



## Mortality of acute-on-chronic liver failure: What is the role of obesity?

### To the Editors:

I read with great interest the study by Hernaez *et al.*, entitled “Prevalence and short-term mortality of acute-on-chronic liver failure: A national cohort study from the USA.”<sup>1</sup> In their paper, the authors illustrate several notable findings regarding risk factors for mortality in patients with acute-on-chronic liver failure (ACLF) via analysis of the Veterans Affairs’ database.

In our previous paper, we demonstrated that class III obesity is a risk factor for the development of ACLF in patients with decompensated cirrhosis by analyzing the United network for Organ Sharing (UNOS) database and the Nationwide Inpatient Sample.<sup>2</sup> Unfortunately due to biases and limitations in both databases, we could not evaluate whether obesity was a risk factor for mortality in patients who had developed the ACLF. In the current study, the authors demonstrate that patients with ACLF have a greater prevalence of obesity based on body mass index (47% vs. 40%), compared to those without ACLF. Furthermore, among each grade of ACLF, the majority of patients had a BMI above 30 (41%–49%). These findings do suggest, at least, that obesity is more prevalent among patients with ACLF.

I am interested to know if the authors have performed or can perform an analysis regarding whether BMI, either as a continuous or categorical variable, was associated with mortality among patients who developed ACLF, particularly with regards to class III obesity. The results, whether positive or negative, would be clinically useful for the risk stratification of our patients with ACLF.

### Conflict of interest

The author declares no conflicts of interest that pertain to this work.

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

### Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2019.01.018>.

### References

- [1] Hernaez R, Kramer JR, Liu Y, Tansel A, Natarajan Y, Hussain KB, et al. Prevalence and short-term mortality of acute-on-chronic liver failure: a national cohort study from the USA. *J Hepatol* 2019;70:639–647.
- [2] Sundaram V, Jalan R, Ahn JC, Charlton MR, Goldberg DS, Karvellas CJ, et al. Class III obesity is a risk factor for the development of acute-on-chronic liver failure in patients with decompensated cirrhosis. *J Hepatol* 2018;69:617–625.

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## Reply to: “Mortality of acute-on-chronic liver failure: What is the role of obesity?”

### To the Editors:

We appreciate the interest and comments by Dr. Sundaram. Out of 19,082 patients with acute-on-chronic liver failure (ACLF) in our study, 17.4% had missing data on body mass index (BMI).<sup>1</sup> Amongst those with non-missing data, obesity class III was present in 10.3%, obesity I-II in 36.4% and 35.9% were non-obese (BMI <30 kg/m<sup>2</sup>). The 28-day mortality rates were 20.5% in patients with class III obesity, 22.9% in those with class II obesity and 28.2% in non-obese patients. We further examined the independent association between mortality and BMI (as continuous and categorical variables). BMI was inversely associated with 28-day mortality (odds ratio [OR] 0.98; 95% CI 0.97–0.98) after adjustment of other demographic and clinical factors. We found a similar association when we examined obesity as a categorical variable. Using obesity classes, and compared to non-obese patients, both obesity class I-II and obesity class III were inversely associated with mortality risk (OR for class I-II 0.73; 95% CI 0.67–0.79; OR for class III 0.62; 95% CI 0.55–0.71).

In summary, despite the high prevalence of obesity in patients with ACLF,<sup>2</sup> these additional analyses show that BMI was inversely associated with mortality in our cohort. The higher risk of mortality observed in normal (and underweight) ACLF patients could at least partly be caused by residual confounding from malnutrition and sarcopenia – both markers of poor prognosis in decompensated cirrhosis. Future cohort studies that prospectively collect data on BMI, anthropometrics, nutrition, and sarcopenia will be important to examine the association between BMI and mortality in ACLF.

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### Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

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### Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2019.02.005>.

## References

Authors names in bold designate shared co-first authorship

- [1] Sundaram V, Jalan R, Ahn JC, Charlton MR, Goldberg DS, Karvellas CJ, et al. Class III obesity is a risk factor for the development of acute-on-chronic liver failure in patients with decompensated cirrhosis. *J Hepatol* 2018;69:617–625.
- [2] **Hernaez R, Kramer JR**, Liu Y, Tansel A, Natarajan Y, Hussain KB, et al. Prevalence and short-term mortality of acute-on-chronic liver failure: a national cohort study from the USA. *J Hepatol* 2019;70:639–647.

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## NAFLD and beneficial effects of lifestyle intervention: Defining the meat of the matter

To the Editor:

It is with great interest that we read the paper of Wong *et al.*<sup>1</sup> In this large population-based study, the authors address a very important issue: is lifestyle modification as important in non-obese non-alcoholic fatty liver disease (NAFLD) as it is in obese NAFLD?

Based on their study results the answer is probably yes: 67% of the non-obese patients and 61% of the obese patients had normalisation of the intrahepatic triglyceride content on MR-spectroscopy after 12 months of lifestyle intervention. The authors subsequently focus on the relative weight loss and variably advice 3–10% (abstract and lay summary) or 5–10% (discussion and conclusion) body weight loss in order to achieve this primary endpoint in non-obese individuals.

What is interesting, however, is that the impact of the lifestyle intervention was independent of the achieved change in absolute body weight and in waist circumference in multivariable analysis. We would therefore like to pose the question whether the authors believe it is the decrease in body weight or the decrease in waist circumference or maybe another component within the lifestyle intervention that reverses NAFLD? And, if the latter is true, then what could that be?

As the authors discuss themselves, body mass index (BMI) is an imperfect measure of adiposity because it cannot distinguish between fat and muscle mass.<sup>2</sup> Indeed, it has been found that waist-to-hip ratio is a better predictor of severe liver disease

than BMI.<sup>3</sup> As stated above, waist circumference was indeed independently associated with reversing non-obese NAFLD in the multivariable analysis. Yet, the actual change in waist circumference over time cannot be deduced from the paper (not shown in text, tables or figures). Also, the relative weight loss (*i.e.* percentage of weight reduction) was in fact not analysed in multivariable fashion at all, merely the absolute change in body weight.<sup>1</sup>

Another matter that caught our attention (although beyond the primary outcome of this study) was the use of the fatty liver index (FLI) for the diagnosis of NAFLD after 6 years of follow-up. As known, the FLI includes waist circumference and BMI, as well as triglycerides and gamma glutamyltransferase (GGT), in its algorithm.<sup>4</sup> The FLI was originally developed on the basis of anthropometric parameters against ultrasound and later validated against actual intrahepatic triglyceride content. However, it is exactly because of this association between anthropometrics and NAFLD, that the choice of FLI in the context of the present study is somewhat unfortunate.<sup>1</sup> The authors state in their results that ‘obese patients had higher FLI at year 6 compared to non-obese patients’ and that ‘obese patients were less likely to have an FLI below 30 than non-obese patients’. These findings are, although true, inherent to the algorithm and therefore redundant. As there is little data on the use of FLI as diagnostic tool for follow-up, it would have been interesting to compare the FLI at baseline against MR-spectroscopy in this study, confirming the robustness of NAFLD diagnosis after 6 years.

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