https://doi.org/10.5664/jcsm.9464

JCSM | Journal of Clinical Sleep Medicine

COMMENTARY

Is it the time to expect long-term outcome data in addition to follow-up data for sleep apnea interventions?

Commentary on Vecchierini MF, Attali V, Collet JM, et al. Mandibular advancement device use in obstructive sleep apnea: ORCADES study 5-year follow-up data. *J Clin Sleep Med*. 2021;17(8):1695–1705. doi:10.5664/jcsm.9308

Mahadevappa Hunasikatti, MD, FCCP

US Food and Drug Administration, Silver Spring, Maryland

Mandibular advancement devices (MADs) are recommended when oral appliance therapy is prescribed by a sleep physician for an adult patient with obstructive sleep apnea (OSA) who is intolerant of continuous positive airway pressure (CPAP) therapy or prefers alternate therapy. Although the efficacy of MADs for reducing the frequency of obstructive events is lower than that of CPAP, their overall effectiveness is similar because of better adherence. Improvements in symptoms and quality of life after 12 months of treatment are similar for MADs and CPAP in studies.[1]

In this issue of the *Journal of Clinical Sleep Medicine*, Vecchierini et al[2] have explored the 5 years of follow-up data of patients using MADs in the ORCADES study. They enrolled eligible patients > 18 years, who had OSA on polysomnography (PSG) or cardiorespiratory polygraphy (PG; apnea-hypopnea index [AHI] > 30 events/h or AHI 5–30 events/h with excessive daytime sleepiness and/or an Epworth Sleepiness Scale [ESS] score > 10) and refused or were noncompliant with CPAP therapy. A total of 331 patients were treated with a custom-made computer-aided design/computer-aided manufacturing (CAD/CAM) bi-block MAD; 5-year follow-up data were available in 172 patients; the median follow-up was 61 months. The majority of patients were male (75%) and 21% were obese. Median (interquartile range) AHI decreased from 26.4 (17.70–37.10) events/h at baseline to 11.05 (6.10–17.30) events/h at 5-year follow-up. There were also statistically significant improvements from baseline in nadir oxygen saturation Peripheral oxygen saturation measured by pulse oximetry (SpO_2) and time with SpO_2 < 90%. At 5 years, 75.5% of patients had an ESS score < 10. Subjective snoring, nocturia, and libido disorders had disappeared in 44.7%, 62.9%, and 74.4% of patients, respectively, at the 5-year follow-up. After 5 years of follow-up in their cohort study, 52% of the initial cohort remained on MAD therapy. Treatment with MAD for 5 years was associated with sustained and clinically relevant improvements in AHI, SpO_2, clinical symptoms, and quality of life, irrespective of baseline OSA severity, consistent with the findings of previous long-term MAD studies.

Long-term follow-up data are not available for many interventions used in patients with OSA. It is commendable that the ORCADES study authors have 5 years of follow-up data with some limitations. AHI was determined using PG or PSG; the same method was used consistently for each patient at each follow-up evaluation. The accuracy of PSG and PG is not measured in the study. Even though during the study the same assessment device (PG or PSG) was consistently used in the same patient, agreement in event scoring between these 2 types of device was not assessed, and the possibility of some discrepancies needs to be acknowledged. There can be significant variation from PSG to PG (home sleep apnea test) in the same patient when conducted simultaneously. Reported sensitivities for a home sleep apnea test range from 86% to 100%, while specificities range from 64% to 100%. While in those with severe disease (AHI > 30 events/h), there is similar high concordance between decisions from laboratory and home studies, at more moderate disease (eg, AHI 5–20 events/h) concordance drops to around 80%.[3] Ioachimescu et al[4] reported diagnostic concordance using WatchPAT (Itamar Medical Ltd, Israel) in 42%, 41%, and 83% of mild, moderate, and severe OSA, respectively (accuracy = 53%). Among patients with peripheral arterial tonometry (PAT) diagnoses of moderate or severe OSA, 5% did not have OSA and 19% had mild OSA; in those with mild OSA, PSG showed moderate or severe disease in 20% and no OSA in 30% of patients (accuracy = 69%). It would be more valid if these patients are subanalyzed who underwent only PSG with known accuracy. As this study was done in 28 centers in France, it is unlikely they used only 1 type of PG.

