Apnea-hypopnea index in sleep studies and the risk of over-simplification

ABSTRACT

According to recent reports, sleep disorders affect 30% of the adult population and 5-10% of children. Obstructive Sleep Apnea Hypopnea Syndrome (OSA) has a considerable epidemiological impact and demand for consultation is growing in our community. Therefore, it is necessary to know the principles of interpretation of diagnostic methods. A suspicion of OSA requires confirmation. According to the guidelines of the Argentine Association of Respiratory Medicine, polysomnography (PSG) is the gold standard for OSA diagnosis, while home sleep testing (HST) can be accepted as a comparatively effective method depending on the clinical situation of the patient. This article questions the use of AHI (apnea-hypopnea index) as the only measurement needed to diagnose OSA and assess its severity. In fact, it is surprising that, despite the large mass of data analyzed during sleep studies, current practices only focus on AHI. More than four decades have passed since OSA was first described. Our tendency to oversimplify complex conditions may prevent us from gaining a deeper and more thorough understanding of OSA. The development and validation of OSA severity scoring systems based on multiple parameters is still a pending issue.

Keywords: Sleep Apnea Syndromes; Severity of Illness Index; Sleep Disorder.
INTRODUCTION

According to recent reports, sleep disorders affect 30% of adults and 5-10% of children. The current obesity epidemic could increase such percentages. In Europe, OSA accounts for 30% of consultations to pulmonologists. In our community consultations due to OSA are also increasing.

According to American Academy of Sleep Medicine guidelines, polysomnography (PSG) is the gold standard for diagnosing OSA, while home sleep testing (HST) can be considered a comparatively effective method (but not an exact equivalent) depending on the clinical situation of the patient (i.e. symptoms, discomfort, risk, history of associated conditions). Such context leads us to ask: How must we interpret information from sleep studies?

Early PSG findings (in the late '70s) identified pauses of breathing (apnea) based on changes in inhaled/exhaled air temperature and resulting damages: fragmented sleep (electroencephalography) and cardiovascular instability (changes in blood pressure or heart rate), which cause sleepiness and The definition of the disease and normal cutoffs are of those time.

Apnea Index (AI) became the first indicator to define OSA since obstructive apnea is its most distinctive element. Subsequent improvements in devices and methods (flow/pressure cannulas) to measure airway collapse added to the complexity of classifying and quantifying obstruction events. Partial collapse (hypopnea) has a similar effect (though it is still unknown to what extent), causing arousals and/or O₂ desaturation. As the effect of partial collapse became recognized, it was included in the definition of OSA creating the AHI index which we now use.

The description of obstructive events should be, in theory, a simple procedure just by following the guidelines for the interpretation of sleep studies, which are updated as new knowledge becomes available. However, the definition of hypopnea remains a major challenge, since there is no consensus over the level of airflow reduction necessary to classify an event as hypopnea. Even in this scenario, physicians make an extensive and oversimplified use of AHI assuming the biological effects of apnea and hypopnea are basically the same and analysis of sleep studies focuses on improving AHI accuracy and defining events with demonstrable consequences in artifact-free recordings.

Some definitions are based only on events associated with significant O₂ desaturation and others try to adjust for underlying variations considering only those respiratory events that cause a physiological response (e.g. micro-arousals). The use of simplified diagnostic strategies has entailed the description of arousal surrogates (movements, change in heart rate or arterial tone) as signs that supplement AHI. Ho et al. studied the impact of different definitions of hypopneas (associated with different thresholds of oxygen desaturation and arousal), in a detachment from the original Sleep Heart Health Study in >6000 subjects and they show that three methods of scoring hypopneas yielded significantly different estimates of the apnea-hypopnea index (AHI), although the relative difference is reduced in severe disease.

Since the original description of AHI, a large body of evidence has linked OSA with clinical consequences like; excessive sleepiness, deterioration in quality of life, traffic accidents, diabetes and insulin resistance, hypertension (HT), stroke, heart failure, and mortality. Almost all studies use AHI as an indicator of exposure to respiratory events during sleep. In addition, intervention studies (CPAP) have shown that OSA treatment is associated with better outcomes when AHI goes down.

It is surprising that despite the large mass of data analyzed during sleep studies, OSA severity rely on AHI. Even though AHI is widely used as a predictor of OSA-related complications, its use has several limitations. First, AHI gives us an idea of the frequency of respiratory events during sleep time, but does not allow us to know the magnitude of oxygen desaturation, which may affect other organs and should be included and interpreted in PSG or HST reports. OSA is a model of intermittent hypoxemia characterized by cycles of hypoxia and re-oxygenation of short duration (15 to 120 seconds) occurring over 6 to 8 hours of sleep for many years. Both animal and human models of chronic intermittent hypoxemia appear to show a significant role in the pathogenesis of OSA comorbidity, including hypertension, cardiovascular events, diabetes, neurocognitive impairments and cancer.

