Journal of Dental Research
2026, Vol. 105(1) 112–119

DOI: 10.1177/00220345251361796
journals.sagepub.com/home/jdr

Mandibular Advancement Device versus CPAP in Severe Obstructive Sleep Apnea

J.T. Colpani[1], Y.-H. Ou[2], A.M. Kosasih[2], F.K.F. Lee[1], S.-P. Chan[3], H.H. Tan[1], R.C.W. Wong[4], C.W. Chin[5], P.A. Cistulli[6,7], and C.-H. Lee[2,3]

Abstract

Severe obstructive sleep apnea (OSA) is linked to adverse cardiovascular outcomes. While continuous positive airway pressure (CPAP) is the standard treatment, mandibular advancement devices (MADs) offer an alternative. This substudy of a randomized trial compared the effectiveness of MADs versus CPAP on 24-h ambulatory blood pressure (BP), sleep-related quality of life, myocardial remodeling, ambulatory heart rhythm, and biomarkers in severe OSA. A total of 144 participants were randomized to MAD ($n=73$) or CPAP ($n=71$) for 12 mo. Median nightly usage was 5.4 (2.9–6.5) h for the MAD group (≥6 h/night: 56.1%) and 4.9 (4.0–6.0) h for the CPAP group (≥6 h/night: 28.3%). The apnea-hypopnea index at baseline and 6 mo was 44.0 (37.6–59.2) and 20.9 (11.7–31.9) events/h in the MAD group and 50.7 (40.7–59.8) and 2.1 (1.2–3.4) events/h in the CPAP group, respectively. MAD treatment reduced asleep mean BP (−4.7 mm Hg, 95% confidence interval [CI]: −8.3 to −4.0, $P=0.015$), asleep systolic BP (−2.0 mm Hg, 95% CI: −10.0 to −4.0, $P=0.047$), and asleep diastolic BP (−4.0 mm Hg, 95% CI: −9.0 to −3.0, $P=0.007$), whereas CPAP showed no significant changes. The between-group differences favored MAD in asleep mean BP (−3.70 mm Hg, 95% CI: −7.40 to 0.00, $P=0.050$) and asleep systolic BP (−4.78 mm Hg, 95% CI: −9.51 to 0.04, $P=0.048$). Both improved sleep-related quality of life, although CPAP had a slightly greater effect on the Epworth Sleepiness Scale (Δ1.63, 95% CI: 0.45 to 2.81, $P=0.007$). No significant changes were observed in cardiac magnetic resonance imaging parameters, ambulatory heart rhythm, or biomarkers. Adverse effects included jaw pain (14.8%) and teeth discomfort (8.2%) with MAD, whereas CPAP users reported dry mouth (50.8%), nasal congestion (23.0%), and air leakage (29.5%). In conclusion, these findings suggested MAD could be an acceptable and effective treatment for patients with severe OSA and hypertension. The study was registered at Clinicaltrials.gov (NCT04119999).

Keywords: Cardiovascular risk, mandibular advancement devices, continuous positive airway pressure, hypertension, blood pressure, quality of life

Introduction

Mandibular advancement devices (MADs) are approved oral appliances for treating obstructive sleep apnea (OSA), particularly in patients with mild to moderate disease or those intolerant to continuous positive airway pressure (CPAP) (Ramar et al. 2015; Lavigne et al. 2020). These devices reposition the mandible forward during sleep, advancing the tongue and soft tissues of the upper airway, which helps reduce airway collapse, stabilize the pharyngeal walls, and improve neuromuscular tone. Compared with CPAP, MADs offer better adherence due to greater comfort, ease of use, portability, and higher partner acceptance (Ramar et al. 2015; Dissanayake et al. 2021; Mohammadieh et al. 2022). Studies suggest that, in appropriately selected patients, MADs provide improvements in daytime sleepiness, blood pressure (BP), and quality of life comparable to those achieved with CPAP (Phillips et al. 2013; Bratton et al. 2015; Pengo et al. 2024).

