ORIGINAL ARTICLE
https://doi.org/10.1590/1806-9282.20201016

Muscle mass and cellular membrane integrity assessment in patients with nonalcoholic fatty liver disease

Iasmin dos Santos Barreto[1], Raquel Oliveira dos Santos[1], Raquel Rocha[1]*, Claudineia de Souza[1], Naiade Almeida[1], Luiza Valois Vieira[1], Rafael Leiróz[2], Manoel Sarno[2], Carla Daltro[1], Helma Pinchemel Cotrim[2]

SUMMARY

OBJECTIVE: To evaluate the association between muscle mass depletion and compromising of the cell membrane integrity and clinical–anthropometric characteristics in patients with nonalcoholic fatty liver disease.

METHODS: This observational study evaluated waist circumference, body mass index, and waist-to-height ratio in patients with nonalcoholic fatty liver disease. Skeletal mass index corrected by weight and impairment of cell membrane integrity were assessed using bioelectrical impedance analysis.

RESULTS: In 56 patients, muscle mass depletion was observed in 62.5% and cell membrane impairment in 28.6%. The metabolic syndrome and elevated aspartate aminotransferase were the only clinical factors associated with mass depletion ($p<0.05$). The linear regression analysis showed association between skeletal mass index and waist-to-height ratio and waist circumference, after adjustments ($p<0.05$). The phase angle value was not different between those with and without mass depletion, and also it did not have correlation with skeletal mass index and clinical parameters ($p>0.05$).

CONCLUSIONS: The prevalence of mass depletion and cell membrane impairment was higher in patients with nonalcoholic fatty liver disease. The muscle mass depletion was associated with central obesity, aspartate aminotransferase elevated, and metabolic syndrome; however, the phase angle is not associated with clinical and anthropometric data.

KEYWORDS: Non-alcoholic fatty liver disease. Skeletal muscle. Bioelectrical impedance. Obesity. Central obesity.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is one of the most prevalent chronic liver diseases in the world, and evidence points that body composition is directly related to the pathogenesis of NAFLD[1]. Thus, visceral obesity is listed as the main factor promoting metabolic changes, since it leads to an imbalance between adipokine secretion, with an increase in inflammatory cytokines and, consequently, influencing insulin resistance (IR) and oxidative stress[2].

However, muscle mass (MM) has also gained prominence in several diseases, including NAFLD[3]. It seems that the connection between the liver, adipose tissue, and muscle occurs

[1]Universidade Federal da Bahia, Escola de Nutrição – Salvador (BA), Brazil.
[2]Universidade Federal da Bahia, Faculdade de Medicina da Bahia – Salvador (BA), Brazil.
*Corresponding author: raquelrocha2@yahoo.com.br

Conflicts of interest: the authors declare there are no conflicts of interest. Funding: This work was supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico - CNPq [MCTI/CNPQ/Universal 14/2014] and institutional support from the Universidade Federal da Bahia.
Received on February 13, 2021. Accepted on July 20, 2021.

through the expression of insulin receptors in these tissues, in view of the anabolic role of insulin, in the presence of IR in myocytes, protein catabolism increases, resulting in MM depletion and, consequently, in sarcopenia[4].

The integrity of the cell membrane can be assessed by bioelectrical impedance analysis (BIA) and identified with the phase angle (PA) value. PA has been studied in several clinical conditions and found that the higher the PA values, the better the integrity of the membrane and thus the better cellular function. Studies show that low PA values are correlated with prognosis of chronic obstructive pulmonary disease, peritoneal dialysis, hemodialysis, and liver cirrhosis, being used as an indicator of nutritional status and prognosis of mortality[5-8].

The aim of this study was to assess whether there is an association between MM reserve, impaired cell membrane integrity, and clinical–anthropometric characteristics in patients with NAFLD.

METHODS

Study design and sample

A cross-sectional, observational study was performed with patients followed up at a nonalcoholic steatohepatitis outpatient clinic. The sample was obtained for convenience between March 2016 and 2017. Inclusion criteria: patients of either sex above 18 years and below 60 years of age. Patients with special needs or diseases that made it difficult to perform anthropometric measurements and ethanol intake ≥140 g/week; patients with thyroid disease, hepatitis A, B, and C, autoimmune disease, Wilson's disease, or hemochromatosis and pregnant and lactating women were not included.

Clinical evaluation

Patients were screened by a team of nutritionists and previously trained students, using a semistructured questionnaire to identify demographic, clinical, and nutritional data.

