

## Long-Term Changes in Body Composition After Direct-Acting Antiviral Therapy in Patients With Hepatitis C

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### ABSTRACT

**AIM:** The long-term changes in body composition (BC) after hepatitis C virus (HCV) eradication are uncertain. This study aimed to evaluate the long-term BC changes after direct-acting antiviral (DAA) therapy.

**MATERIAL AND METHODS:** A total of 119 patients with HCV infection who were treated with DAAs were the subjects of this study. The changes in several BC parameters measured by bioelectrical impedance analysis (BIA) before and at 2 years after the initiation of DAA therapy were investigated. Furthermore, the pretreatment

factors that correlated with changes in several parameters were established by stepwise multiple linear regression analysis.

**RESULTS:** Significant decreases of total body water (TBW) ( $p = 0.001$ ), intracellular water (ICW) ( $p = 0.002$ ), extracellular water (ECW) ( $p < 0.001$ ), and skeletal muscle mass (SMM) ( $p = 0.002$ ) as well as significant increases of body fat mass (BFM) ( $p < 0.001$ ) and percent body fat ( $p < 0.001$ ) were observed. Stepwise multiple regression analysis identified the following as independent predictors for changes in various parameters: sex, body weight (BW), and albumin-bilirubin (ALBI) score for a change in BW; serum albumin level for changes in TBW and ECW; ALBI score, sex, BW, and ratio of branched-chain amino acids to tyrosine (BTR) for a change in BFM; and BTR and BMI  $\geq 25$  kg/m<sup>2</sup> for changes in ICW and SMM.

**CONCLUSIONS:** This study clarified the characteristics of long-term changes in BC after DAA therapy. These changes were influenced by sex, BW, BMI, and some factors related to the hepatic functional reserve.

**Key words:** Body composition; Direct-acting antivirals; Hepatitis C

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### INTRODUCTION

Decreasing skeletal muscle mass (SMM) is a problem for patients with liver disease<sup>[1]</sup>; in particular, the condition characterized by a high loss of muscle mass and low strength is called sarcopenia<sup>[2-4]</sup>. Generally, primary sarcopenia is associated with aging; while secondary sarcopenia is caused by several diseases, malnutrition, or poor activity<sup>[1-4]</sup>. Liver cirrhosis is one of the causal diseases related to sarcopenia, occurring in 20-70% of cirrhotic patients; and sarcopenia is a poor prognostic factor for liver cirrhosis<sup>[5]</sup>.

Hepatitis C virus (HCV) infection is one of the important risk

factors for the development of liver cirrhosis<sup>[6]</sup>. Although interferon (IFN) therapy used to be the only method applied to eradicate HCV, several orally available direct-acting antivirals (DAAs) that can achieve a sustained virologic response (SVR) with few adverse events have been developed<sup>[7]</sup>. Due to the development of these DAAs, DAA therapies have been able to eradicate HCV in almost all patients with hepatitis C<sup>[7-9]</sup>. DAA therapy also can easily treat patients with cirrhosis as well as elderly patients, who are difficult to treat with IFN therapy<sup>[7-9]</sup>.

It is known that viral eradication can improve the inflammation and fibrosis of the liver<sup>[10]</sup>. A change in the SMM after a SVR with DAA therapy has been reported<sup>[11-13]</sup>. However, to the best of our knowledge, there is no published research referring to long-term changes in other body composition (BC) parameters. The aim of this study was to reveal the long-term changes of several BC parameters after achieving a SVR with DAA therapy as well as the pretreatment factors associated with these changes.

## PATIENTS AND METHODS

### Study design and patients

This was a single-center retrospective study that was conducted with the approval of the Ethics Board of our hospital (approval no. 855 for sofosbuvir/ribavirin therapy, approval no. 907 for sofosbuvir/ledipasvir therapy, approval no. 976 for ombitasvir/paritaprevir/ritonavir therapy, and approval no. 1367 for glecaprevir/pibrentasvir therapy) and performed in accordance with the Declaration of Helsinki. Informed consent was signed by all patients before treatment. The inclusion criteria for this study were as follows: patients with chronic hepatitis or compensated cirrhosis with HCV infection, patients who achieved a SVR by DAA therapy, and patients whose BC parameters were examined by bioelectrical impedance analysis (BIA) at pretreatment and at 2 years after the initiation of treatment. In this study, a SVR was defined as the disappearance of serum HCV RNA with the real-time polymerase chain reaction method at 24 weeks after completion of the DAA therapy. The exclusion criteria were as follows: patients who were hepatitis B surface antigen positive, patients with an alcohol consumption  $\geq 20$  g/day, patients with nonalcoholic steatohepatitis, patients with autoimmune hepatitis, patients with primary biliary cholangitis, patients undergoing hemodialysis for chronic kidney disease, patients with hepatocellular carcinoma at treatment, and patients who developed hepatocellular carcinoma or any other malignant disease during the 2 years of this study.