In order to determine what degree of hypoxemia is associated with increased morbidity and mortality in patients with OSA, it is necessary to establish whether different patterns of oxygen desaturation independently predict the development of cardiovascular events and another outcome of interest. In that sense, several publications have observed that patients with OSA the risk of cardiovascular events, recurrence of atrial fibrillation after successful cardioversion, sudden death, and neurocognitive impairments, were observed in those patients with a greater degree of oxygen desaturation.
Second, AHI does not consider the duration of apneas/hypopneas. It is not reasonable to assume that a 10 seconds (s) apnea/hypopnea is equivalent to 30 or 60 s event, in terms of hypoxemia or hypcapnia, development of negative intrathoracic pressure, changes in heart rate or blood pressure and arousal reaction. Third, it is also important to note that AHI do not consider the distribution of nocturnal events. Thus, data related to supine/non-supine AHI or AHI in REM/NREM sleep are reported to illustrate the heterogeneity in the distribution of respiratory events.

Finally, two OSA patients with a similar AHI may differ in terms of severity depending on their age, occupation, daytime symptoms and associated conditions. Likewise, two individuals with the same AHI may present different levels of tolerance and different clinical manifestations. New evidence suggests treatment benefits are not the same for patients with a high AHI and no sleepiness and other published data highlight the impact of hypoxemia on cardiovascular outcomes.

It is necessary to develop a score to assess OSA severity and prognosis which, besides AHI and its different variables (total AHI, supine, non-supine, REM/NREM), should include type and duration of respiratory events, O₂ desaturation index (ODI3/4%, SO₂ mean, Time <90%), symptoms (e.g. sleepiness, which sometimes is difficult to measure objectively), body mass index (BMI), and associated comorbidities, since obese and overweight individuals have been reported to have higher mortality rates. Additionally, the O₂ saturation behavior may not be the same as that of the respiratory flow when the BMI is increased.

Is it possible to consider the following two cases as being equivalent? (1) an individual with OSA with an AHI of 19 events/hour, 34 kg/m² BMI, T90 < at 10% of sleep time, daytime sleepiness, and hypertension; and (2) an individual with an AHI of 19 events/hour, 26 kg/m² BMI, T90 > at 1% of sleep time, without daytime sleepiness and without hypertension. The answer seems obvious. In terms of AHI, both are moderate OSA cases. However, the first one seems more severe (higher BMI, more hypoxemia, and more risk of pulmonary hypertension). Our challenge for the future is to stratify risk and prognosis using sleep studies, BMI, and clinical examination.

Night-to-night AHI variability (a phenomenon identified three decades ago) may result in one patient having a normal PSG one night and mild-to-moderate OSA on a different night. These changes could derive from sleep position, changes in the pharynx, and changes in each night’s REM/NREM ratio. Biological parameters (e.g. changes in nasal resistance, medication, alcohol and drug abuse) may contribute to this variability. However, the pragmatic application of this information is not fully understood yet.

Another source of error to be considered is inter-observer variability in the identification of hypopnea events. It is estimated that 10% of patients evaluated using PSG could fall into the false negative category for OSA. There is also evidence that the respiratory phenomenon is dynamic, and that there are patients who present central phenotypes that after acute episodes change to obstructive or vice versa.

Also, since the estimation of AHI by HST is based on total recording time, rather than total sleep time, AHI is usually 15% lower than PSG AHI, which may result in an underestimation of severity. In this context, oximetry indicators (O₂ desaturation/hour, time <90%) become especially important. Thus, physicians’ decisions may vary depending on PSG or HST values. A European multicenter study that assessed indication of CPAP based on PSG versus HST (respiratory polygraphy) findings in patients at risk for OSA showed remarkable consistency for >20/h AHIs, but a 20% inconsistency for <15/h AHIs.

In summary, though AHI has been extensively used for OSA diagnosis, it entails many limitations when it comes to assessing severity. A high AHI can identify the affected population but intermediate-risk groups are usually left at the mercy of clinicians’ management skills. The development and validation of OSA severity scoring systems based on multiple parameters is still a pending issue.