However, in clinical practice, MADs are typically not recommended for patients with severe OSA because they are less effective than CPAP in reducing the apnea-hypopnea index (AHI), a conventional measure of OSA severity. However, the

[1]Discipline of Endodontics, Operative Dentistry and Prosthodontics, Faculty of Dentistry, National University of Singapore, Singapore
[2]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[3]Department of Cardiology, National University Heart Centre, Singapore
[4]Discipline of Oral and Maxillofacial Surgery, Faculty of Dentistry, National University of Singapore, Singapore
[5]Department of Cardiology, National Heart Centre Singapore, Singapore
[6]Sleep Research Group, Charles Perkins Centre & Northern Clinical School, Faculty of Medicine and Health, University of Sydney, Camperdown, New South Wales, Australia
[7]Department of Respiratory and Sleep Medicine, Royal North Shore Hospital, St Leonards, New South Wales, Australia

A supplemental appendix to this article is available online.

Corresponding Authors:
C.-H. Lee, Department of Cardiology, National University Heart Centre Singapore, 1 E Kent Ridge Road, NUHS Tower Block Level 9, Singapore, 119228, Singapore.
Email: mdclchr@nus.edu.sg
J.T. Colpani, Discipline of Endodontics, Operative Dentistry and Prosthodontics, Faculty of Dentistry, National University of Singapore. 11 Lower Kent Ridge Road, Singapore, 119083, Singapore.
Email: juli.c@nus.edu.sg

clinical relevance of AHI is increasingly questioned (Xu et al. 2023). Severe OSA, if left untreated, is associated with poor BP control and a high incidence of adverse cardiovascular events (Lee et al. 2011; Walia et al. 2014). Moreover, dismissing MADs as a viable alternative leaves many patients with severe OSA who are intolerant to CPAP without an effective treatment option. Consequently, there is growing interest in exploring the potential of MADs for managing severe OSA. A recent meta-analysis suggested MAD may be as effective as CPAP in sleepiness and quality of life, even if the latter is less effective in reducing AHI (Trzepizur et al. 2021). Yet, the comparative effectiveness of the 2 treatments in BP control remains unknown.

In the CRESCENT trial (Ou et al. 2023, 2024), we recruited participants with hypertension and high cardiovascular risk for overnight polysomnography. Those diagnosed with moderate-to-severe OSA were randomly assigned to either MADs or CPAP. Overall, MADs were found to be noninferior to CPAP in improving BP control, and both treatments improved sleep-related quality of life (Ou et al. 2024; Colpani et al. 2025). In this prespecified substudy focusing on participants with severe OSA, we examined the comparative effectiveness of MADs versus CPAP in 24-h ambulatory BP, sleep-related quality of life, and various cardiovascular outcomes.

Materials and Methods

The CRESCENT was an investigator-initiated, randomized, open-label, noninferiority trial (NCT04119999) (Ou et al. 2023, 2024). Between October 2019 and December 2022, a total of 306 adults aged 40 y and older with hypertension and elevated cardiovascular risk were recruited from 3 major public hospitals and completed a supervised, hospital-based, overnight polysomnography using American Academy of Sleep Medicine Type I diagnostic software (Embla RemLogic, Natus Medical Inc.). The exclusion criteria included ongoing treatment for diagnosed OSA; Cheyne–Stokes breathing or predominantly central sleep apnea; secondary hypertension due to renal, endocrine, or vascular problems; unsuitable anatomy for MADs (fewer than 6 teeth per arch, inability to advance the mandible or open the jaw sufficiently, preexisting temporomandibular joint disorders, and severe bruxism), life expectancy less than 1 y, hypertensive crisis, acute coronary syndromes, or acute heart failure in the past 30 d. Among the 306 participants who completed the overnight polysomnography, 144 (47.1%) had severe OSA, defined as an AHI ≥30 events per hour, and they were randomized into the MAD (SomnoDent Flex®, SomnoMed) versus CPAP (AirSense™ 10, Resmed) in a 1:1 ratio. There was a 1-mo acclimatization phase before the trial period began. The total intervention period was 12 mo.