The study participants ( $n = 119$ ) were treated with DAA therapy from August 2015 to September 2019 at our hospital. The regimens of the DAA therapies were sofosbuvir/ledipasvir in 69 patients with genotype 1b HCV infection, ombitasvir/paritaprevir/ritonavir in 9 patients with genotype 1b HCV infection, and sofosbuvir/ribavirin in 27 patients with genotype 2a ( $n = 20$ ) or 2b ( $n = 7$ ) HCV infection, and glecaprevir/pibrentasvir in 14 patients with genotypes 1b ( $n = 10$ ), 2a ( $n = 3$ ), and 2b ( $n = 1$ ). The BC data were measured by BIA using an InBody 770 instrument (InBody Japan, Tokyo, Japan). The parameters analyzed included body weight (BW), body mass index (BMI), total body water (TBW), intracellular water (ICW), extracellular water (ECW), body fat mass (BFM), percent body fat (PBF), SMM, and fat-free mass (FFM). This study compared several BC parameters between at pretreatment and at 2 years after the initiation of treatment. Real-time tissue elastography (RTE) (HI VISION Preirus or Ascendus, Hitachi, Ltd., Tokyo, Japan) was performed before DAA therapy to assess liver fibrosis<sup>[14,15]</sup>.

Subpopulation analyses for the changes of BC between at pretreatment and at 2 years after the initiation of DAA therapy were also performed with respect to cirrhosis, obesity, aging, and the serum albumin level. Patients were determined to have cirrhosis if their computed tomography (CT) or ultrasonography images were consistent with cirrhosis and the patients had esophageal varices on endoscopy or if the imaging showed cirrhosis plus any two of the following: platelet count  $< 13 \times 10^4/\mu\text{L}$ , Fibrosis-4 index  $> 3.25$ <sup>[16]</sup>, or liver fibrosis index by RTE  $> 3.0$ <sup>[14,15]</sup>. Patients who did not meet these definitions were considered as noncirrhotic patients. Cut-off values to establish two groups were set as follows: BMI, 25 kg/m<sup>2</sup>, according to the definition of obesity in Japan<sup>[17]</sup>; age, 65 years old, those  $\geq 65$  years old were defined as older subjects; and serum albumin, 4.0 g/dL, according to a standard value.

### Statistical analysis

Continuous data are shown as the median and range or mean  $\pm$  standard deviation. The paired t-test was used for comparison of each parameter at pretreatment and at 2 years after the initiation of treatment. Independent continuous data were compared using the unpaired t-test. Spearman's correlation was used to evaluate the correlation between two continuous variables. Stepwise multiple linear regression analysis was performed to evaluate the relationships between baseline characteristics and the BC changes. A *P*-value less than 0.05 was considered to be statistically significant. All statistical analyses were performed using the software IBM SPSS Statistics version 27.0 for Windows.

## RESULTS

### Change in BC parameters

The baseline data of the patients at pretreatment are listed in Table 1. The comparisons of the BC parameters of all of the patients between at pretreatment and at 2 years after the initiation of treatment are listed in Table 2. TBW, ICW, ECW, and SMM were significantly decreased; and BFM and PBF were significantly increased.

