Title: Obesity and mortality in COVID-19: cause or association?

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Dear Editor,

We read with great interest the study by Singh et al.,\(^1\) in which the authors have shown the impact of obesity on the 30-day composite outcomes, death or intubation, in patients with coronavirus disease (COVID-19). An appropriate propensity score matching ensured that the two groups had similar confounding risk factors affecting mortality. They also demonstrated higher risks of complications with increasing grades of obesity. However, there are a few concerns that merit further exploration.

First, the prevalence of fatty liver disease in the propensity-matched obese cohort was 5%. However, multiple previous studies in patients with obesity have shown the prevalence to vary from 50% to 90%, and increasing trends with increasing body mass index (BMI).\(^2\,^3\) Patients with non-alcoholic fatty liver disease (NAFLD) may have an accelerated rate of progression to severe COVID-19.\(^4\) Thus, estimating the true prevalence of NAFLD in such a large population, and evaluating its impact on the outcomes, would help in understanding the implications of COVID-19 in patients with obesity.

In the propensity-matched cohort, 368/8112 patients died in the obese cohort (140 and 158 with stage 2 and 3 obesity, respectively). As estimated from the available results, the number of patients who died in the subgroup of stage 1 obesity (3006 cases and controls) in the propensity-matched cohort would be 70 (2.3%) and 90 (3.0%), respectively. These facts interestingly suggest lower mortality rates in patients with stage 1 obesity as compared to high-risk non-obese comparable controls. In another study of more than 17 million patients, stage 1 obesity was associated with an increased risk (Hazard ratio 1.05 (1.0-1.11)) of mortality when adjusted for other risk factors.\(^5\) Whether obesity influences the overall outcomes only after a particular threshold of BMI needs to be further evaluated. Also, it
would be interesting to analyze whether obesity was an independent predictor of poor outcomes, using a regression analysis in the entire COVID-19 cohort.

The authors matched the two cohorts for multiple risk factors for mortality; however, the severity of COVID-19 at presentation, which is an important determinant of outcomes, was not matched. An unequal distribution of patients with greater severity of pneumonia at presentation between the groups could have impacted the outcomes. Other important factors, such as glycemic control, cardiac injury, differences in pharmacotherapy for COVID, and drugs for comorbidities like metformin, statins, aspirin, NSAIDs, might affect the overall outcomes in COVID-19.6,7 Difference in the cause of death in the two groups, if any, would help formulate better treatment strategies. The age distribution of the propensity score matched cohort appears skewed, and further exploratory analysis assessing the overall survival in patients with different age groups would be interesting.

Overall, the study is very well conducted, and we congratulate the authors for achieving this mammoth task of collating and analyzing such a large database.

References:


