What is the Impact of Obesity in PH?

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Obesity is an epidemic affecting a staggering proportion of the population worldwide. The US Surgeon General reports that more than 1 billion adults are overweight (body mass index [BMI] 25-29.9 kg/m^2) and at least 300 million are categorized as obese (BMI >30 kg/m^2).[1]

The impact of obesity in the cardiopulmonary system is well recognized. The cardiac structures undergo a variety of adaptations and functional alterations as excessive adipose tissue accumulates, even in the absence of other comorbidities.[2] One fundamental change that occurs with obesity is increased metabolic need. As a result, the circulating blood volume, plasma volume, and cardiac output increase. This leads to an increase in wall tension and induces left ventricular hypertrophy, which results in a decrease in diastolic compliance. At this stage obese patients present with diastolic heart failure accompanied by pulmonary hypertension. Once the left ventricle is no longer able to adapt to the increase in left ventricular filling pressure and enlargement, systolic dysfunction follows with worsening pulmonary hypertension, often accompanied by right heart failure.

The effect of obesity on respiratory physiology is numerous and includes elevated work of breathing in the presence of heightened demand for ventilation. Mechanically, obesity is associated with respiratory muscle inefficiency and diminished respiratory compliance. The decreased functional residual capacity and expiratory reserve volume are associated with the closure of peripheral lung units, ventilation to perfusion ratio abnormalities, and hypoxemia, which is pronounced in the supine position. These chronic abnormalities result in hypoventilation and sleep apnea syndromes with attenuated hypoxic and hypercapnic ventilatory responsiveness leading to hypoxemia, pulmonary hypertension, and progressive disability.[3]

Thus, obesity appears to be the major risk factor in pulmonary hypertension associated with diastolic dysfunction and chronic hypoxemia/hypoventilation, among others. However, there is no definite evidence to demonstrate direct cause and effect between obesity and pulmonary arterial hypertension (PAH) as shown by the updated consensus document, which does not list obesity as a risk feature for PAH.[4]

This lack of evidence is surprising given the far reaching effects obesity poses on the cardiopulmonary systems. PAH appears to be common among obese patients as demonstrated by its association with appetite suppressant use.[5] One recent study suggests that obesity alone may be a risk factor for PAH.[6] Furthermore, the benefits of weight loss in improving and, in some cases, reversing the symptoms and structural abnormalities associated with PAH have been reported. Patients who underwent bariatric surgery in conjunction with PAH therapy have shown dramatic improvements in exercise performance, hemodynamics, and sleep.[7,8]

Why is there such paucity of direct evidence linking obesity and PAH? Could it be that BMI, an indirect measure of body fat, is an inaccurate surrogate for obesity? This question has been investigated among heart failure patients to determine why patients with higher BMI seemed to have more favorable prognosis (the so called "obesity paradox").[9] One recent study demonstrated that separating BMI into fat and lean mass components resulted in improved correlations between obesity and outcome.[10] Another possibility is that we have not yet identified the factor(s) that link pathological consequence of obesity and PAH, such as insulin resistance.[11] Despite this lack of direct evidence, the deleterious effects of obesity in PAH patients remain irrefutable and the benefits of weight loss, such as through a well tailored exercise regimen, are incomparable.

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