Articles of the Month – November 2020

Diagnostics and consequences of untreated disease

J Sleep Res 2020 Aug;29(4) Epub 2020 May 14.
https://onlinelibrary.wiley.com/doi/full/10.1111/jsr.13066
On the rise and fall of the apnea-hypopnea index: A historical review and critical appraisal - PubMed (nih.gov)

On the rise and fall of the apnea-hypopnea index: A historical review and critical appraisal

Dirk A Pevernagie[1,2], Barbara Gnidovec-Strazisar[3], Ludger Grote[4], Raphael Heinzer[5], Walter T McNicholas[6], Thomas Penzel[7,8], Winfried Randerath[9,10], Sophia Schiza[11], Johan Verbraecken[12], Erna S Arnardottir[13,14]

Abstract

The publication of "The Sleep Apnea Syndromes" by Guilleminault et al. in the 1970s hallmarked the discovery of a new disease entity involving serious health consequences. Obstructive sleep apnea was shown to be the most important disorder among the sleep apnea syndromes (SAS). In the course of time, it was found that the prevalence of obstructive sleep apnea reached the proportions of a global epidemic, with a major impact on public health, safety and the economy. Early on, a metric was introduced to gauge the seriousness of obstructive sleep apnea, based on the objective measurement of respiratory events during nocturnal sleep. The apnea index and later on the apnea-hypopnea index, being the total count of overnight respiratory events divided by the total sleep time in hours, were embraced as principle measures to establish the diagnosis of obstructive sleep apnea and to rate its severity. The current review summarises the historical evolution of the apnea-hypopnea index, which has been subject to many changes, and has been criticised for not capturing relevant clinical features of obstructive sleep apnea. In fact, the application of the apnea-hypopnea index as a continuous exposure variable is based on assumptions that it represents a disease state of obstructive sleep apnea and that evocative clinical manifestations are invariably caused by obstructive sleep apnea if the apnea-hypopnea index is above diagnostic threshold. A critical appraisal of the extensive literature shows that both assumptions are invalid. This conclusion prompts a reconsideration of the role of the apnea-hypopnea index as the prime diagnostic metric of clinically relevant obstructive sleep apnea.

EADSM comment:
Open access article. Very interesting and important knowledge about the indices we use to assess sleep apnea. At first a comprehensive historical overview and then critical comments on the value of indices and possible ways forward. Highly recommended reading

Southwest J Pulm Crit Care 2020;21(4):86-103.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7644074/

The Association Between Obstructive Sleep Apnea Defined by 3 Percent Oxygen Desaturation or Arousal Definition and Self-Reported Cardiovascular Disease in the Sleep Heart Health Study

Stuart F Quan [1 2], Rohit Budhiraja [1], Sogol Javaheri [1], Sairam Parthasarathy [2], Richard B Berry [3]

Abstract

Background: Studies have established that OSA defined using a hypopnea definition requiring a ≥4% oxygen desaturation (AHI4%) is associated with cardiovascular (CVD) or coronary heart (CHD) disease. This study determined whether OSA defined using a hypopnea definition characterized by a ≥3% oxygen desaturation or an arousal (AHI3%A) is associated with CVD/CHD.

Methods: Data were analyzed from 6307 Sleep Heart Health Study participants who had polysomnography. Self-reported CVD included angina, heart attack, heart failure, stroke, previous coronary bypass surgery or angioplasty. Self-reported CHD included the aforementioned conditions but not stroke or heart failure. The association between OSA and CVD/CHD was examined using logistic regression models with stepwise inclusion of demographic, anthropometric, social/behavioral and co-morbid medical conditions. A parsimonious model in which diabetes and hypertension were excluded because of their potential to be on the causal pathway between OSA and CVD/CHD also was constructed.

Results: For CVD, the odds ratios and 95% confidence intervals for AHI3%A ≥30/hour were 1.39 (1.03-1.87) and 1.45 (1.09-1.94) in the fully adjusted and parsimonious models. Results for CHD were 1.29 (0.96-1.74) and 1.36 (0.99-1.85). In participants without OSA according to more stringent AHI4% criteria but with OSA using the AHI3%A definition, similar findings were observed.

