, muscle non-atrophy was seen in 75.0% of patients with serum decorin levels of ≥10,226.8 pg/mL (Figure 2).

Table 1. Patient characteristics

	Reference Value	Median (IQR)	Range (min–max)
N	N/A	39	N/A
Age (years old)	N/A	75 (69-78)	41-84
Sex (female/male)	N/A	19/20	N/A
Body mass index (kg/m^2)	18.5–24.9	22.1 (20.5-24.6)	14-33.6
HCC stage (I/II/III/IV)	N/A	1/17/16/5	N/A
HCV/HBV/Others	N/A	28/3/8	N/A
Skeletal muscle index (cm^2/m^2)	N/A	32.5 (27.3-39.1)	13.8-53.8
Visceral fat area on admission (cm^2/m^2)	N/A	42.7 (34.5-66.7)	5.5-130.6
BCAA supplementation (Yes/No)	N/A	24/15	N/A
Biochemical examinations			
Hemoglobin (g/dL)	13.7-16.8	11.9 (10.7-13)	7.3-16.4
White blood cell count (/μL)	3,300-8,600	3,400 (2,900-4,500)	1,200-6,600
Platelet count (x 10^3/mm^3)	3.3–8.6	8.4 (6.3-14.9)	3.2-23.0
AST (IU/L)	13–30	46 (36-57)	23.0-124.0
ALT (IU/L)	10–30	33 (24-49)	14.0-89.0
ALP (IU/L)	115–359	343 (254-465)	145-1265
GGT (IU/L)	13–64	36 (25-111)	14-218
Total protein (g/dL)	6.6–8.1	7.15 (6.84-7.59)	5.97-9.37
Albumin (g/dL)	4.1–5.1	3.37 (3.11-3.65)	2.31-4.38
Prothrombin activity (%)	80–120	73 (61-88)	36,0-118.0
Total bilirubin (mg/dL)	0.40–1.20	1.08 (0.77-1.3)	0.49-4.28
Total cholesterol (mg/dL)	142–219	146 (119-171.75)	93-235
APRI	N/A	1.65 (1.02–2.81)	0.52–10.72
Child-Pugh score	N/A	6 (5-8)	5-10
AFP (ng/mL)	≤7.0	18.4 (7.1-186.1)	1.3-7174
des-γ-carboxy prothrombin (mAU/mL)	<40	84 (28.75-1206.5)	9-37295
BUN (mg/dL)	8.0-20.0	16 (13.2-19.7)	10.2-31.2
Creatinine (mg/dL)	0.65-1.07	0.69 (0.51-0.85)	0.35-1.92
eGFR (mL/min/1.73 m^2)	>90.0	81.8 (59.7-93.6)	27.4-129.5
Creatine kinase (U/L)	59-248	129.5 (80.75-170.75)	45-386
HbA1c (%)	4.3-5.8	5.7 (5.7-6.5)	4.8-7.9
Ammonia (μg/dl)	12–66	61.5 (41.75-85.25)	18-192
Myokine			
Myostatin (pg/mL)	1,264-8,588	1769.25 (1,045.27-2,448.33)	583.1,04-22733.3
Irisin (ng/mL)	N/A	29.6 (28.3-32.7)	25-76.9
Cathepsin B (ng/mL)	N/A	91.1 (84.1-108.3)	53.9-314.7
Decorin (pg/mL)	N/A	5025.2 (4,304.1-7,906.9)	2,823.9-1,9291.8

Note: Data are expressed as median (interquartile range [IQR]), range, or number. Abbreviations: N/A, not applicable; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HBV, hepatitis B virus; BCAA, branched-chain amino acids; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transpeptidase; APRI, AST to platelet ratio index; AFP, alpha-fetoprotein; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1

Table 2. Correlation analysis between SMI and host factors, tumor factors, and myokine levels

	r	P
Age	-0.00228	0.989
BMI	0.377446	0.0178
ALT	0.124176	0.4513
ALP	0.23206	0.1552
GGT	0.41667	0.0083
Albumin	-0.1942	0.2362
Total bilirubin	0.062688	0.7046
Total cholesterol	-0.05848	0.7273
Ammonia	0.331436	0.0483
Prothrombin activity (%)	0.022398	0.8923
Child-Pugh score	0.112844	0.494
Creatinine	-0.01967	0.9054
eGFR	0.07408	0.654
AFP	-0.42655	0.0068
Des-γ-carboxy prothrombin	0.085112	0.6165
Myostatin	0.146524	0.3734
Decorin	0.374709	0.0188
Irisin	-0.0942	0.5684
Cathepsin B	0.271391	0.0947