Abdominal ultrasonography was used to measure intrahepatic fat, being performed by a single evaluator.

Anthropometric evaluation

Weight and height measurements were obtained with a digital scale (Leader, 200 kg capacity and 100 g precision) and coupled stadiometer[9]. The body mass index (BMI) was calculated, and overweight with BMI ≥ 25.0 kg/m² [10].

Central obesity was identified when waist circumference (WC) ≥ 80 cm for women and ≥ 94 cm for men[11] and waist-to-height ratio (WhtR) >0.5[12].

Muscle mass

MM was measured using BIA (Biodynamics 450®)[13]. The skeletal mass index (SMI) adjusted for weight was calculated[14,15].

Muscle mass depletion was defined when SMI <37% for men and <28% for women[16].

Cell membrane impairment

The cell membrane impairment was evaluated by the PA identified in the BIA, and the cutoff point ≤ the 25th percentile obtained in the statistical analysis of this sample was adopted.

Laboratory evaluation

The registered tests were alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT), alkaline phosphatase (AF), blood glucose, insulin, and triglycerides. IR was calculated by homeostasis model assessment for insulin resistance (HOMA-IR)[17]. Metabolic syndrome was classified according to the International Diabetes Federation[11].

Statistical analysis

The statistical software SPSS version 21.0 was used for data analysis. The patients were grouped according to the MM evaluated, and to compare the means between groups by the Student's *t*-test and the proportions by Pearson's chi-square or Fisher's exact tests. Pearson's correlation was used to analyze the correlation between parametric variables and MM. Associations between MM and continuous variables were assessed by simple and multiple linear regression analyzes. For the multiple linear regression model, variables with p value <0.20, obtained in the bivariate analysis, were considered. The hierarchical selection method was used to construct the regression models and calculate the adjusted determination coefficient (R^2), with a 95% confidence interval (95% CI). The level of significance was $p<0.05$.

RESULTS

General characteristics

All eligible patients were included in the study. Fifty-six patients with NAFLD, with a mean age of 47.7 ± 8.6 years and predominantly females (67.9%), were participated. Of note, 91.1% of the patients were presented with overweight and central obesity. A higher frequency of physically inactive individuals (56.3%), hypertensive individuals (33.9%), and grades II and III steatosis (67.9%) was observed. In a subgroup of 21 patients, 38.1% had IR (Table 1).

Table 1. Clinical and demographic characteristics in a group of patients with nonalcoholic fatty liver disease treated at a referral clinic.

	Total	Muscle Mass		p**
		Depletion	Adequate	
Sex, n (%)				
Male	18 (32.1)	11 (31.4)	7 (33.3)	0.883
Female	38 (67.9)	24 (68.6)	14 (66.7)	
Age (years) $\bar{x}$ (SD)	47.7 (8.6)	47.3 (9.3)	48.6 (7.4)	0.573[a]
Race				
Whites	3 (5.4)	1 (2.9)	2 (9.5)	0.246[b]
Not whites	53 (94.6)	34 (97.1)	19 (90.5)	
Weight (kg) $\bar{x}$ (SD)	78.9 (14.7)	83.5(15.2)	71.3 (10.2)	0.002[a]
BMI (kg/m²) $\bar{x}$ (SD)	30.6 (4.8)	32.4 (4.9)	27.7 (3.1)	<0.001[a]
WHtR $\bar{x}$ (SD)	0.62 (0.07)	0.64 (0.08)	0.58 (0.05)	0.001[a]
WC (cm) $\bar{x}$ (SD)	99.1 (11.1)	103.2(10.8)	92.4 (8.1)	<0.001[a]
Phase angle $\bar{x}$ (SD)	7.3 (2.3)	7.7 (2.7)	6.8 (1.2)	0.102
Physical activity**, n (%)				
Yes	18 (56.3)	12 (57.1)	6 (54.5)	0.888
Not	14 (43.8)	9 (42.9)	5 (45.5)	
Comorbities, n (%)				
IIDM	16 (28.6)	11(68.8)	5 (31.3)	0.541
Dyslipidemia	16 (28.6)	12 (75)	4 (25)	0.360[b]
SHA	19 (33.9)	11 (64.9)	13 (35.1)	0.610
Grade steatosis, n (%)				
Grade I	18 (32.1)	11 (31.4)	7 (33.3)	0.833
Grades II–III	38 (67.9)	24 (68.6)	14 (66.7)	
ALT, n (%)				
Normal	47 (88.7)	29 (85.3)	18 (94.7)	0.402[b]
Increased	6 (11.3)	5 (14.7)	1 (5.3)	
AST, n (%)				
Normal	41 (78.8)	22 (66.7)	19 (100)	0.004[b]
Increased	11 (21.2)	11 (33.3)	0 (0.0)	
GGT, n (%)				
Normal	38 (73.0)	22 (66.7)	16 (84.2)	0.209[b]
Increased	14 (27.0)	11 (33.3)	3 (15.8)	
FA, n (%)				
Normal	38 (82.6)	23 (76.7)	15 (93.8)	0.230[b]
Increased	8 (17.4)	7 (23.3)	1 (6.3)	
TG, n (%)				
Normal	31 (59.6)	19 (57.6)	12 (63.2)	0.693
Increased	21 (37.5)	14 (42.4)	7 (36.8)	
GLICEMIA, n (%)				
Normal	36 (69.2)	21(63.6)	15 (78.9)	0.353[b]
Increased	16 (30.8)	12 (36.4)	4 (21.1)	

