Estimating the probability of OSA in the spinal cord injury population: specific tools are still needed

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Patients with high spinal cord injury (SCI) and tetraplegia have a remarkably high prevalence of sleep-disordered breathing (SDB). Most reports describe obstructive sleep apnoeas (OSAs) and hypopnoeas in this population.[1 2] OSA impairs health-related quality of life (HRQL) in tetraplegic subjects and is associated with cognitive dysfunction, with repercussions mainly on attention, concentration, memory and learning skills.[3 4] Changes in upper airways (UA) in SCI may increase the risk of OSA syndrome (OSAS): increased passive UA collapsibility,[5] greater volume of soft palate and lateral pharyngeal walls, increased nasal resistance and nasal congestion.[6 7] Breathing at lower volumes may also contribute to the higher prevalence of OSAS in this population.[2 8] Coexistent traumatic brain injury, sleep position and medication (opioids, baclofen and benzodiazepines) can affect breathing during sleep with an additional burden of central events[9] or nocturnal hypoventilation. It is quite possible that central events are underestimated in available publications because hypopnoeas are most often not specified as being central or obstructive as proposed by the American Academy of Sleep Medicine (AASM) 2012 guidelines.[10] Despite the high prevalence of SDB and SDB-related symptoms in SCI, adherence to Continuous Positive Airways Pressure (CPAP) is poor: symptomatic patients treated with SDB by CPAP have a long-term adherence to treatment of 50%–63%.[2]

Polysomnography (PSG) is the gold standard for the diagnosis of OSA. However, transportation of the patient for in-laboratory PSG may be as complicated as providing unattended portable PSG in a long-term facility. Providing a simple pragmatic alternative to PSG was therefore the main goal for the study by Graco and colleagues published in *Thorax*.[11] The authors describe the performance of a disease-specific two-stage screening tool for moderate to severe OSAS (defined as apnea-hypopnea index (AHI) >21/hour) in tetraplegic patients with SCI, developed using an existing database of 78 patients who had undergone PSG, and then prospectively validated in a group of 100 subjects with SCI. After selection of relevant variables, the final two-stage model includes a four-item SOSAT questionnaire (SOSAT: *S*creening for *OSA* in *T*etraplegia; level of injury (American spinal injury association scale), self-reported snoring and apnoeas, and sleepiness) combined with nocturnal pulse oximetry (using a >3% desaturation and a threshold index of ≥13/hour). Prevalence of OSAS according to study criteria (AHI ≥21/hour) was 38% in the development group and 53% in the validation group, that is, within previously published results. The combined screening tool (SOSAT and pulse oximetry) had a sensitivity of 77% (95% CI 65% to 87%) and a specificity of 81% (95% CI 68 to 90). Performance was not significantly different from the original OSA-50 questionnaire[12] coupled to pulse oximetry in this population. Noteworthy is the fact that 21 (21%) of the 100 patients with SCI in the development group were misclassified (9 false positives and 12 false negatives).

The study is driven by the difficulties encountered in this population to perform PSG to obtain a formal diagnosis of OSA: high costs, poor availability of PSG, care requirements for SCI patients not necessarily readily available or sometimes not met at all in sleep laboratories. The two-step diagnostic strategy using the SOSAT questionnaire and pulse oximetry is proposed as an alternative to PSG for identifying patients with moderate to severe OSA and implementing treatment.

The authors must be congratulated for this well-documented development and validation study of a new diagnostic strategy in such a large number of patients with chronic SCI, which is a logistic challenge. In a very specific SCI population, the two-step SOSAT strategy outperformed (area under curve: 0.87) scores commonly used to screen moderate to severe OSAS in the general population such as the NoSAS or Stop-Bang scores.[13]

Irrespective of the performance of the two-step SOSAT strategy, one may question the relevance of using a systematic screening tool for OSAS in patients with SCI. Recent epidemiological data from the HyponoLaus cohort have shown that prevalence of moderate-to-severe OSAS (≥15 events/hour) in the general population is much higher than previous estimations, using updated technology: 23.4% (95% CI 20.9 to 26.0) in women and 49.7% (95% CI 46.6 to 52.8) in men.[14] Conversely, the efficacy of treating paucisymptomatic or asymptomatic OSAS as prevention of cardiovascular morbidity has been recently challenged by the Sleep Apnea Cardiovascular Endpoints (SAVE) study.[15 16] This large (n=2717) randomised controlled study of secondary prevention in subjects who had moderate-to-severe OSA and coronary or cerebrovascular disease did not show any benefit of CPAP treatment plus usual care versus usual care alone (usual-care group) on death from cardiovascular or cerebrovascular causes as primary endpoint over a 3.7-year average follow-up period. Despite limitations of the SAVE study (including poor average compliance to CPAP), diagnosing OSAS in asymptomatic individuals and proposing treatment as primary or secondary prevention for cardiovascular events is presently debated and even not recommended by some experts.[16] Therefore, in a group of patients with such a high prevalence of SDB, a pragmatic strategy could be to detect symptomatic individuals (for instance, those with most affected HRQL, and SDB-related sleepiness and cognitive disorders) who are likely to accept and benefit from specific treatment, and, in this subgroup of patients with SCI, to confirm the diagnosis with Level III portable monitors while resorting to PSG only for symptomatic unresolved cases.

