Reply to: "May sarcopenia and/or hepatic encephalopathy improve the predictivity of model for end-stage liver disease?" and "Has the time come for using MELD-Sarcopenia score?"

To the Editor:

We would like to thank Lucidi *et al.*[1] and De *et al.*[2] for their interest in our work[3] and for highlighting some challenging issues regarding the impact of low skeletal muscle mass in liver transplant candidates with cirrhosis.

De *et al.*[2] raised the valid concern that the use of body mass index (BMI) specific cut-off values as proposed by Martin *et al.*[4] although currently most frequently used, may have led to misclassification of sarcopenia in cirrhotic patients with ascites. Ideally, BMI should be calculated based on the dry weight and classified according to, for example, the method of Campillo *et al.* that corrects for the presence and the stage of ascites.[5] However, inherent to the retrospective nature of our study, we were unable to apply this method. Nevertheless, we re-evaluated our data and concluded that only 28 male patients (4.8% of the total study population) might have been wrongly classified as having sarcopenia, while they had a BMI between 25 and 27 (which could have been overestimated due to the presence of ascites) and a skeletal muscle index ranging from 43 to 53 cm^2/m^2. Therefore, we believe that this small fraction may have had only minor influence on the study results if any at all.

Indeed, a cut-off value that can be employed in the general population and is more broadly applicable across different patient populations, is highly warranted. Recently, such values have been proposed, although they have yet to be validated.[6] Therefore, we did apply a cut-off developed for patients with liver cirrhosis specifically by Carey *et al.*[7] to test the robustness of our data. The application of these cut-offs resulted in a poor discriminative performance after correcting for model for end-stage liver disease (MELD) score, which is not surprising, as the MELD-score alone is used as allocation tool on the waiting list because of its strong predictive value. In addition, waiting list placement, disease severity, and prioritization for transplantation on the one hand and skeletal muscle mass on the other hand are all strongly correlated with the MELD score. Altogether, developing a model that significantly improves the predictive value of the MELD, with an excellent concordance index (0.839 in our cohort), remains challenging in an era in which this model is already used to select and prioritize patients.

We agree with Lucidi *et al.*[1] that, ideally, our results should be externally validated, particularly in patients with low MELD-scores who are often not listed for liver transplantation. Our findings in this specific subgroup imply that these patients may be under-prioritized in the current allocation system. Therefore, analysis of the association between skeletal muscle mass and survival of patients with liver cirrhosis who are not listed for transplantation yet, is certainly of interest. But again, such an unselected cohort is hard to identify retrospectively.

Lastly, the MELD score alone is an easy-to-obtain and readily available bedside tool indeed and the addition of CT-evaluation is more labor-intensive and not always readily available. Nevertheless, the majority of listed patients do have computed tomography (CT) images available, as a consequence of the transplantation screening protocol. We acknowledge that consensus regarding cut-off values is of importance and that we should continue to optimize diagnosis of sarcopenia as assessed by CT. Yet, we believe that the optimization of prognostic models is an ongoing process and that opportunistic CT evaluation of skeletal muscle mass could help.

Conflict of interest

The authors who have taken part in this study declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

Please refer to the accompanying ICMJE disclosure forms for further details.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jhep.2018.03.017.

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