

Peer Review File

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Title: Implications of Pre-transplant Sarcopenia and Frailty in Patients with Non-alcoholic Steatohepatitis and Alcoholic Liver Disease

Review Comment

The authors deserve to be congratulated for an excellent review of this important emerging topic. The manuscript is very well written and has important clinical messages. It should be of great interest to the readers.

However, discussion on the following issues should also be considered for inclusion in the manuscript:

Comment 1: What happens to sarcopenia after liver transplantation?

Reply 1: I have expanded on this subject under the heading “Post-Transplant Outcomes” on pages 2-3 of the manuscript. Liver transplant is also compared/contrasted to TIPS on page 7 of the manuscript.

Comment 2: Differential effect on gain of muscle **mass** and muscle **function** in post-transplant period.

Reply 2: The revised section on “Post-Transplant Outcomes” on pages 2-3 more completely addresses changes in both muscle mass and function post-transplant.

Comment 3: Difference in outcomes in peri-transplant and post-transplant period in patients with NASH-related cirrhosis with sarcopenia in comparison those with ALD and sarcopenia – the Lai paper you cite didn’t have a difference in prevalence of sarcopenia between the groups and it doesn’t look like etiology made it into their univariate or multivariate models. Is there another paper somewhere that discusses this better?

Reply 3: I cite several papers by Dr. Lai, but could not find which one is referred to here. Nevertheless, I have incorporated some additional studies to flesh this comment out further. There are two sections in the paper that explicitly address sarcopenia in NAFLD (“Pathophysiology of Sarcopenia in NAFLD” on page 5) and ALD (“Pathophysiology of Sarcopenia in Alcoholic Liver Disease” on page 5). Peritransplant outcomes by etiology have been included in both sections.

Comment 4: Non-linear relationship between severity of cirrhosis and severity of sarcopenia (Alameri HF et al., 2007; Carey EJ et al., 2010). Can mention this but not surprising I believe if you plot MELD vs mortality its also a nonlinear association.

Reply 4: Thank you kindly for these references, I have included them in the section on early-MELD/CTP score mortality under “Pre-transplant Outcomes”, page 3.

Comment 5: Additive effects of alcohol and sarcopenia in alcohol-related liver

disease (ALD)

Reply 5: The exacerbation of sarcopenia by alcohol is addressed on pages 5-6.

Comment 6: Pre-LT sarcopenia is associated with poorer outcomes both pre- and post-transplant period.

Reply 6: Addressed at length on pages 2-3 under the sections “Pre-transplant Outcomes” and “Post-transplant Outcomes.”

Comment 7: Effect of sarcopenic obesity on pre- and post-transplant outcomes – do any of the studies you cite show that there is a “sweet spot” for BMI (it’s often around 28-35) and that patients below/above this do relatively worse? I doubt that you’ll find a paper looking at this directly.

Reply 7: I have added a new paragraph on BMI and transplant outcomes/considerations; this can be found on pages 3-4 as the last paragraph of “Post-transplant Outcomes.”