Continue...

Table 1. Continuation.

	Total	Muscle Mass		p**
		Depletion	Adequate	
HOMA-IR*, n (%)				
Normal	13 (61.9)	8 (57.1)	5 (71.4)	0.656[b]
Increased	8 (38.1)	6 (42.9)	2 (28.6)	
Metabolic syndrome***				
Yes	24 (46.2)	19(57.6)	5 (26.3)	0.029
No	28 (53.8)	14(42.4)	14 (73.7)	

*21 patients; ** Pearson's χ^2 test; ***52 patients; [a]Student's *t*- test; [b]Fisher's exact test. BMI: body mass index; WHtR: waist-to-height ratio; WC: waist circumference; IIDM: type 2 diabetes mellitus; SAH: systemic arterial hypertension; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase; FA: alkaline phosphatase; TG: triglycerides; HOMA-IR: insulin resistance index.

Muscle mass and cell membrane impairment

MM depletion was found in 62.5% of the population patients with NAFLD and cell membrane impairment in 28.6%.

The values of BMI, WHtR, and WC were higher in the group with MM depletion when compared to the group without depletion (p<0.05). MS was present in 57.6% of patients with MM depletion (p=0.03). However, the same finding was not obtained with the HOMA-IR (Table 1). Only AST was related to MM depletion (p=0.004) (Table 1).

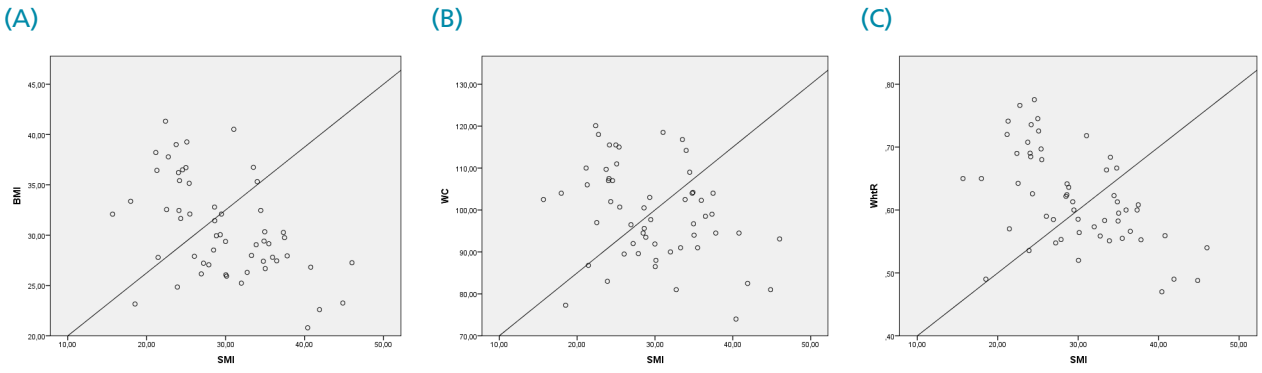
PA showed no difference in relation to MM depletion and none association or correlation with anthropometric, clinical, and biochemical data (p>0.05) (Table 1).

We observed a moderate negative linear correlation between the WHtR and the SMI, in addition to the weak negative correlation with the BMI and WC and SMI (p<0.05) (Figure 1).

Regression analysis

In the analysis of simple linear regression between SMI as independent variables, it was observed that there was a significant relation between WHtR, WC, and BMI with SMI (β= -48.74, 95%CI -69.67 – -27.81; β= -0.194, 95%CI -0.353 – -0.035; β= -0.695, 95%CI -1.029 – -0.360, respectively).

