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COMMENTARY

Muscle mass depletion in chronic liver diseases: An accelerated model of aging or a distinct entity?

**KEYWORDS**

Frailty;
 Sarcopenia;
 Muscle;
 Cirrhosis;
 Myosteatosis;
 MAFLD

Abstract Sarcopenia was initially defined as loss of muscle mass, strength and function related to aging. This phenomenon is a multifactorial process. The evaluation of the geriatric population in which sarcopenia has extensively been studied opens the field for other chronic diseases. Cirrhosis is one of them and the term “sarcopenia” is now also used in this pathological situation. It must be emphasized that the pathophysiology of sarcopenia in cirrhosis is likely different from the pathogenesis in geriatric patients. Furthermore, cirrhosis has heterogeneous causes. Therefore, we need a better understanding of the changes in muscle physiology specifically in chronic liver diseases as well as easy, accurate, reproducible and validated tools, taking into consideration etiology specific aspects to identify sarcopenia in every cirrhotic patient.

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To the Editor,

We read with interest the comment of Razaq et al. [1]. Sarcopenia was indeed defined initially as loss of muscle mass, strength and function related to aging, owing to progressive loss of motoneurons and associated with a reduced number of muscle fibers and size as well as changes in muscle composition [2]. Looking only at muscle mass and composition does not give a full picture of the situation and functional tests are needed. Aging associated sarcopenia is a multifactorial process that occurs due to changes in physical activity, hormone levels, nutrition, mitochondrial dysfunction and systemic inflammation [2,3]. The evaluation of the geriatric population in which sarcopenia has extensively been studied opens the field for other chronic diseases [3]. Cirrhosis is one of those chronic diseases and the term “sarcopenia” is now also used in this pathological situation, as reported not only by consensus of international societies

on the study of the liver [4] but also on clinical nutrition [5]. In this context, the team of Lai et al. validated tools to assess frailty in cirrhosis [6]. It must be emphasized that the pathophysiology of sarcopenia in cirrhosis is certainly not the same as the pathogenesis in geriatric patient [3]. Furthermore, cirrhosis has heterogeneous causes. We propose a three-step approach to tackle these challenges.

First, we need to better understand the changes in muscle physiology specifically in cirrhosis [3]. Some features are certainly common to end-stage liver disease but others are etiology specific [7,8]. A better knowledge of the etiology-specific changes should allow us to propose targeted interventions.

Second, evaluating sarcopenia and frailty needs a qualitative and functional evaluation with specific standardized validated tools. There is currently no gold standard for the diagnosis of sarcopenia. Gait speed and grip strength are interesting [1] and validated tools but must be integrated in a global score. Current studies have focused on methods evaluating only one feature of sarcopenia e.g. muscle mass, muscle function in a specific muscle group. Prospective large-scale multicentric studies are needed to evaluate

Abbreviation: MAFLD, metabolic dysfunction-associated fatty liver disease.

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the best tools/scores in the field of cirrhosis. These studies should allow us to better stratify the risks and to identify the patients in need of interventions. Standardized tools are also important to compare the results of future studies.

Third, it is currently well recognized that sarcopenia is associated with higher morbi-mortality in cirrhosis. Accurate, easy and reproducible tools, taking into consideration etiology specific aspects and/or some cirrhosis specific features such as encephalopathy are needed to identify sarcopenia in every cirrhotic patient in routine clinical practice. The evaluation should be proposed even before the occurrence of cirrhosis. The authors suggest that ultrasound could be performed to measure anterior muscle mass in cirrhotic patients [1]. Obviously, a low-cost, non-irradiating and easily accessible technique would be very practical to perform in routine practice. Nevertheless, cut-off values need to be proposed and validated specifically for patients with chronic liver disease (such as cut-offs proposed for the rectus femoris in patients with chronic kidney disease [9]) to help discriminate patients at greater risk in whom intervention should be proposed. Moreover, the validity of the technique for measurement of intramuscular fat with echo intensity has been criticized [10]. However, this parameter is important as data indicate that myosteatosis is a key indicator of the severity of cirrhosis [11] but also of severe metabolic dysfunction-associated fatty liver disease (MAFLD) before the development of cirrhosis [12,13]. This additional evaluation could allow early intervention. Nevertheless, it is still not clear whether specific treatments/interventions could prevent muscle mass depletion or myosteatosis [14].

Conflict of interest

The authors declare that there is no conflict of interest.

Author's contribution

NL and GD (drafting of the manuscript), PS (critical revision of the manuscript).