The results of the subpopulation analysis are listed in Table 3. In the noncirrhotic group ( $n = 82$ ), TBW, ICW, ECW, and SMM were significantly decreased. Meanwhile, in the cirrhotic group ( $n = 37$ ), BW, BMI, BFM, and PBF were significantly increased; and TBW and ECW were significantly decreased. Although the ICW and SMM tended to decrease in the cirrhotic patients, there was no significant difference; this finding is probably due to the fact that the cirrhotic group had a smaller sample size than the noncirrhotic group. In addition, there was no significant difference in the change of SMM over 2 years between the noncirrhotic group and the cirrhotic group ( $-0.19 \pm 0.67$  kg vs.  $-0.34 \pm 1.1$  kg,  $p = 0.349$ ). The rates of the SMM decrease were 0.41%/year for the noncirrhotic patients and 0.86%/year for the cirrhotic patients ( $p = 0.205$ ). For the patients with a BMI  $< 25$  kg/m<sup>2</sup> ( $n = 92$ ), significant increases were found for BW, BMI, BFM, and PBF; and a significant decrease was found for ECW. In contrast, for the patients with a BMI  $\geq 25$  kg/m<sup>2</sup> ( $n = 27$ ), significant decreases were found for TBW, ICW, ECW, and SMM. For the patients aged  $< 65$  years old ( $n = 48$ ), significant increases were found for PBF. Meanwhile, for patients aged  $\geq 65$  years old ( $n = 71$ ), significant decreases were found for TBW, ICW, ECW, and SMM; and significant increases were found for BFM and PBF. For patients with a serum albumin level  $< 4.0$  g/dL ( $n = 39$ ), significant decreases were found for TBW, ICW, ECW, and SMM; and significant increases were found for BFM and PBF. For patients with a serum albumin level  $\geq 4.0$  g/dL ( $n = 80$ ), significant increases

were found for PBF.

The results of stepwise multiple linear regression analysis showed that the male sex, BW, and ALBI score at pretreatment were independently associated with a change in BW. In addition, the serum albumin level was an independent factor associated with changes in TBW and ECW. Moreover, the ratio of branched-chain amino acids (BCAAs) to tyrosine (BTR) and a BMI  $\geq 25$  kg/m<sup>2</sup> were independently associated with changes in ICW and SMM. Finally, the factors associated with a change in BFM were the ALBI score, male sex, BW, and BTR (Table 4).

### Correlation of BC parameters

There were strong correlations between a change in BW and changes in BFM ( $r = 0.892$ ,  $p < 0.001$ ) and PBF ( $r = 0.789$ ,  $p < 0.001$ ). Furthermore, a change in BW correlated with a change in SMM ( $r = 0.524$ ,  $p < 0.001$ ). When partial correlation analysis was performed with BW change as a control variable, a strong negative correlation was found between a change in BFM and a change in SMM ( $r = -0.978$ ,  $p < 0.001$ ). Additionally, there were strong correlations between a change in SMM and changes in TBW ( $r = 0.979$ ,  $p < 0.001$ ), ICW ( $r = 0.996$ ,  $p < 0.001$ ), and FFM ( $r = 0.982$ ,  $p < 0.001$ ).

## DISCUSSION

This was a study to examine the long-term changes in BC after DAA therapy. To the best of our knowledge, three studies have examined the change in BC, especially the change in SMM, after a SVR with DAA therapy<sup>[11-13]</sup>. Sugimoto *et al.* have examined the BC change using BIA in 30 patients with a SVR after DAA therapy and have reported that there was no significant difference in BW, visceral fat area, or skeletal muscle index (SMI) during a 48-week observation period; but there was a significant increase in the SMI in patients with a low muscle mass<sup>[11]</sup>. In addition, Yoh *et al.* have compared the changes in the SMI in 69 patients between at pretreatment and at 24 weeks after the completion of DAA therapy using BIA. This previous study reported that the BTR is an independent predictor of an increased SMI at 24 weeks after the completion of DAA therapy<sup>[12]</sup>. Moreover, Endo *et al.* have examined the SMI by CT before and after DAA therapy; they concluded that viral eradication with DAA suppresses SMM loss<sup>[13]</sup>. Our study examined not only the SMM but also other BC parameters such as TBW, ICW, ECW, BFM, and PBF. Our findings demonstrated significant decreases in TBW, ICW, ECW, and SMM as well as significant increases in BFM and PBF at 2 years after the initiation of treatment, compared to pretreatment values.

According to multiple regression analysis, the ALBI score was a significant factor associated with a change in BW. As suggested by previous studies, eradication of HCV improves the quality of life of patients<sup>[18]</sup>. It is possible that improvement in the quality of life may have contributed to weight gain. In general, patients with impaired liver function are more likely to experience symptoms such as anorexia and malaise, so it is speculated that patients with impaired liver functional reserve might be more likely to benefit from symptom improvement due to eradication of HCV, resulting in a BW increase.