Conclusion: OSA defined using an AHI3%A is associated with both CVD and CHD. Use of a more restrictive AHI4% definition will misidentify a large number of individuals with OSA who have CVD or CHD. These individuals may be denied access to therapy, potentially worsening their underlying CVD or CHD.

EADSM comment:

Another open access article that puts more light into the question of the puzzle on how to define obstructive sleep apnea and identify consequences of this disease.

J Clin Sleep Med. 2020 Jun 15;16(6):889-898.
Mild obstructive sleep apnea increases hypertension risk, challenging traditional severity classification | Journal of Clinical Sleep Medicine (doi.org)

Mild obstructive sleep apnea increases hypertension risk, challenging traditional severity classification

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Abstract

Study objectives: The association of mild obstructive sleep apnea (OSA) with important clinical outcomes remains unclear. We aimed to investigate the association between mild OSA and systemic arterial hypertension (SAH) in the European Sleep Apnea Database cohort.
Methods: In a multicenter sample of 4,732 participants, we analyzed the risk of mild OSA (subclassified into 2 groups: $mild_{AHI\ 5-<11/h}$ (apnea-hypopnea index [AHI], 5 to <11 events/h) and $mild_{AHI\ 11-<15/h}$ (AHI, ≥11 to <15 events/h) compared with nonapneic snorers for prevalent SAH after adjustment for relevant confounding factors including sex, age, smoking, obesity, daytime sleepiness, dyslipidemia, chronic obstructive pulmonary disease, type 2 diabetes, and sleep test methodology (polygraphy or polysomnography).
Results: SAH prevalence was higher in the $mild_{AHI\ 11-<15/h}$ OSA group compared with the $mild_{AHI\ 5-<11/h}$ group and nonapneic snorers (52% vs 45% vs 30%; P < .001). Corresponding adjusted odds ratios for SAH were 1.789 ($mild_{AHI\ 11-<15/h}$; 95% confidence interval [CI], 1.49-2.15) and 1.558 ($mild_{AHI\ 5-<11/h}$; 95%, CI, 1.34-1.82), respectively (P < .001). In sensitivity analysis, $mild_{AHI\ 11-<15/h}$ OSA remained a significant predictor for SAH both in the polygraphy (odds ratio, 1.779; 95% CI, 1.403-2.256; P < .001) and polysomnography groups (odds ratio, 1.424; 95% CI, 1.047-1.939; P = .025).
Conclusions: Our data suggest a dose-response relationship between mild OSA and SAH risk, starting from 5 events/h in polygraphy recordings and continuing with a further risk increase in the 11- to <150-events/h range. These findings potentially introduce a challenge to traditional thresholds of OSA severity and may help to stratify participants with OSA according to cardiovascular risk.

EADSM comment:
Clear example of the first article above showing that systemic hypertension increases, also in mild sleep apnea and that our present subdivision into disease severities can be questioned. The findings of this article are in line with those of Peppard et al. 2000 in NEJM from the Wisconsin Sleep Cohort study, where they found OR=1.4 for AHI 0.1-4.9, OR=2 for AHI 5-14.9 and OR=2.9 for AHI≥15 compared to no sleep apneas, AHI 0.

Sleep Breath. 2020 Dec;24(4):1759-1765.
https://link.springer.com/article/10.1007/s11325-020-02015-2

Clinical utility of the Epworth sleepiness scale

Nathan A Walker [1], Jag Sunderram [2], Peng Zhang [3], Shou-En Lu [3], Matthew T Scharf [4 5]

Abstract

Purpose: The Epworth sleepiness scale (ESS) is a widely used tool which has been validated as a measure of sleepiness. However, the scores within individual patients referred for clinical sleep services vary considerably which may limit the clinical use of the ESS. We sought to determine the test-retest reliability of the ESS if scores were classified as either normal or sleepy.