REFERENCES

1. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol. 2013;177(9):1006-14. PMID: 23589584 DOI: http://dx.doi.org/10.1093/aje/kws342
2. Tufik S, Santos-Silva R, Taldei JA, Bittencourt LR. Obstructive sleep apnea syndrome in the Sao Paulo Epidemiologic Sleep Study, Sleep Med. 2010;11(5):441-6. DOI: http://dx.doi.org/10.1016/j.sleep.2009.10.005
3. Goodwin JL, Vasquez MM, Silva GE, Quan SF. Incidence and remission of sleep-disordered breathing and related symptoms in 6- to 17-year old children—the Tucson Children’s Assessment of Sleep Apnea Study. J Pediatr. 2010;157(1):57-61. PMID: 20304429 DOI: http://dx.doi.org/10.1016/j.jpeds.2010.01.033
4. World Health Organization. Report of WHO Consultation (WHO Technical Report Series) Obesity: preventing and managing the global epidemic. Online supplement [cited 2018 Feb 5]. Available from: http://www.who.int/nutrition/publications/obesity/WHO_TRS_894/en/
5. Elgart J, Pfirter G, Gonzalez L, Caporale J, Cormillot A, Chiappe ML, et al. Obesity in Argentina: epidemiology, morbimortality and economic impact. Rev Argent Salud Publica. 2010;1(5):6-12.
6. Masa Jiménez JF, Barbé Ilsa F, Capote Gil F, Chiner Vives E, Díaz de Atauri J, Durán Cantolla J, et al.; Working Group. Recursos y demoras en el diagnóstico del síndrome de apneas-hipopneas durante el sueño (SAHS). Arch Bronconeumol. 2007;43(4):188-98. DOI: http://dx.doi.org/10.1157/13100537
7. Rosen DM, Kirsch DB, Chevirin RD, Carden KA, Ramar K, Aurora RN, et al.; American Academy of Sleep Medicine Board of Directors. Clinical Use of a Home Sleep Apnea Test: An American Academy of Sleep Medicine Position Statement. J Clin Sleep Med. 2017;13(10):1205-7. DOI: http://dx.doi.org/10.5664/jcsm.6774
8. Kapur VK, Aueley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, et al. Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med. 2017;13(3):479-504. DOI: http://dx.doi.org/10.5664/jcsm.5696
9. Guilleminault C, Tilkian A, Dement WC. The sleep apnea syndromes. Annu Rev Med. 1976;27:465-84. PMID: 180875 DOI: http://dx.doi.org/10.1146/annurev.me.27.020176.002341
10. Hudgel DW. “Apnea index”: need for improving the description of respiratory variability during sleep. Am Rev Respir Dis. 1986;133(4):706-9. PMID: 2083746
11. Gould GA, Whyte KF, Rhind GB, Airlie MA, Canterall JR, Shapiro CM, et al. The sleep hypopnoea syndrome. Am Rev Respir Dis. 1988;137(4):895-8. PMID: 3354998 DOI: http://dx.doi.org/10.1164/ajrccm/137.4.895
12. Moser NJ, Phillips BA, Berry DT, Harribison L. What is hypopnoea, anyway? Chest. 1994;105(2):426-8. PMID: 8306740
13. Redline S, Sanders M. Hypopnea, a floating metric: implications for prevalence, morbidity estimates, and case finding. Sleep. 1997;20(12):1209-17. DOI: http://dx.doi.org/10.1093/sleep/20.12.1209
14. Rueland WR, Rochford PD, O'Donoghue FJ, Pierce RJ, Singh P, Thorn K, et al. The new AASM criteria for scoring hypopneas: impact on the apnoea-hypopnoea index. Sleep. 2009;32(2):150-7. DOI: http://dx.doi.org/10.1093/sleep/32.2.150
15. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, et al.; Task Force of the American Academy of Sleep Medicine. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012;8(5):597-619.
16. Rapoport DM. POINT: Is the Apnoea-Hypopnoea Index the Best Way to Quantify the Severity of Sleep-Disordered Breathing? Yes. Chest. 2016;149(1):14-6. PMID: 26181884 DOI: http://dx.doi.org/10.1378/chest.15-1319
17. Ho Y, Crainiceanu CM, Punjabi NM, Redline S, Gottlieb DJ. Calibration Model for Apnea-Hypopnea Indices: Impact of Alternative Criteria for Hypopneas. Sleep. 2015;38(12):1887-92. DOI: http://dx.doi.org/10.1093/sleep/5234
18. Vijayan VK. Morbidities associated with obstructive sleep apnea. Expert Rev Respir Med. 2012;6(5):557-66. DOI: http://dx.doi.org/10.1586/ers.12.44
19. Mannarino MR, Di Filippo F, Pirro M. Obstructive sleep apnea syndrome. Eur J Intern Med. 2012;23(7):586-93. DOI: http://dx.doi.org/10.1016/j.ejim.2012.09.004
20. US National Library of Medicine. Opioid use disorder and sleep apnea. National Library of Medicine. 2018;11(1):45-48
