

3. Latest Real World Evidence - Obstructive (OSA) and co-existing Central and Obstructive sleep apnea (CSA-OSA) phenotypes in real-world data

In blog 2 of this series we explored the current understanding of OSA and CSA reported prevalence, software management detection of these events and tailoring treatment parameters based on remote monitoring data. In this 3rd. blog of these series we want to share with you the results of this "Real World Study" by Key Opinion Leader's (KOL's) Pepin et al 2024 1.

The prevalence of CSA in our previous blog was reported to be 5-10% in the ERJ by Randerath et al 2024, however, the authors acknowledged that the prevalence of CSA may be underestimated as epidemiological data are largely based on the AASM reporting criteria 2.

This large real world study was conducted in > 2400 patients referred with suspicion of sleep apnoea. The authors systematically distinguished central versus obstructive hypopneas to define OSA, CSA and coexisting CSA-OSA. Their results report that when CSA was defined by the proportion of central apnoeas (and hypopneas were considered obstructive by default), the prevalence of CSA was 4.59 % (co-existing CSA-OSA: 11.03 %, and OSA: 84.37 %).

When the distinction between obstructive and central hypopneas was used to classify the sleep disordered breathing, the prevalence of CSA was fourfold higher at 19.69 %, indicating that 1 in 5 of these individuals may have CSA, which is a higher prevalence than previously reported. This raises the issue of how important this for sleep medicine clinicians is and how they manage residual central hypopnoeas in their patients.

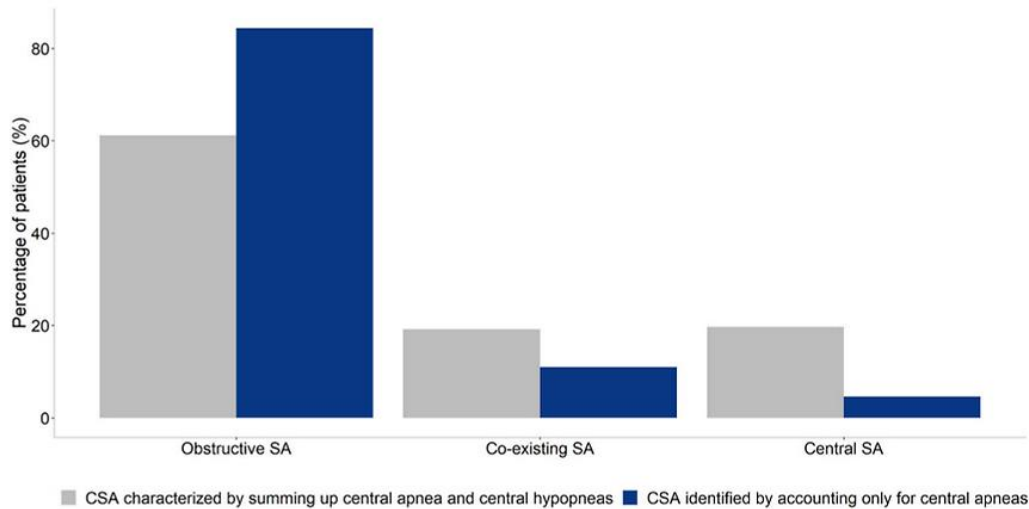


Fig. 1. Prevalence of the different subgroups and scoring rules.

2. [Data from Pepin et al 2024 https://doi.org/10.1016/j.sleep.2024.09.040](https://doi.org/10.1016/j.sleep.2024.09.040)

Pepin et al 2024 highlight crucial differences between reporting of CSA, OSA, and the combined condition CSA-OSA. Does this research, based on a large real-world patient dataset, underscore the importance of accurately differentiating central and obstructive hypopneas during polysomnography (PSG) scoring?

Then following on from this, when patients commence CPAP therapy with remote monitoring, current devices vary significantly on their reporting of residual central apnoeas and hypopnoeas as has been shown by Lebret et al at the ERS 2024, who found that only a limited number of devices were able to categorise hypopnoeas with poor detection of central hypopnoea in the four of the five CPAP devices tested (Article in Press).

The differences between CPAP device reporting central apnoea and hypopnoeas may be explained by different algorithms present in various manufacturers devices. "Is what is being reported what is actually happening in real life". Do all therapy devices detect and report central apnoea and hypopnoeas?

Graphical abstract of Pepin et al 2024 show that OSA and CSA are treated differently highlighting that CSA have a higher burden of comorbidities.

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Hypopnea characterization influences sleep apnea diagnosis and better define central sleep apnea prevalence and specific phenotype