Methods: We measured the ESS in patients presenting to our sleep center at a clinical visit and again when a sleep study was done. Demographic and clinical information was extracted from the electronic medical record.

Results: Average ESS scores were similar on 2 administrations, mean (SD) of 9.8 (5.4) and 10.2 (6.2). Bland-Altman analysis showed upper and lower limits of agreement of 7.5 and -6.7, respectively. No demographic or clinical variables were identified which contributed to the intra-individual variability. Of the patients who presented with an initial ESS < 11, 80% had a second ESS < 11. Of the patients who presented with an initial ESS ≥ 11, 89% had a second ESS ≥ 11. Cohen's kappa for the two administrations of the ESS was 0.67 (95% CI of 0.51-0.83). Using previously published reports, we calculated Cohen's kappa for polysomnographic determination of the apnea-hypopnea index (AHI) with values ranging from 0.26 to 0.69.

Conclusions: Individual ESS scores varied considerably within individual patients, but with classification into either normal or sleepy, the test-retest reliability was substantial and in line with other clinical measures including polysomnographic determination of the AHI.

EADSM comment: For all who are disturbed about the intra-individual variability of the ESS score. This article finds that the score is fairly useful to subdivide into those who have a score < 11 and those who have above this value and are really sleepy.

2020 Nov 3;11:CD013449.
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013449.pub2/full

Myofunctional therapy (oropharyngeal exercises) for obstructive sleep apnoea

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Abstract

Background: Obstructive sleep apnoea (OSA) is a syndrome characterised by episodes of apnoea (complete cessation of breathing) or hypopnoea (insufficient breathing) during sleep. Classical symptoms of the disease - such as snoring, unsatisfactory rest and daytime sleepiness - are experienced mainly by men; women report more unspecific symptoms such as low energy or fatigue, tiredness, initial insomnia and morning headaches. OSA is associated with an increased risk of occupational injuries, metabolic diseases, cardiovascular diseases, mortality, and being involved in traffic accidents. Continuous positive airway pressure (CPAP) - delivered by a machine which uses a hose and mask or nosepiece to deliver constant and steady air pressure- is considered the first treatment option for most people with OSA. However, adherence to treatment is often suboptimal. Myofunctional therapy could be an alternative for many patients. Myofunctional therapy consists of combinations of oropharyngeal exercises - i.e. mouth and throat exercises. These combinations typically include both isotonic and isometric exercises involving several muscles and areas of the mouth, pharynx and upper respiratory tract, to work on functions such as speaking, breathing, blowing, sucking, chewing and swallowing.

Objectives: To evaluate the benefits and harms of myofunctional therapy (oropharyngeal exercises) for the treatment of obstructive sleep apnoea.

Search methods: We identified randomised controlled trials (RCTs) from the Cochrane Airways Trials Register (date of last search 1 May 2020). We found other trials at web-based clinical trials registers.

Selection criteria: We included RCTs that recruited adults and children with a diagnosis of OSA.

Data collection and analysis: We used standard methodological procedures expected by Cochrane. We assessed our confidence in the evidence by using GRADE recommendations. Primary outcomes were daytime sleepiness, morbidity and mortality.

Main results: We found nine studies eligible for inclusion in this review and nine ongoing studies. The nine included RCTs analysed a total of 347 participants, 69 of them women and 13 children. The adults' mean ages ranged from 46 to 51, daytime sleepiness scores from eight to 14, and severity of the condition from mild to severe OSA. The studies' duration ranged from two to four months. None of the studies assessed accidents, cardiovascular diseases or mortality outcomes. We sought data about adverse events, but none of the included studies reported these. In adults, compared to sham therapy, myofunctional therapy: probably reduces daytime sleepiness (Epworth Sleepiness Scale (ESS), MD (mean difference) -4.52 points, 95% Confidence Interval (CI) -6.67 to -2.36; two studies, 82 participants; moderate-certainty evidence); may increase sleep quality (MD -3.90 points, 95% CI -6.31 to -1.49; one study, 31 participants; low-certainty evidence); may result in a