Measurements and Outcomes

The primary outcome for the CRESCENT trial was the 24-h mean arterial BP. Ambulatory BP was measured at 30-min intervals using validated devices (Welch Allyn ABPM 7100, Welch Allyn). Other outcomes included multidimensional questionnaires: sleep-related quality of life (Epworth Sleepiness Scale [ESS] (Johns 1993), the Functional Outcomes of Sleep Questionnaire [FOSQ] (Weaver et al. 1997), and the Sleep Apnea Quality of Life Index [SAQLI]) (Flemons and Reimer 1998), cardiac magnetic resonance imaging (MRI), ambulatory electrocardiogram (ECG) monitoring, and cardiovascular biomarkers (high-sensitivity C-reactive protein, N-terminal pro B-type natriuretic peptide, high-sensitivity cardiac troponin T). Adherence in the MAD group was monitored using an embedded compliance recorder (DentiTrac, Braebon). The CPAP group's adherence was tracked through a cloud-based platform (AirView, ResMed).

The primary aim of this substudy was to compare the effectiveness of MADs versus CPAP on improving 24-h mean BP. We hypothesized that MAD would be more effective than CPAP at 12-mo follow-up. Secondary aims included comparing MADs versus CPAP in terms of (1) improvement in quality of life, (2) change in cardiovascular biomarkers, and (3) reversal of myocardial remodeling. We hypothesized that MADs would be more effective than CPAP for these secondary outcomes. The Institutional Review Board approved the trial (The Domain Specific Review Board-C: 2019/00359, approved on August 28, 2019). All participants provided written informed consent.

Statistical Analysis

The sample characteristics of participants diagnosed with severe OSA at baseline who completed the 12-mo follow-up were summarized with mean ± standard deviation (SD), median (interquartile range), and frequency (%). Data analyses were carried out on the following endpoints: (1) ambulatory BP monitoring, (2) sleep-related quality-of-life questionnaires, (3) cardiac MRI, (4) ambulatory ECG monitoring, and (5) cardiovascular biomarkers, with Wilcoxon–Mann–Whitney test and Fisher's exact test. Change analyses between baseline and 12-mo outcomes were ascertained with the Wilcoxon signed ranked and McNemar's tests.

Confirmatory analyses of the relative reduction in 24-h mean arterial BP, changes in sleep-related quality of life, myocardial remodeling, ambulatory ECG monitoring, and cardiac biomarkers, comparing MADs and CPAP between baseline and 12-mo follow-ups, used analysis of covariance estimated with ordinary least squares. All statistical analyses were performed with Stata BE version 17.0 (Stata Corp).

Results

Population Demographics

A total of 144 participants were diagnosed with severe OSA. These included 73 randomized to the MAD group and 71 randomized to the CPAP group. The flowchart outlining the study design is provided in Appendix Figure 1. The baseline

Table 1. Baseline Demographic and Clinical Characteristics of the Study Participants.