According to multiple regression analysis, the serum albumin level was associated with changes in TBW and ECW. It is well known that the albumin level increases after DAA therapy<sup>[11]</sup>. Since albumin regulates interstitial fluid by colloid osmotic pressure, it was hypothesized that an increase in the serum albumin level is associated with an increase in the colloid osmotic pressure, leading to decreases

**Table 1** Baseline data before DAA therapy ( $n = 119$ ).

Variable	Number or Median (Range)
Age (years)	68 (29-88)
Sex (Male/Female)	53/66
Body weight (kg)	56.5 (34.4-96.2)
Body mass index (kg/m <sup>2</sup> )	22.5 (14.9-34.6)
Total bilirubin (mg/dL)	0.7 (0.1-2.0)
Albumin (g/dL)	4.2 (2.5-5.0)
AST (U/L)	37.6 (16.8-172.6)
ALT (U/L)	31.9 (8.4-312.2)
$\gamma$ GTP (U/L)	29.2 (10.3-296.0)
ALBI score	-2.86 (-3.53 to -1.45)
Platelet count (104/ $\mu$ L)	14.7 (2.6-32.8)
BTR	5.3 (2.1-8.5)
Cirrhosis/Noncirrhosis	37/82

DAA: direct-acting antiviral; AST: aspartate aminotransferase; ALT: alanine aminotransferase;  $\gamma$ GTP: gamma-glutamyltransferase; ALBI: albumin-bilirubin; BTR: branched-chain amino acid-to-tyrosine ratio.

**Table 2** Comparison of body composition parameters between at pretreatment and at 2 years after the initiation of treatment ( $n = 119$ )

Variable	Pretreatment	2 years after initiation of treatment	P-value
Body weight (kg)	57.40 $\pm$ 10.64	57.89 $\pm$ 10.81	0.084
Body mass index (kg/m <sup>2</sup> )	22.74 $\pm$ 3.46	22.92 $\pm$ 3.46	0.104
Total body water (L)	30.79 $\pm$ 5.96	30.47 $\pm$ 6.01	0.001
Intracellular water (L)	18.77 $\pm$ 3.75	18.59 $\pm$ 3.81	0.002
Extracellular water (L)	12.03 $\pm$ 2.22	11.88 $\pm$ 2.22	<0.001
Body fat mass (kg)	15.62 $\pm$ 6.43	16.54 $\pm$ 6.21	<0.001
Percent body fat (%)	26.84 $\pm$ 8.57	28.19 $\pm$ 8.37	<0.001
Skeletal muscle mass (kg)	22.48 $\pm$ 4.90	22.24 $\pm$ 4.98	0.002

in TBW and ECW.

Multiple regression analysis showed that the ALBI score, male sex, BW, and BTR were independently associated with a change in BFM. The reason that the ALBI score was an independent factor for a change in BFM is speculated to be the same as that for a change in BW, as described above. The BTR is calculated as the ratio of BCAAs to tyrosine, and it is correlated with the serum albumin level and the Child-Pugh score<sup>[19,20]</sup>. In cirrhotic patients, a decrease of the serum BCAA level, which is caused by ammonia detoxification<sup>[21]</sup> and energy generation<sup>[22]</sup>, results in a reduction of the Fisher's ratio or the BTR. The reason that the BTR was an independent factor for a change in BFM in this study is uncertain. Nevertheless, a possible explanation is that the BTR contributes to an increased SMI after DAA therapy, as reported previously<sup>[12]</sup>, and our study also identified a relationship between the BTR and a change in SMM. A poor ability of muscle synthesis in patients with a low BTR tends to lead to a decrease in SMM or difficulties with increasing the SMM. Furthermore, when partial correlation analysis was performed with BW as a control variable, there was a strong negative correlation between a change in SMM and a change in BFM in our study. Therefore, in patients with a low BTR, a decrease in the SMM or suppression of muscle synthesis might result in an increase in the BFM.

An increase in the BFM is generally thought to be detrimental as it causes arterial sclerosis triggered by hypernutrition. However, according to the results of this study (a high ALBI score was an independent factor for an increased BFM), an increased BFM would be caused by improvement of the nutritional status in patients with

**Table 3** Comparison of body composition parameters between at pretreatment and at 2 years after the initiation of treatment- Subpopulation analyses-