Abbreviations: BMI, body mass index; ALT, alanine aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transpeptidase; eGFR, estimated glomerular filtration rate; AFP, alpha-fetoprotein

Table 3. Independent factors for SMI

Variable	Estimate	95% CI	P
Age	7.694225	-20.93564-36.324089	0.5875
BMI	1.1135081	0.261119-1.9658973	0.0121
Cathepsin B	0.0151027	-0.068423-0.0986281	0.7148
Myostatin	-0.000696	-0.001615-0.0002227	0.1325
Irisin	-0.081161	-0.398381-0.2360594	0.6055
Decorin	0.0010772	8.4233e-6-0.002146	0.0483
Child-Pugh score	-0.045779	-1.889424-1.7978657	0.9599

Abbreviations: SMI, skeletal muscle index; BMI, body mass index

Figure 1. Differences in host factors, tumor factors, and myokine levels between the muscle atrophy and non-atrophy groups of patients with chronic liver disease. (A) BMI, (B) GGT, (C) ammonia, (D) AFP, (E) myostatin, (F) cathepsin B, (G) irisin, and (H) decorin. Differences in each factor between the muscle atrophy and non-atrophy groups were analyzed with the Wilcoxson rank sum test. The level of statistical significance was set at P<0.05.

Abbreviations: BMI, body mass index; GGT, γ-glutamyltransferase; AFP, alpha-fetoprotein; N.S., not significant

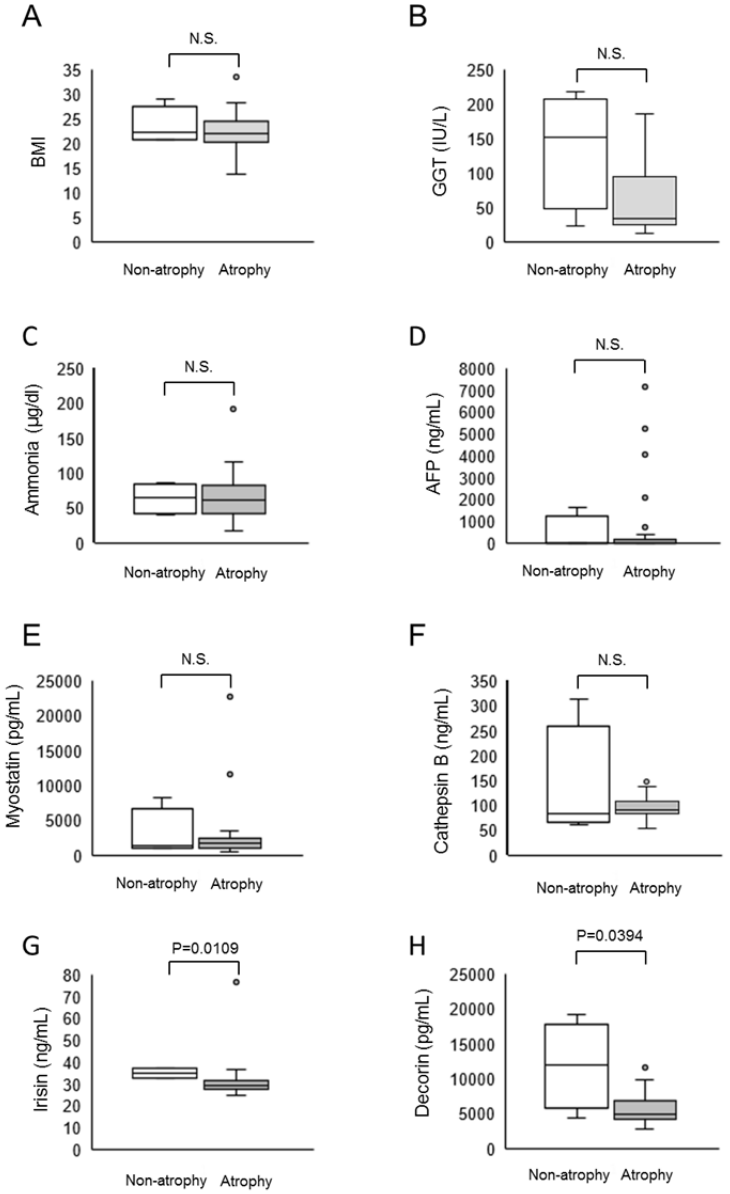
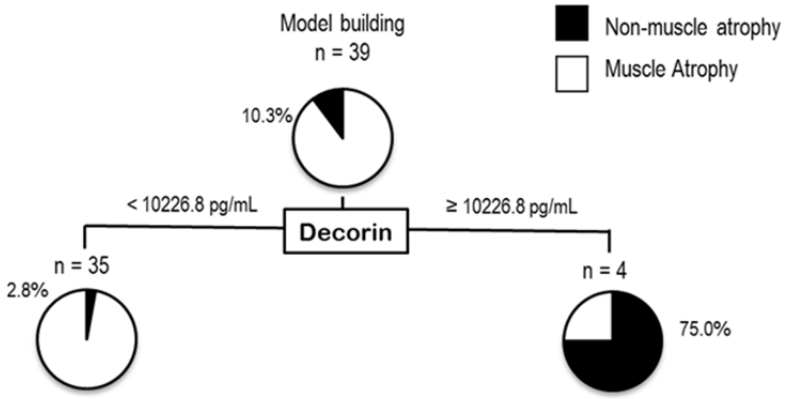


