

Increased Severity of COVID-19 in People with Obesity: Are We Overlooking Plausible Biological Mechanisms?

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TO THE EDITOR: The relationship between obesity and more severe disease in patients with coronavirus disease (COVID-19) is intriguing. Recent articles published in *Obesity* (1-3) discuss the possible effects of increased proinflammatory cytokines and disturbances of lung function in people with obesity, but we believe that they overlook an important player in this scenario, which is endothelial dysfunction.

Endothelial dysfunction is present in obesity and is indeed a final common pathway of a cluster of comorbidities, such as hypertension, diabetes, and dyslipidemia. In obesity, the severity of endothelial dysfunction correlates

with the degree of visceral adiposity, and studies have indicated the roles of proinflammatory factors and oxidative stress (3). In addition to that chronic scenario, acute endothelial damage occurs, induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (which binds to the transmembrane angiotensin-converting enzyme II receptor). Vascular endothelial cell apoptosis ensues and, in conjunction with the acute “cytokine storm,” promotes the settings for lung microvascular dysfunction, vascular leakage, alveolar edema, and ultimately hypoxia. Proinflammatory cytokines also increase the expression of adhesion molecules, resulting in endothelial activation and procoagulant changes, worsening microvascular flow and tissue perfusion (4). In this context, the acronym “MicroCLOTS” (microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome) was recently suggested to describe a progressive endothelial pulmonary syndrome with microvascular thrombosis (5).

Therefore, we believe that among several possible pathophysiologic mechanisms leading to adverse prognosis in people with obesity and COVID-19, endothelial dysfunction is a central one, as it combines the effects of obesity

and its associated comorbidities with the acute effect of SARS-CoV-2. This should turn our attention to the endothelium; if we overlook that, we may be overlooking important plausible biological mechanisms underlying the association between obesity and more serious COVID-19 outcomes. **O**

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