Parameters of Body Composition	Noncirrhotic patients (n = 82)			Cirrhotic patients (n = 37)		
	Pretreatment	2 years after initiation of treatment	P-value	Pretreatment	2 years after initiation of treatment	P-value
Body weight (kg)	56.97 ± 11.17	57.00 ± 11.10	0.922	58.35 ± 9.45	59.87 ± 9.98	0.016
Body mass index (kg/m <sup>2</sup> )	22.42 ± 3.50	22.42 ± 3.43	0.992	23.46 ± 3.32	24.04 ± 3.29	0.015
Total body water (L)	30.73 ± 6.18	30.50 ± 6.13	0.015	30.92 ± 5.51	30.41 ± 5.80	0.028
Intracellular water (L)	18.78 ± 3.91	18.64 ± 3.92	0.013	18.73 ± 3.42	18.47 ± 3.62	0.067
Extracellular water (L)	11.95 ± 2.28	11.86 ± 2.24	0.033	12.19 ± 2.11	11.94 ± 2.20	0.009
Body fat mass (kg)	15.26 ± 6.57	15.58 ± 6.14	0.218	16.43 ± 6.12	18.66 ± 5.90	<0.001
Percent body fat (%)	26.36 ± 8.81	26.93 ± 8.37	0.098	27.88 ± 8.02	30.98 ± 7.75	<0.001
Skeletal muscle mass (kg)	22.50 ± 5.12	22.31 ± 5.11	0.015	22.43 ± 4.44	22.09 ± 4.73	0.065
	BMI <25 kg/m <sup>2</sup> (n = 92)			BMI ≥25 kg/m <sup>2</sup> (n = 27)		
Body weight (kg)	53.94 ± 8.19	54.72 ± 9.10	0.008	69.21 ± 9.61	68.70 ± 9.15	0.496
Body mass index (kg/m <sup>2</sup> )	21.31 ± 2.16	21.59 ± 2.44	0.012	27.63 ± 2.45	27.44 ± 2.43	0.532
Total body water (L)	29.98 ± 5.66	29.78 ± 5.78	0.066	33.55 ± 6.24	32.82 ± 6.30	<0.001
Intracellular water (L)	18.27 ± 3.56	18.16 ± 3.66	0.1	20.45 ± 3.97	20.03 ± 4.05	<0.001
Extracellular water (L)	11.71 ± 2.11	11.62 ± 2.13	0.047	13.10 ± 2.29	12.79 ± 2.29	0.001
Body fat mass (kg)	13.23 ± 4.61	14.29 ± 4.92	<0.001	23.77 ± 4.94	24.21 ± 3.34	0.556
Percent body fat (%)	24.58 ± 7.79	26.02 ± 7.83	<0.001	34.51 ± 6.46	35.59 ± 5.45	0.165
Skeletal muscle mass (kg)	21.83 ± 4.65	21.69 ± 4.78	0.109	24.67 ± 5.18	24.12 ± 5.29	<0.001
	Age < 65 years old (n = 48)			Age ≥ 65 years old (n = 71)		
Body weight (kg)	61.31 ± 11.09	61.89 ± 11.01	0.288	54.76 ± 9.53	55.19 ± 9.86	0.161
Body mass index (kg/m <sup>2</sup> )	23.09 ± 3.53	23.28 ± 3.31	0.342	22.51 ± 3.43	22.68 ± 3.55	0.181
Total body water (L)	33.42 ± 5.92	33.26 ± 5.86	0.347	29.02 ± 5.33	28.59 ± 5.37	<0.001
Intracellular water (L)	20.52 ± 3.71	20.47 ± 3.74	0.619	17.58 ± 3.31	17.32 ± 3.33	<0.001
Extracellular water (L)	12.90 ± 2.22	12.79 ± 2.15	0.133	11.44 ± 2.04	11.27 ± 2.06	0.001
Body fat mass (kg)	15.95 ± 6.77	16.73 ± 5.98	0.077	15.41 ± 6.23	16.41 ± 6.40	0.001
Percent body fat (%)	25.54 ± 8.21	26.64 ± 7.30	0.028	27.71 ± 8.75	29.23 ± 8.91	<0.001
Skeletal muscle mass (kg)	24.77 ± 4.85	24.70 ± 4.88	0.619	20.93 ± 4.32	20.58 ± 4.34	<0.001
	Albumin <4.0 g/dL (n = 39)			Albumin ≥4.0 g/dL (n = 80)		
Body weight (kg)	59.66 ± 9.91	60.43 ± 10.10	0.107	56.30 ± 10.88	56.66 ± 10.99	0.319
Body mass index (kg/m <sup>2</sup> )	24.14 ± 3.47	24.45 ± 3.47	0.107	22.06 ± 3.27	22.18 ± 3.21	0.399
Total body water (L)	31.26 ± 5.90	30.60 ± 5.94	<0.001	30.57 ± 6.01	30.41 ± 6.08	0.171
Intracellular water (L)	18.92 ± 3.71	18.56 ± 3.70	<0.001	18.69 ± 3.80	18.60 ± 3.89	0.224
Extracellular water (L)	12.34 ± 2.21	12.04 ± 2.26	<0.001	11.87 ± 2.23	11.80 ± 2.21	0.14
Body fat mass (kg)	17.29 ± 5.94	18.97 ± 5.89	0.001	14.81 ± 6.55	15.35 ± 6.05	0.056
Percent body fat (%)	28.81 ± 7.63	31.23 ± 7.76	<0.001	25.87 ± 8.88	26.71 ± 8.30	0.022
Skeletal muscle mass (kg)	22.67 ± 4.82	22.20 ± 4.83	<0.001	22.38 ± 4.96	22.27 ± 5.08	0.222