Multiple linear regression demonstrated that anthropometric parameters were associated with the dependent variable in all models. It is evident that the WHtR is a much stronger predictor in the depletion of MM. Note that the association of central obesity indicators (WHtR and WC) and total body mass improves the prediction of change in SMI, explaining 43.0% of this (Table 2).



*Pearson's correlation. BMI: body mass index; WC: waist circumference; WhtR: waist-to-height ratio; SMI: skeletal muscle mass index.

Figure 1. Correlation between: (A) BMI and SMI (r= -0.493; p<0.001); (B) WC and SMI (r= -0.312; p=0.019); (C) WhtR and SMI (r= -0.536; p≤0.001) in patients with nonalcoholic fatty liver disease.

Table 2. Linear regression selected from anthropometric variables associated with skeletal muscle mass index in a group of patients with nonalcoholic fatty liver disease treated at a referral clinic.

Skeletal muscle mass index (%)												
	Model 1				Model 2				Final model			
Variable	β adjusted	P	CI	R^2	β adjusted	P	CI	R^2	β adjusted	P	CI	R^2
WHtR	-0.54	<0.001	-69.67 – -27.81	0.29	-1.08	<0.001	-138.8 – -58.50	0.38	-0.79	0.004	-118.9 – -24.02	0.43
BMI	–	–	–		–	–	–		-0.59	0.048	-1.650 – -0.006	
WC	–	–	–		0.63	0.006	0.115– 0.657		0.90	0.001	0.241 – 0.860	

Model 1: adjusted by the BMI and WC variables; Model 2: adjusted by the BMI variable; Model 3: adjusted by BMI, WC, and WHtR. WHtR: waist-to-height ratio; BMI: body mass index; WC: waist circumference; CI: confidence interval.

DISCUSSION

More than half of the patients with NAFLD evaluated in this study had MM depletion and approximately one-third cell membrane impairment. The cell membrane impairment does not seem to be associated with the clinical and anthropometric characteristics of these patients; however, skeletal MM was associated with metabolic syndrome, elevated AST, and central obesity indicators (WHtR and WC).

The MM depletion had also a high prevalence in a study with Caucasian patients with NAFLD, using the same cutoff points adopted in the present study[18] and studies with Asian patients with NAFLD[19,20]. Koo et al.[21] observed that the occurrence of nonalcoholic steatohepatitis (NASH) may be associated with MM depletion.

In patients with NAFLD, a reduction in the MM can synergistically increase visceral fat.[22] The association of central obesity with the reduction in MM was the main finding in this study, corroborating with data from the literature[20,23].

IR has been identified as the link between MS and NAFLD[24]. Furthermore, it is also suggested as a key factor in the genesis of sarcopenia, since when there is IR in myocytes, less activation of mTOR (target of rapamycin in mammals) occurs, leading to an imbalance between the synthesis and increase of protein catabolism and, consequently, depleting to MM[4]. Although the association between IR and MS is reported[25,26], the same result was found only for MS in the present study.

Some studies observed that MM depletion affects the severity of liver disease, with worsening fibrosis[19,25]. It is noted that there is an inverse relationship between MM and ALT and AST levels in patients with NAFLD, independently of obesity[26,27]. In this study, AST was the only liver enzyme to be associated with MM and such findings were similar to the studies by Moon et al.[23]) and Petta et al.[18]

Studies that assess the correlation of PA with muscle 8 and other anthropometric and biochemical parameters are scarce. Petta et al.[18] calculated the PA in Italian patients with NAFLD and found the mean PA similar to that of the present study (6.9±1.0). This cohort adopted the cutoff point of PA<5.4 to define sarcopenia, obtaining a prevalence of 5.7%.

The main positive points of this study include the use of practical, low-cost, and easy-to-use methods in clinical practice to assess MM and central adiposity. So far, most of the studies published have been carried out on the Eastern population who have different eating habits, lifestyle, and body composition than the Western population. However, the small sample size, the absence of liver biopsy, and loss of data in variables, such as IR, are the factors, which robust statistical analyses, however, tried to minimize the limitation of this study.

In conclusion, the high prevalence of MM depletion found in the patients with NAFLD is a cause for concern, considering the association with high AST and what has already been described in the literature regarding the progression of the disease to steatohepatitis and fibrosis in the presence of MM depletion. One-third of patients with NAFLD also had impaired cell membrane integrity and it is known that this integrity is important for maintaining adequate cell function. However, further studies are needed to better assess this condition in patients with NAFLD.

