Is Pulmonary Hypertension Common in Uncomplicated OSA?

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Obstructive sleep apnea (OSA) and its clinical counterpart, obstructive sleep apnea hypopnea syndrome (OSAHS), encompass the pathophysiology of upper airway obstruction during sleep. The defining event for OSA is an unstable upper airway leading to flow limitation (hypopnea) or complete obstruction (apnea). The working definition of OSAHS for clinical research is restless sleep, includes disruptive snoring, and daytime sleepiness (including fatigue, unrefreshing sleep, and inattention); both are to be accompanied by more than 5 events (apneas and/or hypopneas) during sleep [1].

Some efforts are being made to refocus working definitions for OSAHS away from counting only respiratory events to the describing appearance of arousals from sleep as the events that lead to daytime sleepiness/fatigue/inattention and even hypertension [2]. Here the literature seems to point to arousals as being as an important factor determining changes in blood pressure during sleep [3], but the effects on daytime (wakefulness) cardiovascular function are, in animal models, quite modest [4].

What about hypoxemia? There is a debate concerning the necessity and implications for working definitions of an apnea or hypopnea to include a fall in oxygen saturation as a defining criterion for apnea or hypopnea [5]. The fall in oxygen saturation that is a consequence of an apnea or hypopnea represents the sum total of pre-event gas exchange and event length and type [6]. In the case of an individual with a normal alveolar-arterial gradient, the

fall in oxygen saturation may not be very great despite a considerable fall in PaO_2 ; in contrast, a person who is hypoxic during the day will have a greater fall in oxygen saturation for a similar change in PaO_2 with sleep onset or sleep apnea. In any event episodic changes in oxygenation can be quantified [7] and experimentally correlated with triggering sustained changes in blood pressure, increases in pulmonary artery pressure and up-regulation of systems than have long-lasting effects on cardiovascular homeostasis [8]. Therefore, episodic hypoxemia appears important.

The report in this issue of *Respiration* by Alchanatis et al. [9] has a focus on pulmonary hypertension as a feature of uncomplicated OSA. One notable feature is its design. First, there is case control in regard to estimated pulmonary artery pressures in the presence or absence of sleep apnea in people matched for age, BMI and (normal) lung function. (OSAHS was higher.) Second, there was demonstrated an acceptable correlation between direct measurements and the noninvasive estimates of pulmonary artery measurements. Third, there was a good follow-up of the patients. Those with OSA and pulmonary artery pressures >20 mm Hg (the defining event for pulmonary hypertension in this report) were older, heavier, and had a slightly lower (but normal) PaO_2 during wakefulness. Their finding indicates that pulmonary hypertension can occur in patients without overt cardiopulmonary problems.

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An important finding is that a fall in pulmonary artery pressure occurred even in those with wakefulness values of pulmonary artery pressure within the normal range before treatment. Most studies suggest that the reversibility of pulmonary hypertension may take a long time (>18 months) to resolve [10], and this time course would be in contrast to the more rapid improvement in systemic blood pressure and sympathetic nerve activity [11]. Some of the slow reversal of pulmonary artery pressure is ascribed to patient adherence to therapy, but could be secondary to other features like pulmonary artery remodeling as a function of the length of illness or more often by cardiopulmonary co-morbidity. In the present study there are issues in regard to the recruitment numbers and capture of all potential subjects, but their observation – the fairly rapid (within 6 months) fall in pulmonary artery pressures with CPAP in patients without overt cardiopulmonary dysfunction – is an important observation requiring more mechanistic studies. Indeed, only 2 of 6 patients remained with pulmonary pressures >20 mm Hg. In any event, it appears that pulmonary artery pressures can be added to other physiologic measures like systemic blood pressure as short-term objective outcomes of therapy for OSAHS [12, 13].

The findings in this paper are consistent with the notion that in sleep clinics many patients (20–40%) with OSAHS have pulmonary hypertension at the time of diagnosis [10, 14–17]. One usually assumes that this occurs as a result of an enrichment of risk factors including co-morbidity and the length of illness that results in referral to a specialty clinic. Although recognition of sleep apnea is rather uncommon in primary care [18], there are papers that suggest that OSA can be recognized in primary care offices by the presence of new-onset pre-tibial edema and/or unexplained pulmonary hypertension [19, 20]. What is unresolved in these studies as well as in the current literature is whether or not pulmonary hypertension by itself can be the sole presenting feature of OSAHS or is captured by current recognition strategies that focus on presenting symptoms like snoring and sleepiness rather than abnormal physical or laboratory findings.

In summary, pulmonary hypertension can often occur in OSA uncomplicated by other cardiopulmonary disorders, and effective treatment is accompanied by a fall in pulmonary pressures. Whether cor pulmonale can be the presenting feature, independent of other cardinal symptoms or be a defining feature of the illness remains an open question.

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