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Frailty, sarcopenia and mortality in cirrhosis: what is the best assessment, how to interpret the data correctly and what interventions are possible?

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Summary

Cirrhosis-induced sarcopenia plays a deleterious role in patients on the waiting list of transplantation. Liver frailty index (LFI) calculation based on easy measurable clinical parameters (muscle strength and balance data) seems therefore accurate for identifying patients at risk for waiting list mortality. However, some questions remain open such as the difficult clinical testing of patients with encephalopathy, the comparison of these clinical data with the radiological evaluation of muscle quantity and quality, the attitude to adopt towards these patients identified as fragile (emergency versus futile transplantation?) and the possible benefit of interventions (nutrition and/or exercise). Finally, recent data show that the deterioration of the muscle condition occurs early prior to the development of advanced fibrosis (specifically in fatty liver disease). This underlines the interest of evaluating the muscle compartment during the pathogenesis of liver diseases, also before the emergence of cirrhosis.

Sarcopenia, defined as a critical reduction in skeletal muscle mass associated with poor outcomes, has been shown to carry an increased risk of morbidity and mortality in end-stage liver disease and in particular in patients on the waiting list of transplantation [1].

Recently, a large prospective multicentre study evaluating the frailty at baseline and frailty evolution in cirrhotic patients on the transplant list was published [2]. Frailty was determined by an objective liver frailty index (LFI) calculation based on measurable muscle strength and balance data. Interestingly, for similar MELD scores (around 18 points), transplant list mortality was significantly higher in patients with high baseline frailty and a worsening of this LFI, reassessed every 3 months. Importantly, an objective clinical assessment of frailty seems thus possible. However, after an analysis of these data, three important questions emerge.

Firstly, patients with severe encephalopathy are unfortunately excluded from the “clinical” evaluation of frailty [2]. As a reminder, encephalopathy as a clinical manifestation of end-stage liver disease is common in patients requiring a transplant. It is obvious that the calculation of the LFI would be biased by the presence of encephalopathy and not representative of frailty in this situation. The other “classical” measures on radiological

images evaluating muscle quantity (in order to detect sarcopenia) but also muscle quality (muscle composition) are therefore needed in these patients [3]. According to this point of view, it would be interesting to compare the LFI score (when it is feasible) and these radiological measurements.

Secondly, we wonder how to correctly interpret the results of those evaluations. Is a high LFI or low skeletal muscle index an urgent call for liver transplantation priority or one important information for clinicians helping them to avoid futile transplantation? It seems logical to postulate that our attention and priority should be given to the most fragile patients [4]. However, on the contrary, shouldn't we consider denying transplantation for patients with very high frailty scores in whom it would be too late to benefit from transplantation? In a context of shortage of liver grafts and known impact of sarcopenia on post-transplant mortality [5], this question is to be asked.

Thirdly, the interesting data on frailty/sarcopenia related risk call for further intervention studies. This task would probably be complex and broad with multiple objectives. Those include targeting and correcting frailty, trying to improve nutritional status and survival to finally allow the patient to be in a better condition to reach the transplant, or even avoid it... Recommendations have been published in this context [6]. However, we know from previous dietary intervention studies that these interventions are effective (ameliorate survival or total body protein) in the case of mild cirrhotic disease (Child A) but not in the case of more severe disease (Child B or C) [7,8]. We therefore want to insist that one should not wait too long for nutritional interventions in the cirrhotic patient. Adapted physical activity has also been proposed in patients on the waiting list of transplantation with some benefits but also limited data [1]. The benefit of a combined intervention (nutrition and exercise) to increase muscle strength and general condition in cirrhotic patients and pre-transplant patients needs to be evaluated. According to the recent study on frailty [2], specific subgroups of patients, such as subjects with metabolic dysfunction-associated fatty liver disease (MAFLD), seem to be particularly affected by frailty deterioration over time and thus require special attention and further studies. Changes in muscle size/composition may indeed play a role in the progression of all decompensated liver diseases [9], but also specifically in the pathogenesis of MAFLD before cirrhosis development [10,11].

Taken together, frailty evaluation through the objective LFI allows an objective longitudinal clinical evaluation of the patients. Further studies are needed to compare this clinical index with even more objective radiological data, as well as in liver disease pathogenesis, before the occurrence of cirrhosis, especially in MAFLD [12,13]. Altogether, this information opens

important debates on listing priority and possible impact of nutrional and physical interventions.

Declaration of interests

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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