21. Usmani ZA, Chai-Coetzer CL, Antic NA, McEvoy RD. Obstructive sleep apnoea in adults. Postgrad Med J. 2011;87(1049):148-56. PMID: 21466350 DOI: http://dx.doi.org/10.1136/postgradmedj-2012-131340
22. Heatley EM, Harris M, Battersby M, McEvoy RD, Chai-Coetzer CL, Antic NA. Obstructive sleep apnoea in adults: a common chronic condition in need of a comprehensive chronic condition management approach. Sleep Med Rev. 2013;17(7):349-55. DOI: http://dx.doi.org/10.1016/j.smr.2012.09.004
23. Gami AS, Howard DE, Olsson EF, Somers VK. Day-night pattern of sudden death in obstructive sleep apnea. N Engl J Med. 2005;352(12):1206-14. DOI: http://dx.doi.org/10.1056/NEJMoa041832
24. Yaffe K, Lafran AM, Harrison SL, Redline S, Spira AP, Ensrud KE, et al. Sleep-disordered breathing, hypnotics, and risk of cognitive impairment and dementia in older women. JAMA. 2011;306(6):613-9. PMID: 21828324 DOI: http://dx.doi.org/10.1001/jama.2011.1115
25. Martinez-Garcia MA, Duran-Cantolla J, Montserrat JM. [Sleep apnea-hypopnea syndrome in the elderly]. Arch Bronconeumol. 2010;46(9):479-88. Spanish. PMID: 20580480
26. McEvoy RD, Antic NA, Heely E, Luo Y, Ou Q, Zhang X, et al.; SAVE Investigators and Coordinators. CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea. N Engl J Med. 2016;375(10):919-31. PMID: 27571048 DOI: http://dx.doi.org/10.1056/NEJMoa160599
27. Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M, Martínez-Alonso M, Carmona C, Barceló A, et al; Spanish Sleep and Breathing Network. Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. JAMA. 2012;307(20):2161-8. PMID: 22618923
28. Heintz R, Var S, Marques-Vidal P, Martí-Soler H, Andries D, Tobbback N, et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. Lancet Respir Med. 2015;3(4):310-8. DOI: http://dx.doi.org/10.1016/S2213-2600(15)00043-0
29. Kendzerska T, Gershon AS, Hawker G, Leung RS, Tomlinson G. Obstructive sleep apnea and risk of cardiovascular events and all-cause mortality: a decade-long historical cohort study. PLoS Med. 2014;11(2):e1001599.
30. Valsecchi G, Bubademeza MA, Gui M. Association of sleep time in supine position with apnoea-hypopnoea index as evidenced by successive polysomnography. Sleep. 2017;21(2):289-94. DOI: http://dx.doi.org/10.1001/sleep.sjx014-0140-15
31. Global BMI Mortality Collaboration, Di Angelantonio E, Bhupathi SwN, Wormser D, Gao P, Kaptoge S, Berrington de Gonzalez A, et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. Lancet. 2016;388(10046):776-86. DOI: http://dx.doi.org/10.1016/S0140-6736(16)30175-1
32. Le Bon O, Hoffmann G, Tecco J, Stamer I, Noseda A, Pecl I, et al. Mild to moderate sleep respiratory events: one negative night may not be enough. Chest. 2008;133(5):535-9. DOI: http://dx.doi.org/10.1378/chest.118.2.353
33. Masa JF, Corral J, Bousi J, Somers VK. Sleep apnea-hypopnea syndrome and cardiovascular disease: an outcome-based definition of hypopneas. Am J Respir Crit Care Med. 2008;177(10):1150-5. PMID: 18276938 DOI: http://dx.doi.org/10.1164/rccm.200712-1884OC
34. Kuragala R, Murali NS, Friedman PA, Ammass GM, Gersh BJ, Ballman KV, et al. Obstructive sleep apnea and the recurrence of atrial fibrillation. Circulation. 2003;107(20):2589-94. PMID: 12743002
35. Gami AS, Howard DE, Olsson EF, Somers VK. Day-night pattern of sudden death in obstructive sleep apnea. N Engl J Med. 2005;352(12):1206-14. DOI: http://dx.doi.org/10.1056/NEJMoa041832
36. Marshall NS, Wong KK, Cullen SR, Knuiman MW, Grunstein RR. Sleep apnea and 20-year follow-up for all-cause mortality, stroke, and cancer incidence and mortality in the Busselton Health Study cohort. J Clin Sleep Med. 2014;10(4):355-62. DOI: http://dx.doi.org/10.5066/jcsm.3600
37. Punjabi NM, Newman AB, Young TB, Resnick HE, Sanders MH. Sleep-disordered breathing and cardiovascular disease: an outcome-based definition of hypopneas. Am J Respir Crit Care Med. 2008;177(10):1150-5. PMID: 18276938 DOI: http://dx.doi.org/10.1164/rccm.200712-1884OC
38. Borsini, et al. Sleep Sci. 2018;11(1):45-48