The findings of this study reinforce the importance of evaluating the indicators of central adiposity and MM in patients with NAFLD, considering that the indicators of central obesity remained independently associated with MM depletion.

ACKNOWLEDGMENT

The authors thank all the patients involved in this study for their cooperation and the nutrition students, namely, Geisa de Jesus Santos and Jilmara Fiuza de Oliveira

ETHICAL STATEMENT

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the research ethics committee of the School of Nutrition of the Federal University of Bahia (Opinion nº 774.353 / 2014). Informed consent was obtained from all participants. The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/)

AUTHORS' CONTRIBUTIONS

ISB: Conceptualization, Data curation, Formal analysis, Project administration, Writing – original draft, Writing – review & editing. **RR:** Conceptualization, Resources, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **ROS:** Project administration, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **CAS:** Project administration, Data curation, Writing – original draft, Writing – review & editing. **NAS:** Project administration, Resources, Data curation, Writing – original draft, Writing – review & editing. **LVV:** Project administration, Writing – original draft, Writing – review & editing. **GJS:** Project administration, Writing – original draft, Writing – review & editing. **JFO:** Project administration, Writing – original draft, Writing – review & editing. **HPC:** Resources, Writing – original draft, Writing – review & editing. **CD:** Resources, Formal analysis, Writing – original draft, Writing – review & editing. **RLPDS:** Data curation, Writing – original draft, Writing – review & editing. **MACS:** Data curation, Writing – original draft, Writing – review & editing.

REFERENCES

1. Ko YH, Wong TC, Hsu YY, Kuo KL, Yang SH. The Correlation Between Body Fat, Visceral Fat, and Nonalcoholic Fatty Liver Disease. Metab Syndr Relat Disord. 2017;15(6):304-11. https://doi.org/10.1089/met.2017.0001
2. Pang Q, Zhang JY, Song SD, Qu K, Xu XS, Liu SS, et al. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. https://doi.org/10.3748/wjg.v21.i5.1650
3. Seko Y, Mizuno N, Okishio S, Takahashi A, Kataoka S, Okuda K, et al. Clinical and pathological features of sarcopenia-related indices in patients with nonalcoholic fatty liver disease. Hepatol Res. 2019;49(6):627-36. https://doi.org/10.1111/hepr.13321
4. Wijarnpreecha K, Panjawatanan P, Thongprayoon C, Jaruvongvanich V, Ungprasert P. Sarcopenia and risk of nonalcoholic fatty liver disease: a meta-analysis. Saudi J Gastroenterol. 2018;24(1):12-7. https://doi.org/10.4103/sjg.SJG_237_17
5. Garlini LM, Alves FD, Ceretta LB, Perry IS, Souza GC, Clausell NO. Phase angle and mortality: a systematic review. Eur J Clin Nutr. 2019;73(4):495-508. https://doi.org/10.1038/s41430-018-0159-1
6. Han BG, Lee JY, Kim JS, Yang JW. Clinical Significance of Phase Angle in Non-Dialysis CKD Stage 5 and Peritoneal Dialysis Patients. Nutrients. 2018;10(9):1331. https://doi.org/10.3390/nu10091331
7. Maddocks M, Kon SSC, Jones SE, Canavan JL, Nolan CM, Higginson IJ, et al. Bioelectrical impedance phase angle relates to function, disease severity and prognosis in stable chronic obstructive pulmonary disease. Clin Nutr. 2015;34(6):1245-50. https://doi.org/10.1016/j.clnu.2014.12.020
8. Peres WA, Lento DF, Baluz K, Ramalho A. Phase angle as a nutritional evaluation tool in all stages of chronic liver disease. Nutr Hosp. 2012;27(6):2072-8. https://doi.org/10.3305/nh.2012.27.6.6015
9. Lohman TG, Roche AF, Martorell R. Anthropometric standardization reference manual. Medicine & Science in Sports & Exercise. 1988;24. 177 p.
10. World Health Organization. Consultation on obesity: preventing and managing the global epidemic [Internet]. Geneva: World Heal Organ. 1998[cited on mar. 25, 2016];894:i-xii,1-253. Available from: https://apps.who.int/iris/handle/10665/42330
11. Alberti G, Zimmet P, Shaw J, Grundy SM. he IDF consensus worldwide de nation of the metabolic syndrome [Internet]. Brussels: IDF Communications. 2006[cited on mar. 25, 2016];50:514211. Available from: https://www.idf.org/e-library/consensus-statements/60-idfconsensus-worldwide-definitionof-the-metabolic-syndrome.html
12. Pitanga FJ, Lessa I. Razão cintura-estatura como discriminador do risco coronariano de adultos. Rev Assoc Med Bras (1992). 2006;52(3):157-61. https://doi.org/10.1590/s0104-42302006000300016
13. Kyle UG, Bosaeus I, Lorenzo AD, Deurenberg P, Elia M, Go M, et al. Bioelectrical impedance analysis-part II: utilization in clinical practice. Clin Nutr. 2004;23(6):1430-53. https://doi.org/10.1016/j.clnu.2004.09.012
14. Janssen I, Heymsfield SB, Wang ZM, Ross R. Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. J Appl Physiol (1985). 2000;89(1):81-8. https://doi.org/10.1152/jappl.2000.89.1.81
15. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc. 2002;50(5):889-96. https://doi.org/10.1046/j.1532-5415.2002.50216.x
16. Peng TC, Wu LW, Chen WL, Liaw FY, Chang YW, Kao TW. Nonalcoholic fatty liver disease and sarcopenia in a Western population (NHANES III): The importance of