Figure 2. Decision-tree algorithm for muscle non-atrophy in patients with chronic liver disease. The subjects were classified according to the indicated cut-off value for the serum decorin level. The pie graphs indicate the proportion of patients with muscle atrophy (white) and patients with non-muscle atrophy (black) in each group.



Discussion

In this study, we found that serum decorin levels were significantly associated with skeletal muscle mass in patients with LC. In addition, both serum decorin levels and BMI were independent negative risk factors for skeletal muscle atrophy in patients with LC. Moreover, serum decorin level was identified as the first divergence variable for non-muscle atrophy in a decision-tree analysis. Thus, decorin may be an important myokine regulating sarcopenia in patients with LC.

Skeletal muscle atrophy is an independent prognostic factor for patients with LC [6, 7]. We investigated an association between SMI and host and tumor factors. In a correlation analysis and the least square analysis, a significant association was seen between SMI and BMI. Previous studies reported that skeletal muscle mass is significantly correlated with BMI in healthy children, adolescents, and older individuals [31], suggesting that our results are good agreement with previous reports. Age is also well-known factor for sarcopenia [32]; however, age was not a factor associated with SMI in this study. This may be related to age distribution of the enrolled patients. The interquartile range of age is 69 to 78 years old and the age distribution of 75% of enrolled subjects was within 10 years. The most of patients were distributed over a set range and age might not be a factor associated with SMI in this study.

Skeletal muscle mass is also known to be associated with liver dysfunction and malnutrition in patients with LC [33]. On the other hand, in this study, no significant association was seen between SMI and various liver function tests, including serum albumin and bilirubin levels. It remains unclear why most liver function tests were not significantly associated with SMI in this study. However, Montano-Loza et al. previously demonstrated that skeletal muscle mass does not correlate with the degree of liver dysfunction [6]. These data, along with our results, suggest that, in patients with LC, the etiology of sarcopenia is more complex than simple aging, malnutrition, and liver function. Various factors, including physical activity, may be associated with skeletal muscle atrophy in patients with LC.

In this study, we first evaluated the correlation between SMI and myokine levels. We found that the serum decorin level was significantly correlated with SMI in patients with LC. In addition, serum decorin level was an independent negative risk factor for skeletal muscle atrophy. Moreover, the serum decorin level was identified as the first divergence variable in the decision-tree analysis for skeletal muscle mass. The reason for the correlation with SMI and serum decorin levels remains unclear. Kanzleiter T et al. showed that decorin is secreted from the myotubes in response to exercise and plays a role in the exercise-related restructuring processes of skeletal muscles in healthy young men [24]. Furthermore, previous studies demonstrated possible mechanisms for decorin-induced muscle hypertrophy. Decorin directly binds to myostatin, a potent inhibitor of muscle growth, and enhances the proliferation and differentiation of C2C12 myoblasts through suppressing myostatin activity, leading to muscle hypertrophy [34]. Alternatively, decorin is also known to induce myogenic satellite cell proliferation and differentiation by regulating cellular responsiveness to TGF-beta1, resulting in muscle hypertrophy [35]. There are various factors associated with skeletal muscle mass in patients with LC. However, our data, along with these previous reports, suggest that decorin may be an important regulator for skeletal muscle mass in patients with LC.