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References

- [1] Razaq S, Kara M, Özçakar L. Measure grip strength, gait speed and quadriceps muscle in cirrhosis. Comment to "Frailty, sarcopenia and mortality in cirrhosis: what is the best assessment, how to interpret the data correctly and what interventions are possible?". *Clin Res Hepatol Gastroenterol* 2021. In preparation.
- [2] Larsson L, Degens H, Li M, Salvati L, Lee II Y, Thompson W, et al. Sarcopenia: aging-related loss of muscle mass and function. *Physiol Rev* 2019;99:427–511, <http://dx.doi.org/10.1152/physrev.00061.2017>.
- [3] Sinclair M. Controversies in diagnosing sarcopenia in cirrhosis—moving from research to clinical practice. *Nutrients* 2019;11, <http://dx.doi.org/10.3390/nu11102454>.

- [4] Merli M, Berzigotti A, Zelber-Sagi S, Dasarathy S, Montagnese S, Genton L, et al. EASL clinical practice guidelines on nutrition in chronic liver disease. *J Hepatol* 2019;70:172–93, <http://dx.doi.org/10.1016/j.jhep.2018.06.024>.
- [5] Bischoff SC, Bernal W, Dasarathy S, Merli M, Plank LD, Schütz T, et al. ESPEN practical guideline: clinical nutrition in liver disease. *Clin Nutr* 2020;39:3533–62, <http://dx.doi.org/10.1016/j.clnu.2020.09.001>.
- [6] Lai JC, Dodge JL, Kappus MR, Dunn MA, Volk ML, Duarte-Rojo A, et al. Changes in frailty are associated with waitlist mortality in patients with cirrhosis. *J Hepatol* 2020;73:575–81, <http://dx.doi.org/10.1016/j.jhep.2020.03.029>.
- [7] Bhanji RA, Narayanan P, Moynagh MR, Takahashi N, Angirekula M, Kennedy CC, et al. Differing impact of sarcopenia and frailty in nonalcoholic steatohepatitis and alcoholic liver disease. *Liver Transpl* 2019;25:14–24, <http://dx.doi.org/10.1002/lt.25346>.
- [8] Clarembau F, Bale G, Lanthier N. Cirrhosis and insulin resistance: current knowledge, pathophysiological mechanisms, complications and potential treatments. *Clin Sci* 2020;134:2117–35, <http://dx.doi.org/10.1042/CS20200022>.
- [9] Wilkinson TJ, Gore EF, Vadasz N, Nixon DGD, Watson EL, Smith AC. Utility of ultrasound as a valid and accurate diagnostic tool for sarcopenia. *J Ultrasound Med* 2021;40:457–67, <http://dx.doi.org/10.1002/jum.15421>.
- [10] Watanabe Y, Ikenaga M, Yoshimura E, Yamada Y, Kimura M. Association between echo intensity and attenuation of skeletal muscle in young and older adults: a comparison between ultrasonography and computed tomography. *Clin Interv Aging* 2018;13:1871–8, <http://dx.doi.org/10.2147/CIA.S173372>.
- [11] Montano-Loza AJ, Angulo P, Meza-Junco J, Prado CMM, Sawyer MB, Beaumont C, et al. Sarcopenic obesity and myosteatosis are associated with higher mortality in patients with cirrhosis. *J Cachexia Sarcopenia Muscle* 2016;7:126–35, <http://dx.doi.org/10.1002/jcsm.12039>.
- [12] Lanthier N, Rodriguez J, Nachit M, Hiel S, Trefois P, Neyrinck AM, et al. Microbiota analysis and transient elastography reveal new extra-hepatic components of liver steatosis and fibrosis in obese patients. *Sci Rep* 2021;11, <http://dx.doi.org/10.1038/s41598-020-79718-9>.
- [13] Nachit M, Kwanten WJ, Thissen J-P, Op De Beeck B, Van Gaal L, Vonghia L, et al. Muscle fat content is strongly associated with NASH: a longitudinal study in patients with morbid obesity. *J Hepatol* 2021, <http://dx.doi.org/10.1016/j.jhep.2021.02.037>. In press.
- [14] Lanthier N, Stärkel P, Dahlqvist G. Frailty, sarcopenia and mortality in cirrhosis: what is the best assessment, how to interpret the data correctly and what interventions are possible? *Clin Res Hepatol Gastroenterol* 2021;45(2):101661, <http://dx.doi.org/10.1016/j.clinre.2021.101661>.

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