Reply to “Sarcopenia does not worsen outcomes in patients with refractory ascites under Transjugular Intrahepatic Portosystemic Shunt Placement- Preliminary evidence?”

By Amine Benmassaoud, Emmanuel Tsochatzis

To the editor :

We would like to thank Dr Anand and Dr Sharma for their interest in our study and their comments. Sarcopenia is a well-known poor prognostic factor in patients with cirrhosis and is associated with increased mortality before and after liver transplantation[1]. We recently reported on the impact of baseline sarcopenia in a cohort of 107 patients that underwent transjugular intrahepatic portosystemic shunt (TIPSS) insertion for refractory ascites due to cirrhosis[2]. In our retrospective study with a median patient follow-up of 14.2 months, we found that baseline sarcopenia, as defined by validated sex-specific cut-offs of skeletal muscle index at the third lumbar vertebrae, was not associated with *de novo* hepatic encephalopathy (HE) or mortality. In fact, muscle mass tended to increase following TIPSS insertion in those with repeated cross-sectional imaging. Together, this suggests that baseline sarcopenia should not be seen as a contra-indication for the insertion of a TIPSS for refractory ascites as their outcomes are not worse than those without sarcopenia.

Regarding the criticisms of our paper by Dr Anand and Dr Sharma, we acknowledge that there were significant differences in the distribution of sex with regard to baseline prevalence of sarcopenia. Consistent with the literature, our study highlighted that sarcopenic patients were more likely to be male and have a lower body mass index [3]. Unlike sarcopenia cut-offs that have been validated for males and females separately based on its association with mortality in

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We thank Dr. Sharma and Dr. Anand for their comments and critical review of our paper.

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patients with cirrhosis, this is not the case yet for BMI. We therefore conducted univariate and multivariate analyses and showed that sarcopenia, sex, and BMI were not associated with *de novo* HE or mortality. Although sex did not appear to have an impact on outcome, it is likely that males and females are subject to a different set of risk factors that can lead to worse outcome. Unfortunately, our manuscript is not powered to specifically identify sex-based predictors of worse outcome in this patient population.

Another key point raised is the retrospective study design and possibility of selection bias. We agree that due to the retrospective nature, individuals without baseline imaging had to be excluded as sarcopenia could not be assessed. As baseline imaging is mandatory before proceeding with TIPSS, it is more likely that images were performed at the patient's local center and images reviewed but not uploaded in our system. Besides a lower creatinine in those with imaging, there was no other significant difference. In addition, we do not believe that there was a selection bias as our intent was to focus on patients with TIPSS insertion for refractory ascites only. Presence of sarcopenia is unlikely to have played a major role in selecting patients as it was not assessed *a priori* and is not part of current selection criteria. Crucially, baseline degree of liver dysfunction was the same between both groups, specifically the MELD and Child Pugh score, medians and interquartile ranges.

Finally, we firmly believe that 14 months of median follow-up is sufficient to form conclusions in a vulnerable group of patients with cirrhosis and refractory ascites, where life expectancy is limited without a liver transplantation. We therefore disagree with the statement that studies with longer follow up are required. Although our study was retrospective, its results are robust

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and the message clear for current clinical practice: sarcopenia does not adversely impact outcomes in patients with refractory ascites undergoing TIPS, therefore such patients should not be deterred from having the procedure.

References:

1. Kalafateli M, Mantzoukis K, Choi Yau Y, et al. Malnutrition and sarcopenia predict post-liver transplantation outcomes independently of the Model for End-stage Liver Disease score. J Cachexia Sarcopenia Muscle 2017;8:113-121.
2. Benmassaoud A, Roccarina D, Arico F, et al. Sarcopenia Does Not Worsen Survival in Patients With Cirrhosis Undergoing Transjugular Intrahepatic Portosystemic Shunt for Refractory Ascites. Am J Gastroenterol 2020.
3. Ebadi M, Tandon P, Moctezuma-Velazquez C, et al. Low subcutaneous adiposity associates with higher mortality in female patients with cirrhosis. J Hepatol 2018;69:608-616.

Deleted: We thank the editors and Dr. Sharma for the opportunity to further discuss our findings. ¶