

# What is more affected in patients with obstructive sleep apnea: the right or the left heart?

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Obstructive sleep apnea (OSA) is a chronic disease, which, in predisposed subjects, causes repeated episodes of upper airway collapse, apnea, and arousals during sleep. Intraluminal airway pressure and pharyngeal muscle activity are widely recognized as major determinants of the size and collapsibility of the upper airways.<sup>1</sup> Excessively negative intrathoracic pressure, generated during inspiratory efforts against the collapsed upper airway, chronically occurs during sleep. The pulmonary artery, being an elastic low pressure system, may be easily stretched by the repetitive negative intrathoracic pressure.<sup>2</sup> The persistent mechanical stress during sleep may be likely responsible for pulmonary artery dilation in OSA.<sup>3</sup> Furthermore, repetitive hypoxia-induced pulmonary arterial vasoconstriction, occurring during obstructive sleep apneas, may promote remodeling of pulmonary vasculature, resulting in pulmonary artery dilation, with consequent pulmonary hypertension (PH).<sup>4</sup>

The study of Dobrowolski et al<sup>5</sup> clearly demonstrates the existing relationship between pulmonary artery dilation and the presence of newly diagnosed severe OSA in patients with resistant hypertension (RHTN). OSA and RHTN are known to have a negative impact on left ventricular morphology and function,<sup>6</sup> while in the present study, the authors<sup>5</sup> established the effects of OSA and RHTN on right ventricular morphology and systolic function and on the parameters associated with pressure in pulmonary circulation. Among the studied parameters, the main pulmonary artery diameter of 25 mm or higher at diastole turned out to be particularly useful in selecting patients suspected of severe OSA.<sup>5</sup> Very recently, Kawano et al<sup>7</sup> reported similar conclusions in patients with severe OSA, which was independently associated with an abnormal increase in the right descending pulmonary artery

diameter, suggesting that severe OSA may cause pulmonary artery dilation.

Taken these original and interesting studies together, we have observed a common limitation, likely due to an ethical issue. Indeed, both papers did not evaluate pulmonary arterial pressure by right cardiac catheterization, nor evaluated the left ventricular alterations, so we could not clarify the exact associations among the severity of OSA, pulmonary artery dilation, and pulmonary artery pressure. In addition, these studies found a positive linear correlation between the pulmonary artery dimension and severity of OSA, without considering the role of the body mass index (BMI) in OSA, since the body fat distribution and BMI have been invariably recognized to be strongly correlated to the apnea-hypopnea index, and thus to the severity of OSA.<sup>8</sup>

OSA typically causes only mild PH, which generally does not require treatment. However, these patients often present with more severe degrees of PH when they have comorbid conditions contributing to hypoxemia, such as obesity hypoventilation syndrome.<sup>9</sup> In addition, cardiomyopathy characterized by eccentric ventricular hypertrophy and diastolic heart failure is a well-recognized condition in severely obese patients. The chronically elevated left ventricular filling pressure might be transmitted into the pulmonary venous system, leading to elevated pulmonary venous pressures, arteriolar remodeling, and ultimately to persistent elevated pulmonary vascular resistance.<sup>10</sup> The interplay between OSA, insulin resistance, and elevated left ventricular filling is likely responsible for endothelial dysfunction, with consequent PH in obese individuals. Thus, obesity may promote endothelial pulmonary dysfunction, while the coexistence with OSA might accelerate progression to PH.<sup>11,12</sup>

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On the other hand, the severity of apnea-related hypoxemia is associated with a gradual deterioration of left ventricular diastolic function, as well as endothelial function of the large artery. A positive relationship has been found between the severity of OSA and subclinical indicators of myocardial or vascular dysfunction.<sup>13</sup> Furthermore, in 2 recent studies,<sup>14,15</sup> endothelial brachial artery dysfunction has been revealed in mild OSA<sup>14</sup> and in minimally symptomatic OSA with obesity (mean BMI, 32.6 kg/m<sup>2</sup>).<sup>15</sup> Such endothelial dysfunction was also significantly decreased by continuous positive airway pressure (CPAP) treatment.<sup>14,15</sup> In other words, CPAP improved endothelial function, but not arterial stiffness, in patients with minimally symptomatic OSA.<sup>15</sup> Thus, minimally symptomatic OSA may be a cardiovascular risk factor. In addition, more recent observations have demonstrated that the duration of OSA and its severity are important factors related to higher values of the intima-media thickness of the common carotid artery, and hence with a higher risk of atherosclerosis.<sup>16</sup>

Based on these robust and substantial data, we warmly emphasize that left and right ventricular function, as well as endothelial function are not preserved in patients with OSA. The need to early investigate these systems in patients with OSA seems to be essential to improve the quality of life and prognosis of these patients. Their dysfunction might depend on the length of disease or might be increased by the coexistence of other important comorbidities, such as resistant systemic hypertension and obesity. The use of CPAP with its effects on the endothelium should be soon mandatory in known or at-risk OSA patients in order to preserve both left and right ventricular function, as well as large-artery endothelial functions, reducing the risk for these patients to early suffer from left (acute myocardial infarction, atherosclerosis) or right (pulmonary hypertension, chronic cor pulmonale) heart diseases.

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