Variable	MAD (n = 73)	CPAP (n = 71)	*P* Value
Demographic characteristics			
Age (y), median (IQR)	61 (54–67)	61 (56–65)	0.942
Male sex, *n* (%)	65 (89.0)	58 (81.6)	0.211
BMI (kg/m^2), median (IQR)	28.4 (25.9–31.0)	28.5 (26.2–31.2)	0.544
Neck circumference (cm), median (IQR)	40.5 (37.7–42.5)	39.7 (37.0–42.5)	0.578
Waist circumference (cm), median (IQR)	97.5 (93.2–105.2)	98.5 (93.3–108.5)	0.716
Hip circumference (cm), median (IQR)	101.5 (98.2–106.5)	104.0 (98.0–109.5)	0.341
Waist/hip ratio, median (IQR)	1.0 (0.9–1.0)	1.0 (0.9–1.0)	0.450
BMI 23 to <27.5 (kg/m^2), *n* (%)	26 (37.1)	26 (38.2)	
BMI ≥ 27.5 (kg/m^2), *n* (%)	44 (62.9)	42 (61.8)	0.895
Hypertension duration, y, *n* (%)			
<5	12 (16.4)	17 (23.9)	0.703
5 to 10	13 (17.8)	10 (14.0)	
>10	30 (41.1)	28 (39.4)	
Unknown	18 (24.7)	16 (22.5)	
Number of blood pressure–lowering medications, *n* (%)			
1	14 (19.2)	26 (36.6)	
2	39 (53.4)	21 (29.6)	0.020
3	13 (17.8)	18 (25.4)	
≥4	7 (9.6)	6 (8.5)	
Cardiovascular risk, *n* (%)			
Diabetes mellitus	45 (61.6)	45 (63.4)	0.830
Previous stroke	5 (6.9)	4 (5.6)	0.763
Coronary artery disease	41 (56.2)	40 (56.3)	0.983
Chronic kidney disease	6 (8.22)	8 (11.3)	0.537
Age≥75 y	1 (1.4)	1 (1.4)	0.984
Smoker	4 (5.5)	3 (4.2)	0.726
Hyperlipidemia	55 (75.3)	59 (83.1)	0.252
Atrial fibrillation	3 (4.1)	3 (4.2)	0.972
Previous myocardial infarction	18 (24.7)	22 (31.0)	0.397
Previous PCI	33 (45.2)	35 (49.3)	0.623
Previous CABG	6 (8.2)	6 (8.5)	0.960

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; BMI, body mass index; CABG, coronary artery bypass surgery; CPAP, continuous positive airway pressure; IQR, interquartile range; MAD, mandibular advancement device; PCI, percutaneous coronary intervention.

demographic and clinical characteristics of the participants in the MAD and CPAP group are shown in Table 1. Overall, the 2 groups were well balanced. About 62% of the participants had obesity, based on the Asian cutoff of ≥27.5 kg/m^2. There was a high prevalence of cardiovascular risk factors, with about 56% of the participants having coronary artery disease.

The baseline ESS and in-laboratory polysomnography findings are shown in Table 2. About two-thirds of the participants in both the MAD and CPAP groups were nonsleepy. The AHI was 44.0 (37.6 to 59.2) events per hour in the MAD group and 50.7 (40.7 to 59.8) events per hour in the CPAP group. The number of patients who completed the 12-mo follow-up was 61 for both the MAD (83.6%) and CPAP (85.9%) groups.

Treatment with MAD and CPAP and Device Adherence

In the MAD group, the percentage of mandibular protrusion at the beginning of the acclimatization was 70.1 ± 1.9% (absolute advancement: 10.1 ± 1.7 mm). During the acclimatization phase, the device was progressively titrated based on participant comfort and symptom control. It increased to 95.8% ± 8.1% at the end of acclimatization (beginning of the treatment phase). At 12-mo follow-up, the mean protrusion was 88.0% ± 17.3% (absolute advancement: 9.7 ± 1.7 mm). The median duration of MADs usage during the 12-mo treatment period was 5.4 (2.9 to 6.5) h per night. Overall, 70.7% (29/41) of participants used the MADs for ≥4 h per night, and 56.1% (23/41) used it for ≥6 h per night.

In the CPAP group, the 95th percentile pressure was 9.9 ± 3.3 cm H_2O at baseline and 10.8 ± 2.4 cm H_2O at 12 mo. The median duration of CPAP usage during the 12-mo treatment period was 4.9 (4.0 to 6.0) h per night. Overall, 75.0% (45/60) of participants used CPAP for ≥4 h per night, and 28.3% (17/60) used it for ≥6 h per night.