malnutrition and impaired liver function.

The rate of SMM decrease was 0.86%/year in cirrhotic patients in this study. In contrast, Hanai *et al* have reported that the rate of SMM decrease is 1.3%/year in cirrhotic patients with Child-Pugh class A chronic liver disease<sup>[23]</sup>. Comparison of this previous report to our result indicates that eradication of HCV with DAAs can suppress a reduction of SMM in cirrhotic patients. Multiple regression analysis showed that the BTR and a BMI ≥ 25 kg/m<sup>2</sup> were independently associated with a change in SMM. Our results that the BTR contributes to a SMM change were in agreement with those of a previous study<sup>[12]</sup>. BCAAs, especially leucine, are related to protein synthesis<sup>[24-26]</sup>. Therefore, it is possible that patients with a low BTR show a low increase or a decrease of SMM due to a low protein synthesis capacity. Furthermore, obesity is known to be a risk factor for a decrease in SMM<sup>[2,27]</sup>.

The BTR and a BMI ≥ 25 kg/m<sup>2</sup> were also independently associated with a change in ICW, and these factors were the same as those associated with a change in SMM. It is known that FFM and

ICW are well correlated<sup>[28]</sup>. Therefore, it is possible that the same factors were selected as a result of changes in SMM.

The limitation of this study is that the number of patients analyzed was small. Therefore, the results of this study may not be sufficient to be generalizable.

In conclusion, at 2 years after DAA treatment, the TBW, ICW, ECW, and SMM values were decreased; and the BFM and PBF values were increased. Sex, weight, and some factors related to the hepatic functional reserve were associated with these BC changes after DAA therapy.

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**Table 4** Stepwise multiple linear regression analysis for changes of body composition.

	$\beta$	SE	Standardized $\beta$	t	P-value
Change for body weight, R2 = 0.201					
(Constant)	10.1	2.603		3.881	<0.001
Male	2.658	0.59	0.427	4.508	<0.001
BW (kg)	-0.092	0.028	-0.314	-3.275	0.001
ALBI	1.977	0.662	0.258	2.988	0.003
Change for total body water, R2 = 0.077					
(Constant)	-3.012	0.878		-3.429	<0.001
Albumin (g/dl)	0.648	0.211	0.277	3.068	0.003
Change for intracellular water, R2 = 0.103					
(Constant)	-0.721	0.228		-3.17	0.002
BTR	0.116	0.042	0.249	2.779	0.006
BMI $\geq 25$ (kg/m <sup>2</sup> )	-0.291	0.133	-0.196	-2.193	0.03
Change for extracellular water, R2 = 0.092					
(Constant)	-1.414	0.376		-3.756	<0.001
Albumin (g/dl)	0.306	0.091	0.303	3.383	<0.001
Change for body fat mass, R2 = 0.313					
(Constant)	11.07	2.153		5.141	<0.001
ALBI	1.819	0.661	0.268	2.752	0.007
Male	2.62	0.498	0.474	5.257	<0.001
BW	-0.063	0.023	-0.245	-2.735	0.007
BTR	-0.496	0.202	-0.243	-2.461	0.015
Change for skeletal muscle mass, R2 = 0.106					
(Constant)	-0.943	0.297		-3.177	0.002
BTR	0.153	0.055	0.25	2.801	0.006
BMI $\geq 25$ (kg/m <sup>2</sup> )	-0.391	0.173	-0.202	-2.259	0.026

BW: body weight; ALBI: albumin-bilirubin score; BTR: branched-chain amino acid-to-tyrosine ratio; SE: standard error; BMI, body mass index.

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