large reduction in Apnoea-Hypopnoea Index (AHI, MD -13.20 points, 95% CI -18.48 to -7.93; two studies, 82 participants; low-certainty evidence); may have little to no effect in reduction of snoring frequency but the evidence is very uncertain (Standardised Mean Difference (SMD) -0.53 points, 95% CI -1.03 to -0.03; two studies, 67 participants; very low-certainty evidence); and probably reduces subjective snoring intensity slightly (MD -1.9 points, 95% CI -3.69 to -0.11 one study, 51 participants; moderate-certainty evidence). Compared to waiting list, myofunctional therapy may: reduce daytime sleepiness (ESS, change from baseline MD -3.00 points, 95% CI -5.47 to -0.53; one study, 25 participants; low-certainty evidence); result in little to no difference in sleep quality (MD -0.70 points, 95% CI -2.01 to 0.61; one study, 25 participants; low-certainty evidence); and reduce AHI (MD -6.20 points, 95% CI -11.94 to -0.46; one study, 25 participants; low-certainty evidence). Compared to CPAP, myofunctional therapy may result in little to no difference in daytime sleepiness (MD 0.30 points, 95% CI -1.65 to 2.25; one study, 54 participants; low-certainty evidence); and may increase AHI (MD 9.60 points, 95% CI 2.46 to 16.74; one study, 54 participants; low-certainty evidence). Compared to CPAP plus myofunctional therapy, myofunctional therapy alone may result in little to no difference in daytime sleepiness (MD 0.20 points, 95% CI -2.56 to 2.96; one study, 49 participants; low-certainty evidence) and may increase AHI (MD 10.50 points, 95% CI 3.43 to 17.57; one study, 49 participants; low-certainty evidence). Compared to respiratory exercises plus nasal dilator strip, myofunctional therapy may result in little to no difference in daytime sleepiness (MD 0.20 points, 95% CI -2.46 to 2.86; one study, 58 participants; low-certainty evidence); probably increases sleep quality slightly (-1.94 points, 95% CI -3.17 to -0.72; two studies, 97 participants; moderate-certainty evidence); and may result in little to no difference in AHI (MD -3.80 points, 95% CI -9.05 to 1.45; one study, 58 participants; low-certainty evidence). Compared to standard medical treatment, myofunctional therapy may reduce daytime sleepiness (MD -6.40 points, 95% CI -9.82 to -2.98; one study, 26 participants; low-certainty evidence) and may increase sleep quality (MD -3.10 points, 95% CI -5.12 to -1.08; one study, 26 participants; low-certainty evidence). In children, compared to nasal washing alone, myofunctional therapy and nasal washing may result in little to no difference in AHI (MD 3.00, 95% CI -0.26 to 6.26; one study, 13 participants; low-certainty evidence).
Authors' conclusions: Compared to sham therapy, myofunctional therapy probably reduces daytime sleepiness and may increase sleep quality in the short term. The certainty of the evidence for all comparisons ranges from moderate to very low, mainly due to lack of blinding of the assessors of subjective outcomes, incomplete outcome data and imprecision. More studies are needed. In future studies, outcome assessors should be blinded. New trials should recruit more participants, including more women and children, and have longer treatment and follow-up periods.

EADSM comment: Comprehensive Cochrane review about the evidence for myofunctional therapy in OSA. Another article; by Kezirian et al. 2020 in AJRCCM (included in EADSM literature for July) defined the evidence based therapies for OSA that we have today and concluded that myofunctional therapy needed more evidence in order to be recommended for clinical practice. They wrote “Oral myofunctional therapy involves the selection from among a number of exercises based on assessment of a speech language pathologist, and published studies have not outlined a specific, uniform exercise protocol for OSA or a protocol that could guide exercise selection”. It seems clear that more knowledge is needed, before these types of therapies can be implemented in the clinic, based on evidence.