Indeed, screening for and treating OSA should be targeted and has different rationales and impacts according to specific patient groups. Irrespective of symptoms, it is for instance relevant to confirm and treat OSAS in subjects with refractory systemic hypertension to improve efficacy of treatment.[17 18] Similarly, it seems reasonable to detect and treat severe OSA as a secondary prevention strategy in patients who have survived a stroke.[19] Bariatric surgery is also an opportunity to screen for OSAS in order to decrease perioperative morbidity.[20] Goals in patients with COPD with OSA are different as treatment may have a positive impact on exacerbations, readmission and survival.[21] Conversely, it may be less relevant to screen for OSAS in

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asymptomatic individuals without comorbidities other than SCI.

Confirming the obstructive, central or mixed nature of SDB in SCI and excluding nocturnal hypoventilation cannot be attained using the proposed two-step SOSAT strategy. Graco and colleagues state that the proportion of central (central apnea index: 1.4/hour) or mixed (1.0/hour) events is low in their study population.[11] However, no information is provided as to classification of hypopnoeas as central or obstructive according to 2012 AASM recommendations and the majority (74%) of the events reported in the validation group are hypopnoeas. Given the non-negligible probability of medication-induced events in this population, this raises the question of whether one can consider desaturations and a positive SOSAT as sufficient to exclude central or mixed apnoea syndromes.[9] SCI may also impair respiratory muscle function and therefore this population is also prone to nocturnal hypoventilation. As correctly noticed by the authors, studies concerning prevalence of hypoventilation in patients with SCI are lacking. Given this uncertainty, and because an appropriate diagnosis of SDB is important to decide which type of positive pressure treatment is better adapted to the patient, exploring SDB in SCI should in our opinion also include at least a combination of Level III portable monitors (PG) and transcutaneous transcutaneous carbon dioxide ($PtcCO_2$). Measurement of $PtcCO_2$ is presently considered as a reliable surrogate marker of partial pressure of carbon dioxide ($PaCO_2$), at least when performed by experienced teams.[22] In the study presented in *Thorax*, mean/median SpO_2 is not provided and it is thus difficult to exclude nocturnal alveolar hypoventilation, all the more since it has been recently demonstrated that only very conservative SpO_2 thresholds can reliably exclude nocturnal hypoventilation in neuromuscular patients.[23]

Finally, one out of five patients in the validation sample were misclassified (9 false positives and 12 false negatives). Considering the burden related to CPAP treatment in patients with SCI, a more solid strategy seems warranted to confirm the diagnosis. As previously mentioned, adherence to treatment is at best average in SCI (50% to 63%)[2]; among other difficulties, nasal congestion (related to unopposed parasympathetic activity) decreases tolerance to CPAP. Conversely, given the high prevalence of OSA in this group and the negative predictive value of 76%, the proposed strategy is not appropriate to exclude OSA if the patient is symptomatic.

We agree with Graco and colleagues that PSG is indeed often difficult to implement in the general population, and even more in patients with SCI. Sleep studies using Level III portable monitors (PG) are easier to perform and now widely available at reasonable costs. Strategies using PG are accepted as non-inferior to PSG in diagnostic strategies in the general population,[24 25] in children,[26] in heart failure[27] or in severe neurological impairment such as multiple system atrophy.[28] In a population with such a high prevalence of SDB, PG with manual scoring of events has to be tested as another strategy than that suggested by Graco and colleagues, allowing to identify and quantify central events, and to improve diagnostic accuracy. Underdiagnosis of SDB with PG is however also possible,[29 30] and a negative PG with suggestive symptoms should be in indication for PSG.

Current knowledge in OSA tends to show that diagnosing OSA must not aim to detect all prevalent cases, but should rather focus on subjects most likely to benefit from treatment either because they are clearly symptomatic or because of significant comorbidities. These are the patients who are more likely to improve their quality of life and symptoms under treatment. Comparing the proposed questionnaire and pulse oximeter-based strategy with a symptom-focused use of Level III portable monitors (PG) and transcutaneous CO_2, leaving PSG to symptomatic unresolved cases warrants further trials with a patient-oriented outcome as a primary outcome.

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