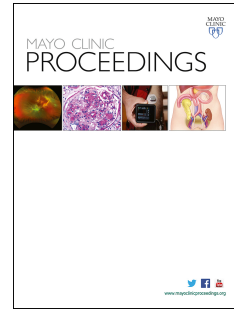


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Obesity is Associated with More Critical Illness in COVID-19

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Obesity is Associated with More Critical Illness in COVID-19

To the Editor: In follow-up to recent major state-of-the-art review on Obesity and Outcomes in SARS-CoV-2 (COVID-19),¹ we have additional data regarding the relationship of obesity with outcomes in patients with COVID-19. Clearly, obesity and metabolic syndrome have been shown to affect both innate and adaptive immunity, leading to increased infection severity.^{1,2}

This is very important since current statistics indicate that three-fourths of the United States (US) population are either overweight or obese by body mass index (BMI) criteria, and currently over 42% meet criteria for obesity by BMI ≥ 30 kg/m². More alarmingly, currently over 9% of the US population meet criteria for severe or morbid obesity (Class III obesity) by BMI ≥ 40 kg/m².^{1,2} Certainly, many other countries across the globe are experiencing marked increases in the prevalence and severity of obesity,^{1,2} which may be particularly problematic in COVID-19 and other such pandemics. We performed a rapid review and meta-analysis to evaluate whether obesity is associated with worse outcomes in patients with COVID-19.

The present study was conducted in accordance with the PRISMA guidelines. We performed a comprehensive search in the MEDLINE and medrxiv.org databases for studies published between January 01, 2019 and May 31, 2020. The following key words were used for search in different combinations: “Coronavirus 2019”, “Covid-19”, “SARS-CoV2”, “Obesity”, “Body mass index”, and “Outcomes”. Studies reporting the relationship between BMI (non-obese vs. obese) and outcomes among hospitalized

patients with Covid-19 were included for analysis. Three reviewers (AS, A.G. and A.R.) screened the study titles and abstracts for relevance followed by full manuscript evaluation. The following data was collected from included studies: baseline characteristics, proportion of subjects classified by BMI categories ($< 30 \text{ kg/m}^2$ vs. $>30 \text{ kg/m}^2$), and percentage of hospitalized patients. The primary outcome was critical illness [need for intensive care unit (ICU), invasive mechanical ventilation (IMV) or mortality] as defined per individual study protocol. We used the Cochrane review manager 5.3 for study analysis. Pooled odds ratio (OR) and 95% confidence intervals (CI) were calculated using random-effects models and Mantel-Haenszel method. Heterogeneity was assessed using I^2 statistic. Initial search resulted in 266 studies out of which 13 (N=7196) were identified to report outcomes in patients with Covid-19 based on BMI.³⁻¹⁵ Critical illness was defined as need for ICU care or need for IMV or composite of ICU care, IMV, hospice or death. Pooled analysis showed that obesity was associated with increased odds of critical illness among patients hospitalized with Covid-19 [OR 1.39 (1.21-1.60)] (**Figure**). Low heterogeneity was evident across studies ($I^2= 19\%$) (**Figure**).

In this rapid review and meta-analysis, obesity was associated with a 39% increased risk of critical illness, defined by individual study protocol as ICU admission, need for IMV, or hospice admission or death. Considering the very high prevalence of obesity among adults in the US and worldwide, and even severe obesity approaching nearly a tenth of US adults, this increased critical illness is a worrisome sign.²

Patients with obesity also have more endothelial dysfunction, as well as respiratory and renal diseases that could worsen COVID-19 outcomes. However, probably most

importantly, COVID-19 coronavirus attaches to the angiotensin converting enzyme 2 (ACE2) receptors in the lungs and organs.¹ Obese patients have insulin resistance and activation of the renin angiotensin aldosterone system.¹ The presence of ACE2 may enable the entry of SARS-CoV-2 into adipocytes, which makes adipose tissue an important viral reservoir.¹ Therefore, adipose tissue, which is more abundant in obesity, might also be infected by SARS-CoV-2 and allow spread to other organs, thus explaining the more severe COVID-19 disease in obesity.¹ The prevention of obesity in the first place and, especially, its progression to more severe forms, is desperately needed for future pandemics, as well as for the primary and secondary prevention of diabetes mellitus and cardiovascular disease.² In this COVID-19 pandemic, clinicians should recognize the marked increased risks associated with obesity, and these patients need more aggressive triage and treatment.

Our study has several limitations. Due to lack of patient level data, the results in our study were not adjusted to baseline patient characteristics. Several studies analyzing the relationship between obesity and clinical outcomes have reported results after adjusting for different confounders. Due to differences in the variables used to adjust results in these studies, we have not performed the pooled analysis of those adjusted confidence interval and odds ratio. Further, studies did not have long term follow up data and most patients were still hospitalized without a definite outcome i.e. mortality, thus caution should be exercised before extrapolation of our results to long term outcomes.

Despite these study limitations, however, our data of a 39% increase in worse outcomes associated with obesity strongly supports the recent paper in *Mayo Clinic Proceedings*.¹

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Figure legend:

Figure: Forest Plot comparing the odds of critical illness between obese (BMI>30 kg/m²) versus non-obese (BMI<30 kg/m²) patients hospitalized with Covid-19 infection.

