Author response: Is obesity a risk factor for the development of acute on chronic liver failure in patients with decompensated cirrhosis?

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Dear Dr. Yu and colleagues:

Thank you for your interest in our manuscript, "Class III obesity is a risk factor for the development of acute on chronic liver failure in patients with decompensated cirrhosis."[1] In your letter, there are several points raised regarding the statistical methodology and the variables incorporated in the study. We would like to address these comments.

With regards to statistical methodology, the authors suggest the use of propensity score matching (PSM). PSM can be a useful tool by accounting for covariates that predict receiving the "treatment," which in the case of our study would be Class III obesity. However, PSM is not always appropriate or necessary in all retrospective observational studies. PSM is traditionally considered when there are few units (in this case patients) in the comparison group (obese group) who are comparable to the treatment group (in this case patients with Class III obesity). That is not the case in our study. Furthermore, we had sufficient sample size to adjust for the key covariates mentioned by the authors, using Cox proportional hazards regression due to the large number of patients available in the registries, which makes PSM unnecessary. Therefore, while PSM is a potentially valuable tool, it is not needed nor of added value in the type of study we published. We refer the authors to the following articles that demonstrate that regression analysis is the methodology of choice for studies with a large sample size such as ours,[2,3] and in fact that use of PSM with a larger sample size can lead to significant loss of statistical power.

The authors also state that additional variables should be included in our model from the UNOS database analysis, specifically mentioning hemoglobin, portal hypertension, and gamma-glutamyl transferase (GGT) level. These variables could not be incorporated, however, as they are not available in the registry. Nonetheless, we would like to address each of these variables. Regarding the variable of hemoglobin, we did attempt to account for this in the Nationwide Inpatient Sample analysis, by creating a variable for clinically significant anemia, which required both a diagnostic code for anemia and a procedure code for red blood cell transfusion. As expected, this variable was significantly associated with ACLF in our multivariable regression model. We are uncertain regarding the authors suggestion of incorporating portal hypertension and assume they are referring to hepatic venous pressure gradient. Again, this is not available in the UNOS database and is not commonly assessed in a clinical setting among patients with decompensated cirrhosis in the United States. Regardless, all patients evaluated had decompensation in the form ascites or hepatic encephalopathy, which demonstrates that they all had clinically significant portal hypertension as outlined in the AASLD guidelines.[4] Finally, regarding GGT level, this also is unavailable in the registries studied. Regardless, although GGT level may associated with ALCF development, there is no evidence that GGT level alone demonstrates a physiologic difference between our patient groups that cannot be accounted for by other variables we have included.

Sincerely,

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