Treatment Efficacy on AHI

Residual AHI in the MAD group was determined by a home-based sleep study using a wrist-worn sleep monitoring device (WatchPAT®□ 200, Itamar Medical; the 3% hypopnea scoring rule was used) and in the CPAP group by the in-built sensor in

Table 2. Baseline Epworth Sleepiness Scale and Polysomnography Findings.

Variable	MAD ($n=73$)	CPAP ($n=71$)	*P* Value
Daytime sleepiness severity, *n* (%)			
Nonsleepy, ESS≤10	48 (65.8)	47 (66.2)	0.404
Mildly sleepy, ESS 11–14	15 (20.6)	18 (25.3)	
Moderately sleepy, ESS 15–17	5 (6.9)	5 (7.0)	
Severely sleepy, ESS 18–24	5 (6.9)	1 (1.4)	
TST, min, median (IQR)	351.0 (291.0–383.0)	378.0 (330.0–395.0)	0.066
AHI, events per hour, median (IQR)	44.0 (37.6–59.2)	50.7 (40.7–59.8)	0.098
ODI, events per hour, median (IQR)	35.8 (25.2–48.6)	44.0 (31.8–52.5)	0.036
Patients with ODI, *n* (%)			
<15 events per hour	5 (6.9)	2 (2.8)	
15 to <30 events per hour	25 (34.3)	12 (16.9)	0.020
≥30 events per hour	43 (58.9)	57 (80.3)	
RDI, events per hour, median (IQR)	44.1 (37.6–59.3)	51.2 (40.7–59.8)	0.095
Patients with RDI, *n* (%)			
<15 events per hour	0 (0.0)	0 (0.0)	
15 to <30 events per hour	0 (0.0)	0 (0.0)	0.999
≥30 events per hour	73 (100.0)	71 (100.0)	
Arousal index, events per hour, median (IQR)	20.5 (11.5–28.0)	21.6 (12.6–31.9)	0.293
Patients with arousal index, *n* (%)			
<15 events per hour	25 (34.3)	20 (28.2)	
15 to <30 events per hour	32 (43.8)	32 (45.1)	0.675
≥30 events per hour	16 (21.9)	19 (26.8)	
Oxygen saturation, median (IQR)			
Mean SpO_2 (%)	94.0 (93.0–95.0)	94.0 (92.0–95.0)	0.683
Minimum SpO_2 (%)	80.0 (74.0–84.0)	78.0 (72.0–83.0)	0.685

AHI, apnea-hypopnea index; CPAP, continuous positive airway pressure; ESS, Epworth Sleepiness Scale; IQR, interquartile range; MAD, mandibular advancement device; ODI, oxygen desaturation index; RDI, respiratory disturbance index; SpO_2, saturation of peripheral oxygen.

the CPAP machine. For the MAD group, the AHI reduced from 44.0 (37.6 to 59.2) at baseline to 20.9 (11.7 to 31.9) events per hour at 6 mo. For the CPAP group, the corresponding values were 50.7 (40.7 to 59.8) and 2.1 (1.2 to 3.4) events per hour.

Treatment efficacy was defined a priori by the following criteria: (1) AHI <5 events/h, (2) ≥50% reduction, or (3) ≥20% reduction with final AHI <15 events/h. At 6 mo, 5.2% of the MAD group and 92.3% of the CPAP group achieved a residual AHI of <5 events per hour. In addition, 74.1% of the MAD group and 100% of the CPAP group achieved a ≥50% reduction in AHI. Furthermore, 51.7% of the MAD group and 96.9% of the CPAP group achieved a ≥20% reduction in AHI with a final AHI of <15 events per hour.

At the 12-mo follow-up, residual AHI data were available for only the CPAP group, where 91.7% of users maintained an AHI of <5 and 100% sustained a ≥50% reduction in AHI. As per the study protocol, the home-based sleep study for the MAD group was not performed at the 12-mo follow-up in order to minimize the risk to the study participants during the COVID-19 pandemic.