Serum myostatin levels were not significantly correlated with SMI in patients with LC in this study. Although serum myostatin levels in patients with end-stage liver disease were reported to be 4 times higher than those in healthy volunteers [36], Merli et al. examined gene expression for myostatin in the biopsied rectus abdominis muscles of patients with liver disease and reported that there was no difference in myostatin levels between the patients and controls [37]. Thus, alteration in serum myostatin levels is controversial in patients with LC. The reason for the lack of association between serum myostatin levels and SMI remains unclear. However, one possibility is that hyperammonemia is known to induce myostatin expression [38]. Ammonia transcriptionally upregulates myostatin via a p65 nuclear factor-kappa B mediated mechanism. Hyperammonemia also activates autophagy and is an activator of reactive oxygen species in patients with LC [38]. In this study, the median blood ammonia level was within normal limits. In addition, no significant difference was seen in blood ammonia levels between the muscle atrophy and non-muscle atrophy groups. Taken together, muscle atrophy may not be associated with myostatin levels in this study because of the low prevalence of hyperammonemia.

In this study, serum irisin levels were not associated with skeletal muscle mass in patients with LC. Irisin is reported to induce muscle hypertrophy through upregulation of satellite cell activation and downregulation of protein degradation [39]. Kim et al. reported that serum irisin levels were positively correlated with muscle mass in overweight adults [40]. It remains unclear why serum irisin was not associated with skeletal muscle mass in this study. Circulating irisin levels are the result of the sum of the irisin produced by different depots of adipose tissue and skeletal muscle [41]. In addition, Choi et al. showed that serum irisin levels were not different between patients with sarcopenia and control subjects [42]. Moreover, the low accuracy of commercial ELISA kits for irisin has been reported [43]. Thus, the expression site of irisin and methodological issues could be one reason for the lack

of association between serum irisin levels and skeletal muscle mass.

Recently, cathepsin B was identified as a myokine [16]. In this study, the serum cathepsin B level was associated with the Child-Pugh score; however, there was no association between serum cathepsin B level and muscle mass. Yamamoto et al. reported that serum cathepsin B levels increased 1.9-fold in the fibrotic liver compared to the normal liver [18]. Cathepsin B induces lysosomal proteolysis; however, there is no study reporting an association between serum cathepsin B levels and skeletal muscle mass. Moon et al. reported that circulating cathepsin B levels are associated with memory function [16]. Taken together, cathepsin B may not be involved in muscle hypertrophy in patients with LC.

There are limitations of this study. Muscle mass of patients with LC was not compared to that in healthy subjects in this study. Healthy control group is necessary to confirm muscle atrophy in this cohort. However, diagnosis of muscle atrophy was based on the Japan Society of Hepatology guidelines for sarcopenia in patients with liver disease [2]. The guideline for diagnosis of sarcopenia is specialized for patients with liver disease and has high diagnostic ability. The assessment criteria are now used for sarcopenia studies and the patients who meet the criteria are thought to be in sarcopenia [5, 44].

Another limitation is that we did not investigated the impact of myokine on prognosis in patients with LC. In this study, we first found that serum decorin level was associated with muscle mass in cirrhotic patients with HCC. Since muscle mass is reported to be associated with prognosis in patients with LC and HCC [6, 7, 45], further study will be focused on the impact of serum decorin level on prognosis in cirrhotic patients with HCC.

In conclusion, we showed that the serum decorin level was significantly associated with skeletal muscle mass and was an independent negative risk factor for skeletal muscle atrophy in patients with LC. In addition, a decision-tree analysis revealed that the serum decorin level was the most distinguishable factor for skeletal non-muscle atrophy in patients with LC. Thus, decorin may be an important myokine regulating sarcopenia in patients with LC.

Abbreviations

LC, liver cirrhosis; HCC, hepatocellular carcinoma; TGF, transforming growth factor; CT, computed tomography; L3, the third lumbar; SMI, skeletal muscle index; VFA, visceral fat area; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ- glutamyltransferase; eGFR, estimated glomerular filtration rate; AFP, alpha fetoprotein; APRI, AST to platelet ratio index; IQR, interquartile range; BMI, body mass index.

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