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## Obstructive Sleep Apnea: A Big Issue. The Need for Screening Tools

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Obstructive Sleep Apnea (OSA) is characterized by pharyngeal collapse and occlusion during sleep, causing intermittent hypoxia, sudden reduction of intrathoracic pressure, systemic and pulmonary arterial blood pressure fluctuations and frequent awakenings with consequent sleep disruption [1]. It has been increasingly recognized as a serious health problem worldwide that affects 3-7% of adult men and 2-5% of adult women in the general population [2]. The syndrome increases health-care utilization [3,4] and is often associated with significant morbidity and mortality [5,6]. OSA has been clearly shown as a risk factor for serious health problems which include hypertension, atrial fibrillation, coronary artery disease, stroke [7], metabolic disorders [8] and excessive daytime sleepiness [1,2,9]. The OSA patients without documented or perceived sleepiness have reaction times to drive significantly increased (about half a second), compared to healthy people and are therefore at greater risk of being involved in motor vehicle crashes (2 to 7 fold increase) than the general population [10]. The risk is more relevant for commercial motor vehicle operators due to the weight and size of the vehicles they drive and/or the number of passengers they transport [11]. It has also been shown that snoring and daytime sleepiness, which are the characteristics of OSA, are tightly associated with occupational injuries [12,13]. Untreated OSA in the general adult population is significantly related to neuropsychological impairment [14], altered quality of life in areas related to vitality, social functioning, and mental health [9] and increased mortality rate [6]. OSA is treatable and its under-recognition has important consequences.

Despite the abundance of scientific evidence, OSA is still undiagnosed. Studies have estimated that nearly 80% of men and 93% of women with moderate-to-severe sleep apnea are undiagnosed [15]. This is due to multiple causes, such as lack of knowledge on the part of physicians and the limited access that patients have to diagnosis and treatment [16]. Unfortunately, predictive criteria are still unsatisfactory. Identifying new predictive tools with extensive applications would therefore be useful. To address this critical issue, it is necessary to identify reliable and inexpensive screening systems to detect subjects at risk for the disease.

In certain subgroups of the population, such as obese subjects [15,17] and professional drivers [11] the prevalence of OSA is higher than in the general population. Obesity parameters are important predictors [18], although not all OSA patients are obese and not all obese subjects have OSA.

Effective screening procedures could help to distinguish subjects with high risk of OSA. The Berlin questionnaire [19] showed a sensitivity of 86% in primary care patients, 62.5% in patients undergoing pulmonary rehabilitation, 57-68% in sleep laboratory patients, and 68.9 at AHI>5, 78.6 at AHI>15 and 87.2 at AHI>30 in surgical patients. The STOP questionnaire, which incorporates snoring tiredness, observed apneas, elevated BP, validated in surgical patients to identify subjects with a high risk of OSA demonstrated a moderately high level of sensitivity and specificity [20]. The STOP-Bang scoring, which incorporates Body Mass Index (BMI), age, neck size, and gender with the STOP questionnaire, has demonstrated a higher sensitivity and negative predictive values, especially for patients with moderate

to severe OSA, but low specificity and positive predictive values [21]. A recent meta-analysis [22] that included the STOP-Bang, American Society of Anesthesiologists (ASA), and Berlin questionnaires concluded that only the ASA and STOP-Bang questionnaires had sufficient power to identify patients with OSA in the perioperative setting.

The STOP-Bang questionnaire has good sensitivity for identifying patients with high or moderate OSA but not for finding mild OSA, and its use leads to a high number of false-positives (i.e., men>50 years with a history of hypertension). The identification of new markers of OSA would be useful. Because increased upper airway collapsibility is one of the main determinants of OSA [23,24], the response to the application of Negative Expiratory Pressure (NEP) could be a predictor of this disorder [25-31]. The basis of the technique is to apply a negative pressure at the start of expiration during spontaneous breathing. In normal subjects, an increase in expiratory flow is observed. In subjects with airway obstruction, however, the flow measured under NEP will not exceed spontaneous flow. In subjects with upper airway collapsibility and under NEP, the flow shows a transient decrease, caused by airway collapse. NEP has been evaluated as a tool to predict OSA with different assessing methodologies [25-31]. Van Meerhaeghe et al. [25] concluded that NEP might be useful in predicting OSA with an AHI  $\geq$  15 in a clinic-based population with a sensitivity of 81.9% and a specificity of 69.1%. Tamisier et al. [29] reported a predictive positive value of 96.6% and a predictive negative value of 76.9% and a trend of a lower quantitative index in severe patients who express more highly collapsible upper airway. Romano et al. [31] showed how the NEP test may be very reliable to identify subjects with AHI<30 when the test is negative (negative predictive value of 100%), and to identify subjects with  $AHI \ge 5$  when the test is positive (positive predictive value of 98.1%). NEP test may provide an objective assessment to identify patients with high risk of OSA and could be adopted as a screening test for the evaluation of suspected severe OSA patients, as it appears a very reliable diurnal test to objectively predict this respiratory disorder. A limitation of these investigations was that most of the population studied consisted of subjects attending a sleep laboratory. Further investigations are needed to better detect how the NEP test could be useful to identify mild and moderate OSA in subjects. Probably NEP test could be even more powerful in association with questionnaires investigating anthropometrics data and signs and symptoms.

Useful applications of screening tools could be in assessing the

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fitness of specific categories, such as commercial drivers, workers with jobs who are at an increased risk for accidents, or identifying undiagnosed OSA patients in the preoperative period who are known to have a higher incidence of difficult intubations, postoperative complications, and increased intensive care unit admissions. It is important to heighten public awareness of the potential hazards and health risks that surround undiagnosed sleep apnea; therefore, diagnosing and treating sleep apnea are important medical and social issues.

## Conclusions

OSA is a significant public health problem because of its significant influence on the quality of life and the social impact. Effective screening procedures could help to distinguish subjects with different probabilities of being affected by OSA. The identification of simple, non-invasive, predictive, and reliable tools to detect OSA would be useful in several fields. The evaluation of flow limitation during wakefulness using the NEP technique looks promising to predict OSA and probably may be even more useful when combined with specific questionnaires.

However, upper airway collapsibility predictive of sleep collapsibility evaluated by the NEP test requires measurement standardization for OSA screening in awake subjects. There is a need for simple things that work.

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