sarcopenia definition. Clin Nutr. 2019;38(1):422-8. https://doi.org/10.1016/j.clnu.2017.11.021

17. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28(7):412-9. https://doi.org/10.1007/BF00280883
18. Petta S, Ciminnisi S, Marco V, Cabibi D, Camm C. Sarcopenia is associated with severe liver fibrosis in patients with non-alcoholic fatty liver disease. Aliment Pharmacol Ther. 2017;45(4):510-8. https://doi.org/10.1111/apt.13889
19. Kang MK, Park JG, Lee HJ, Kim MC. Association of low skeletal muscle mass with advanced liver fibrosis in patients with non-alcoholic fatty liver disease. J Gastroenterol Hepatol. 2019;34(9):1633-40. https://doi.org/10.1111/jgh.14607
20. Mizuno N, Seko Y, Kataoka S, Okuda K, Furuta M, Takemura M, et al. Increase in the skeletal muscle mass to body fat mass ratio predicts the decline in transaminase in patients with nonalcoholic fatty liver disease. J Gastroenterol. 2019;54(2):160-70. https://doi.org/10.1007/s00535-018-1485-8
21. Koo BK, Kim D, Joo SK, Kim JH, Chang MS, Kim BG, et al. Sarcopenia is an independent risk factor for non-alcoholic steatohepatitis and significant fibrosis. J Hepatol. 2017;66(1):123-31. https://doi.org/10.1016/j.jhep.2016.08.019
22. Choi KM. Sarcopenia and sarcopenic obesity. Korean J Intern Med. 2016;31(6):1054-60. https://doi.org/10.3904/kjim.2016.193
23. Moon JS, Yoon JS, Won KC, Lee HW. The role of skeletal muscle in development of nonalcoholic fatty liver disease. Diabetes Metab J. 2013;37(4):278-85. https://doi.org/10.4093/dmj.2013.37.4.278
24. Aller R, Fernández-Rodríguez C, lo Iacono O, Bañares R, Abad J, Carrión JA, et al. Consensus document. Management of non-alcoholic fatty liver disease (NAFLD). Clinical practice guideline. Gastroenterol Hepatol. 2018;41(5):328-49. https://doi.org/10.1016/j.gastrohep.2017.12.003
25. Shida T, Akiyama K, Oh S, Sawai A, Isobe T, Okamoto Y, et al. Skeletal muscle mass to visceral fat area ratio is an important determinant affecting hepatic conditions of non-alcoholic fatty liver disease. J Gastroenterol. 2018;53(4):535-47. https://doi.org/10.1007/s00535-017-1377-3
26. Lee YH, Jung KS, Kim SU, Yoon HJ, Yun YJ, Lee BW, et al. Sarcopaenia is associated with NAFLD independently of obesity and insulin resistance: Nationwide surveys (KNHANES 2008-2011). J Hepatol. 2015;63(2):486-93. https://doi.org/10.1016/j.jhep.2015.02.051
27. Hong HC, Hwang SY, Choi HY, Yoo HJ, Seo JA, Kim SG, et al. Relationship between sarcopenia and nonalcoholic fatty liver disease: the Korean Sarcopenic Obesity Study. Hepatology. 2014;59(5):1772-8. https://doi.org/10.1002/hep.26716