The authors state that relevant and statistically significant reductions in the ESS score from baseline (median [interquartile range]: 11 [8–15]) were seen after 36 months (7 [5–10]; $P < .0001$) and were sustained over 5 years (6 [4–10]; $P < .0001$). However, the ESS at baseline of 11 shows that they were not having excessive sleepiness. In general, ESS scores can be interpreted as follows: 0–10 indicates normal daytime sleepiness, 11–12 mild daytime sleepiness, 13–15 moderate daytime sleepiness, and 16–24 indicates severe daytime sleepiness.[5] We have to compare the reductions found in the study with that of CPAP. With other studies with CPAP, mean change in ESS was −4.5 (95% confidence interval: −5.6 to −3.5), with a mean

(standard deviation) self-reported compliance of 4.5 (2.8) hours. Of the participants, 39% reported feeling "much less sleepy," 14% "moderately less sleepy," 13% "little less sleepy," 31% "no change," and 2% "little more sleepy." No patients reported feeling "moderately more sleepy" or "much more sleepy." There was a significant correlation between self-reported CPAP compliance and change in ESS.[6]

Their claim that there were statistically significant improvements from baseline in nadir SpO_2 and time with $SpO_2 <$ 90% (Table 2) is not clinically meaningful as, at baseline, the total number of minutes spent < 90% was only 6 minutes, and with intervention it decreased to 1 minute, 1 minute, and 2 minutes at 6 months, 2 years, and 5 years, respectively. A hypoxic burden of 60% minutes/hour corresponds to a 3% reduction in SpO_2 below baseline for 20 minutes during every hour of sleep.[7]

Despite these limitations, long-term follow-up data of this study have opened viable alternative therapy for patients who may not be able to tolerate or who refuse PAP therapy. Maybe it is time for us to see if there is any change in the outcome of these patients in terms of blood pressure (systolic, diastolic, mean blood pressure), quality of outcome, ESS, overall health care utilization, hospitalization, reduction in accidents, major cardiac events, and stroke reduction—not limited only to AHI/oxygen saturation/ESS parameters alone.[8]

The laudable goal of the authors of "improving patient outcomes" can only be realized if they can demonstrate outcome data. They already have long-term clinical data that may need to be followed further to see if there is any change in the outcome, an opportunity that should not be missed. We hope that they can continue to follow their cohort of patients with PSG to have, preferably 10 years' worth of, long-term clinically meaningful outcome data.

CITATION

Hunasikatti M. Is it the time to expect long-term outcome data in addition to follow-up data for sleep apnea interventions? *J Clin Sleep Med*. 2021;17(8):1519–1520.

REFERENCES

1. Schwartz M, Acosta L, Hung YL, Padilla M, Enciso R. Effects of CPAP and mandibular advancement device treatment in obstructive sleep apnea patients: a systematic review and meta-analysis. *Sleep Breath*. 2018;22(3):555–568.
2. Vecchierini MF, Attali V, Collet JM, et al. Mandibular advancement device use in obstructive sleep apnea: ORCADES study 5-year follow-up data. *J Clin Sleep Med*. 2021;17(8):1695–1705.
3. Pack AI. Point: does laboratory polysomnography yield better outcomes than home sleep testing? Yes. *Chest*. 2015;148(2):306–308.
4. Ioachimescu OC, Allam JS, Samarghandi A, et al. Performance of peripheral arterial tonometry-based testing for the diagnosis of obstructive sleep apnea in a large sleep clinic cohort. *J Clin Sleep Med*. 2020;16(10):1663–1674.
5. Guo Q, Song WD, Li W, et al. Weighted Epworth sleepiness scale predicted the apnea-hypopnea index better. *Respir Res*. 2020;21(1):147.
6. Patel S, Kon SSC, Nolan CM, et al. The Epworth sleepiness scale: minimum clinically important difference in obstructive sleep apnea. *Am J Respir Crit Care Med*. 2018;197(7):961–963.
7. Azarbarzin A, Sands SA, Stone KL, et al. The hypoxic burden of sleep apnoea predicts cardiovascular disease-related mortality: the Osteoporotic Fractures in Men Study and the Sleep Heart Health Study. *Eur Heart J*. 2019;40(14):1149–1157.
8. Aurora RN, Collop NA, Jacobowitz O, Thomas SM, Quan SF, Aronsky AJ. Quality measures for the care of adult patients with obstructive sleep apnea. *J Clin Sleep Med*. 2015;11(3):357–383.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication May 24, 2021
Submitted in final revised form May 24, 2021
Accepted for publication May 24, 2021
Address correspondence to: Mahadevappa Hunasikatti, MD, FCCP, US Food and Drug Administration, 10903 New Hampshire Avenue, Silver Spring, MD 20993; Email: drhunasikatti@gmail.com

DISCLOSURE STATEMENT

This article reflects the views of the author and should not be construed to represent Food and Drug Administration's views or policies. The author reports no conflicts of interest.