Sleep 2020 Nov 4;zsaa222.
Mandibular advancement splint response is associated with the pterygomandibular raphe | Sleep | Oxford Academic (oup.com)

Mandibular advancement splint response is associated with the pterygomandibular raphe

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Abstract

Mandibular advancement increases the lateral dimensions of the nasopharyngeal airway via a direct connection from the airway to the ramus of the mandible. The anatomical structure in this region is the pterygomandibular raphe, but a tendinous component is not always present. Whether tendon presence influences treatment outcome is unknown.

Study objectives: To investigate whether presence of tendinous pterygomandibular raphe could predict treatment outcome, and how it affects lateral wall mechanical properties.

Methods: 105 subjects with obstructive sleep apnoea completed detailed anatomical MRI with and without mandibular advancement. The study design was case control. Variables were compared between participants with and without the tendon present.

Results: Amount of maximum mandibular advancement decreased when pterygomandibular tendon was present (4.0 ± 1.2mm present versus 4.6 ± 1.4mm absent, p= 0.04). Pterygomandibular raphe tendon absent subjects had a lower post treatment apnea hypopnea index (16 ± 12 events/hour tendon present versus 9 ± 9 events/hour absent, p= 0.007) and were more likely to have complete response (63% versus 36%, p= 0.02). However, tendon absent subjects were more likely to not complete the study (χ 2 (3) =10.578, p= 0.014). Tendon absent subjects had a greater increase in midline antero-posterior airway diameter (1.6 ± 1.7 mm versus 0.6 ± 2.3 mm, p= 0.04).

Conclusion: When pterygomandibular raphe tendon is absent, treatment response and amount of maximum advancement improves, possibly at the expense of reduced splint tolerability. Tendon presence may help predict a group less likely to respond to mandibular advancement splint therapy.

EADSM comment: Interesting findings on new prediction possibilities for mandibular advancement devices, although not always clinically available. The findings might also give new insight into the mechanism of action of these devices.

Ear Nose Throat J
2020 Nov 4;145561320969251.

https://journals.sagepub.com/doi/full/10.1177/0145561320969251

Effectiveness of Continuous Positive Airway Pressure Versus Mandibular Advancement Device in Severe Obstructive Sleep Apnea Patients With Mandibular Retrognathia: A Prospective Clinical Trial

Haichun Lai[1], Wei Huang[1], Wei Chen[1], Desheng Wang[1]

Free article

Abstract

Aim: Some obstructive sleep apnea (OSA) patients may have mandibular retrognathia (ANB > 4.7° and SNB < 76.2°). Currently, there are no studies that have compared the effectiveness of continuous positive airway pressure (CPAP) versus mandibular advancement device (MAD) in severe OSA patients with mandibular retrognathia. We explored the efficacy of CPAP versus MAD for the treatment of severe OSA patients with mandibular retrognathia.

Methods: A total of 105 patients were enrolled. Outcomes were assessed by using polysomnography, Epworth Sleepiness Scale (ESS), Snore Scale (SS), Self-rating Anxiety Scale (SAS), and compliance, before treatment and after 6 and 12 months of treatment.

Results: Continuous positive airway pressure was superior to MAD in improving polysomnographic outcomes and SS score, but reported compliance was higher on MAD. There is no significant difference between the 2 treatments in terms of ESS score and SAS score. Obstructive sleep apnea patients with mandibular retrognathia showed greater improvement than those without mandibular retrognathia in terms of apnea-hypopnea index and oxygen desaturation index after MAD.

Conclusion: Continuous positive airway pressure and MAD are both effective in treating severe OSA patients with mandibular retrognathia. Mandibular advancement device is a good alternative to CPAP in severe OSA patients with mandibular retrognathia. Mandibular advancement device is more effective in treating OSA patients with mandibular retrognathia than those without. **Trial registration:** ChiCTR2000032541.

EADSM comment: Although retrospective data always are difficult to interpret, this study gives new insight into a possible “odontological” phenotype responding to OA therapy.