

New Challenges for Sleep Apnea Research: Simple Diagnostic Tools, Biomarkers, New Treatments and Precision Medicine

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In the last decades, we witnessed an extraordinary development in the sleep apnea field characterized by multidisciplinary approaches that allowed us to get significant progress in our understanding of sleep apnea burden, pathophysiology consequences and developing effective treatments¹. We rapidly learned that one of the main sleep apnea forms – namely Obstructive sleep apnea (OSA) is very common in the general population² and especially in patients with cardiovascular diseases³. Similarly, central sleep apnea (CSA) is a frequent sleep disorder observed in patients with decompensate heart failure⁴. Far beyond being common clinical conditions, evidence derived from experimental, translational and clinical observational studies consistently showed that OSA is associated with multiple consequences including increased cardiovascular risk⁵⁻⁸ and that CSA is associated with worst prognosis in patients with heart failure⁹.

However, all this “euphoria” came across to several challenges and realities: 1) we are not able to provide a massive strategy to improve sleep apnea underdiagnosis considering the availability of sleep laboratories and current long waitlists^{10,11}; 2) the main treatment for sleep apnea (namely continuous positive airway pressure, CPAP) is not systematically available in some Countries and has significant challenges to reach long-term good adherence; 3) we observed considering variability on sleep-related symptoms and cardiovascular endpoints improvements even in those patients with good adherence to sleep apnea treatment¹²; 4) we lack effective alternative treatments, especially for severe forms of sleep apnea. In parallel to these issues, there was growing interest to explore effective screening questionnaires¹³ and to expand OSA diagnosis using portable monitors and other potential tools to effectively identify OSA at very low cost^{14,15}.

Moreover, there is a recent interest in exploring biomarkers for sleep apnea. Much more interesting than non specific biomarkers such as C-reactive protein, recent approach using metabolomics, proteomics, microRNAs techniques (among others) gained attention to potentially identify sleep apnea signatures, biomarkers of risk¹⁶⁻¹⁸ and to predict response to OSA treatment¹². In contrast to the “wake-up call” for sleep apnea, we have recent learned that that mild OSA seems to be not associated with significant neurocognitive and cardiovascular impairment¹⁹. In addition, the recent neutral effects of CPAP on asymptomatic or minimally symptomatic high risk OSA patients^{20,21} contribute to the recent statement from the US Preventive Services Task Force (USPSTF) to determine insufficient evidence to assess the balance of benefits and harms of screening for OSA in asymptomatic adults²². The recent potential harmful effects of Adaptive Servo Ventilation (ASV) for CSA in patients with heart failure²³ made us to reflect if CSA is a compensatory mechanism of heart failure or other factors such as low compliance, high dropouts and specific algorithm machines contribute to these results²⁴.

Therefore, the superb progress on sleep apnea field was accompanied by more questions and challenges to address in future investigations. Particular interest included

(but not limited) to advancements in new diagnostic strategies (who? how? where?), developments of useful biomarkers of risk (and not merely urine and blood exams to screening OSA), selection of patients who will most have benefit from treatment (Precision Medicine)²⁵ and alternative effective treatments for OSA and CSA. By the way, all these challenging research agenda are quite not surprisingly, considering the complexity of sleep...

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