Methods

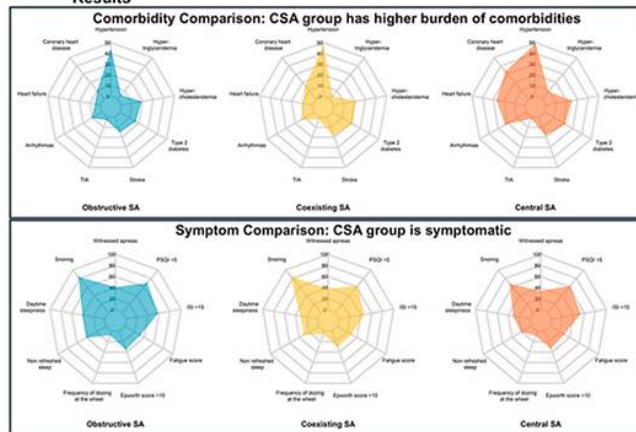
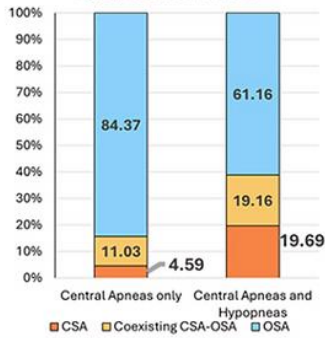
The prevalence of central sleep apnea (CSA) was examined in 2,400 patients referred to the sleep lab for suspicion of sleep apnea. In patients with apnea hypopnea index (AHI) was ≥ 15 /hour, 2 methods to determine CSA burden were used to assign the sleep apnea (SA) group:

1. Obstructive sleep apnea (OSA) if the percent of central apneas was $< 20\%$ of AHI, CSA if the percent of central apneas was $> 50\%$ of AHI, or co-existing CSA-OSA if the percent of central apneas was $20\%-50\%$ of AHI.
2. Like the first method, however, the number of central apnea + central hypopnea events was compared to AHI.

Using the CSA definition including central hypopneas, the profiles of the 3 sleep apnea (SA) cohorts were then compared.

Results

CSA diagnosis was 4x higher using central hypopneas: Only 4.59% of patients were defined as CSA when ignoring hypopnea class, compared to 19.69% when accounting for hypopnea classification.



Conclusion

Central sleep apnea prevalence is severely underestimated when counting hypopneas as obstructive events. Central sleep apnea patients are suffering from more cardiovascular and metabolic comorbidities than OSA patients and experience a similar symptomatic burden. Correct hypopnea scoring during PSG is important for proper therapeutic decision and therapy success.

These findings may have implications for manufacturers of sleep apnoea devices and sleep clinicians. Firstly, CPAP/APAP device algorithms report residual central apnoea and hypopnoeas differently as has been demonstrated in a recent study by Midelet et al 2021 in 3102 patients 3. and the Lebret et al 2024 study (In Press). Midlet et al 2021 found that the residual AHI reported by one CPAP brand was significantly lower than the residual AHI reported by other CPAP brands. They confirmed that statistically significant differences exist between CPAP brands when reporting residual AHI (Including central hypopnoeas) and this discrepancy may be clinically relevant in a subgroup of individuals. The recent data presented by Lebret et al 2024 (In Press) also found wide variation between devices reporting residual central apnoea and hypopnoeas.

A recent publication by Kundel et al 2024 provides and expert panel review on CSA. The panel emphasises the need for comprehensive studies on the clinical implications of CSA, distinguishing between central and obstructive hypopneas, and developing standardised diagnostic protocols. They advocate for improved endo-phenotyping and further research on combination therapies and nocturnal supplemental oxygen, along with comparative effectiveness trials to enhance therapeutic outcomes in CSA 4.

Clinicians should consider CPAP/APAP devices that accurately report residual central apnoeas and hypopneas, as highlighted by Pepin et al's study. A nuanced treatment approach is necessary, considering sleep apnoea type, comorbidities, and patient experiences. The study advocates for precise, personalised diagnosis and management of sleep apnoea 1.

Modern CPAP devices provide advanced features like improved event detection, accurate leakage compensation, refined event classification, automatic pressure adjustments, and remote monitoring for more precise management. They can detect subtle breathing irregularities and optimise therapy automatically. The issue lies not in technological capability but in consistent clinical implementation. Finally, recently published French recommendations suggest that CPAP devices censoring central events and/or reports censoring central hypopneas should not be used in patients with central events on the initial diagnostic test 5.

In blog 4 of these series we will discuss that CSA is more prevalent in the real-life setting. Pepin et al 2024 exposes a significant disconnect: we possess the technology to precisely diagnose different types of sleep apnoea, yet we aren't consistently using it. This can lead to a significant undercounting of CSA, a condition often misdiagnosed as OSA or a mixed apnoea type. This misdiagnosis may have clinical consequences, as treatment effectiveness may vary significantly in people with CSA phenotypes.

1. [Multidimensional phenotyping to distinguish among central \(CSA\), obstructive \(OSA\) and co-existing central and obstructive sleep apnea \(CSA-OSA\) phenotypes in real-world data \(sciencedirectassets.com\)](#)
2. [Central sleep apnoea: not just one phenotype \(ersjournals.com\)](#)
3. [Apnea-hypopnea index supplied by CPAP devices: time for standardization? - PubMed \(nih.gov\)](#)
4. [kundel-et-al-2024-insights-recommendations-and-research-priorities-for-central-sleep-apnea-report-from-an-expert-panel \(1\).pdf](#)
5. **Launois-Rollinat S, Gentina T, Meslier N, Portel L, Priou P, Gagnadoux F, Jaffuel D. [French consensus on central sleep apnea and hypopnea syndrome \(SAHCS\) in adults. Part 1: Definitions and Diagnostic Modalities - ScienceDirect. https://doi.org/10.1016/j.msom.2023.12.188](https://doi.org/10.1016/j.msom.2023.12.188)**