Editorial

Liver cirrhosis and sarcopenia: a dreadful combination

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Patients with liver cirrhosis, irrespective of etiology, have increased risk of liver-related and all-cause mortality (1). Also, the severity of cirrhosis determines health outcomes. For instance, patients with compensated cirrhosis have a nearly five-fold increased risk of death, while those with decompensated cirrhosis have approximately a 10-fold increased risk compared with the general population (1). Furthermore, the median survival time of patients with compensated cirrhosis is 12 years, while it is only 1.8 years in those with decompensated cirrhosis (2). Moreover, the presence of intercurrent conditions, such as sarcopenia (loss of skeletal muscle mass and function) may also compromise the prognosis of patients with cirrhosis (3).

In line with that, Tantai *et al.* have reported in a recent meta-analysis (22 studies evaluating 6,965 patients with cirrhosis) that sarcopenia is significantly associated with increased mortality risk (4). They found that the 1-, 3-, and 5-year cumulative probabilities of survival in patients with sarcopenia were 76.6%, 64.3%, and 45.3%, respectively. By comparison, the cumulative probabilities of survival were 93.4%, 82.0% and 74.2%, respectively, in cirrhotic patients without sarcopenia. Upon performing sensitivity analysis and excluding patients with hepatocellular carcinoma, the results were similar. Overall, patients with coexisting cirrhosis and sarcopenia had an ~2.6 times higher risk of death than those without sarcopenia (4).

Several previous meta-analyses had also demonstrated an association between the presence of sarcopenia and a lower survival rate in patients with cirrhosis (5,6). An evident limitation of these meta-analyses is that the majority of included studies were retrospective cohorts. Similarly, in the meta-analysis conducted by Tantai *et al.*, most studies (18 out of 22) were retrospective cohorts (4). However, in this meta-analysis, a more comprehensive study search was performed, as they added 16 new studies not previously included in prior meta-analyses, and excluded overlapping cohorts/small studies (4).

Several diagnostic modalities are available for sarcopenia,

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such as computed tomography (CT), magnetic resonance imaging (MRI), dual-energy X-ray absorptiometry (DEXA) or bioelectrical impedance analysis (BIA) (7). This fact, along with the lack of consensus for the use of a particular diagnostic modality or specific cut-off points for the diagnosis of sarcopenia, results in a higher degree of heterogeneity among studies. At this point, it is important to highlight that the majority of studies included in the meta-analysis from Tantai *et al.* diagnosed sarcopenia based on CT or MRI-based modalities, avoiding some level of heterogeneity.

The prevalence of sarcopenia in patients with cirrhosis ranges from 30% to 70%, depending on the tools utilized for the diagnosis of sarcopenia, etiology and severity of the cirrhosis (8). For instance, in the meta-analysis by Tantai *et al.*, patients with Child-Pugh class C cirrhosis had a higher prevalence of sarcopenia (46.7%) than those with Child-Pugh class B (37.9%) or class A (28.3%) cirrhosis. The prevalence was also found to be higher in alcohol-related cirrhosis (49.6%) compared to those with other liver disease etiologies (33.4%), and was higher in males (41.9%) than in females (28.7%) (4). Therefore, these findings confirm that sarcopenia is a highly prevalent condition among patients with liver cirrhosis and is a key factor in the prognosis of the disease.

Since sarcopenia worsens the prognosis of patients with cirrhosis, it would be advisable to screen all patients with cirrhosis for sarcopenia. Indeed, the European Association for the Study of the Liver (EASL), the American Association for the Study of Liver Diseases (AASLD), and the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend screening for sarcopenia with emphasis on early detection (9,10). However, as previously discussed, there is considerable heterogeneity among the preferred imaging modality and cut-offs used for diagnosis of sarcopenia in patients with cirrhosis.

The gold standard tool for the assessment of sarcopenia in patients with cirrhosis is CT, through the measure of the cross-sectional area of the abdominal skeletal muscles at the 3rd lumbar vertebra (L3) level (9). This cross-sectional area of the abdominal skeletal muscles yields skeletal muscle index (SMI) when normalized to the patient's height, which is a well-validated modality for the diagnosis of sarcopenia in patients with cirrhosis. Using this CT-based index, sarcopenia is defined as L3-SMI <50 cm^2/m^2 for men and <39 cm^2/m^2 for women (Western cut-off); or as L3-SMI <36.5 cm^2/m^2 for men and 30.2 cm^2/m^2 for women (Asian cut-off) (9,10).

In addition, several medical societies recommend incorporating handgrip strength (HGS) in the definition of sarcopenia. European Working Group on Sarcopenia in Older People-2nd meeting (EWGSOP2) definition incorporates low HGS (<27 kg for men and <16 kg for women) with low SMI (defined by the Western or the Asian cut-offs). Sarcopenia diagnosed by a combination of low HGS and population-specific L3-SMI cut-off is the best predictor for mortality (11). To enhance its predictability, sarcopenia has been added to the model for End Stage Liver Disease (MELD) score. When sarcopenia coexists, it is equivalent to adding 10 extra points to the patients' MELD score. The MELD-sarcopenia score led to an improvement in mortality prediction in comparison to the MELD score (12).

Of the 22 studies evaluated by Tantai *et al.*, 50% of them include patients with hepatocellular carcinoma with a variable prevalence (8–46%), a pathology that clearly constitutes a subgroup with a high morbidity and mortality rate. Apart from the efforts of the authors to homogenize the studies, this type of subgroup still constitutes an additional challenge to establish an adequate way to measure the impact on prioritization strategies, mainly in liver transplant settings or procedures with curative intent.

Prevention or treatment of sarcopenia in patients with cirrhosis should be considered a health priority. Improvement in nutrition with branched chain amino acids (BCAA) have been shown to improve muscle mass in numerous studies (13). However, BCAA supplementation is not recommended beyond emphasizing the importance of meeting daily overall protein targets from a diverse range of protein sources (10). In addition, regular physical activity has been shown to protect patients with cirrhosis from developing sarcopenia and physical deconditioning (13). Likewise, testosterone supplementation has been shown to improve muscle mass is selected patients with cirrhosis (14). Overall, further robust longitudinal randomized trials are required to examine the benefits of these or other therapeutic approaches in the management of sarcopenia in patients with liver cirrhosis.

In summary, sarcopenia is highly prevalent among patients with cirrhosis and has a major impact on their survival. Sarcopenia assessment should become a part of routine care in patients with cirrhosis. The early diagnosis of sarcopenia should be considered as an essential part of the management of patients with liver cirrhosis, along with appropriate nutritional assessment and treatment, in order to improve the prognosis of this fragile population.

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Footnote

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