24-h Ambulatory BP

Overall, 83.6% (61/73) of the participants in the MAD group and 85.9% (61/71) of the participants in the CPAP group completed the ambulatory BP monitoring at 12-mo follow-up. Details of the ambulatory BP at the baseline and at 12-mo follow-ups are shown in Table 3.

Within- and between-group BP changes from baseline to 12 mo are shown in the Figure. MAD was associated with a reduction in 24-h diastolic BP, asleep mean BP, asleep systolic BP, and asleep diastolic BP, while CPAP was associated with an increase in BP. The between-group difference in asleep mean BP (−3.70 mm Hg, 95% confidence interval [CI] −7.40 to 0.00, $P=0.050$) and asleep systolic BP (−4.78 mm Hg, 95% CI −9.51 to −0.04, $P=0.048$) favored the MADs. A sensitivity analysis, excluding participants with medication changes during the 12-mo treatment period and adjusting for baseline differences in oxygen desaturation index and number of antihypertensive medication use, showed that the findings remained unchanged (Appendix Table 1).

Sleep-Related Quality-of-Life Questionnaires

The details of the sleep-related quality-of-life questionnaire change are shown in Table 4. From baseline to 12 mo, the ESS scores improved in both the MAD group (Δ −3.0 [−7.0 to −1.0], $P<0.001$) and the CPAP group (Δ −4.0 [−7.5 to −1.0], $P<0.001$). The between-group difference in changes in ESS favored the CPAP group (Δ 1.63 [0.45 to 2.81], $P=0.007$). The Functional Outcomes of Sleep Questionnaire (FOSQ) scores improved in both the MAD group (Δ 0.6 [−0.5 to 1.6], $P=0.010$) and the CPAP group (Δ 0.9 [−0.1 to 3.6], $P<0.001$). The

Table 3. Ambulatory Blood Pressure at Baseline and 12 mo.

	MAD		CPAP	
	Baseline ($n=72$)	12 mo ($n=61$)	Baseline ($n=67$)	12 mo ($n=61$)
24-h , mm Hg, median (IQR)				
Mean BP[a]	96.5 (91.0–102.5)	95.0 (90.3–101.3)	96.0 (90.0–100.0)	95.3 (89.0–100.3)
Systolic BP	126.5 (119.0–135.5)	126.0 (119.0–133.0)	126.0 (120.0–134.0)	127.0 (119.0–135.0)
Diastolic BP	81.00 (77.0–86.0)	79.0 (76.0–84.0)[b]	80.0 (74.0–86.0)	79.0 (74.0–86.0)
Awake, mm Hg, median (IQR)				
Mean BP	98.0 (93.0–102.5)	97.0 (92.3–103.0)	97.0 (93.0–104.0)	97.3 (91.7–102.0)
Systolic BP	128.5 (121.0–136.5)	129.0 (122.0–135.0)	130.0 (122.0–136.0)	129.0 (120.0–137.0)
Diastolic BP	83.0 (78.0–88.0)	81.0 (77.0–86.0)	81.0 (76.0–88.0)	81.0 (75.0–87.0)
Asleep, mm Hg, median (IQR)				
Mean BP	93.0 (87.0–101.0)	91.3 (83.0–96.7)[b]	91.0 (85.0–99.0)	91.0 (85.7–99.7)
Systolic BP	124.5 (115.0–132.0)	121.0 (112.0- 130.0)[b]	122.0 (112.0–132.0)	123.0 (113.0–135.0)
Diastolic BP	78.0 (71.0–85.0)	74.0 (69.0–80.0)[b]	76.0 (70.0–84.0)	76.0 (69.0–84.0)

BP, blood pressure; CPAP, continuous positive airway pressure; IQR, interquartile range; MAD, mandibular advancement device.
[a]Mean BP is calculated as one-third of the sum of systolic BP and 2 times the diastolic BP.
[b]Change from baseline to 12 mo, $P<0.05$.

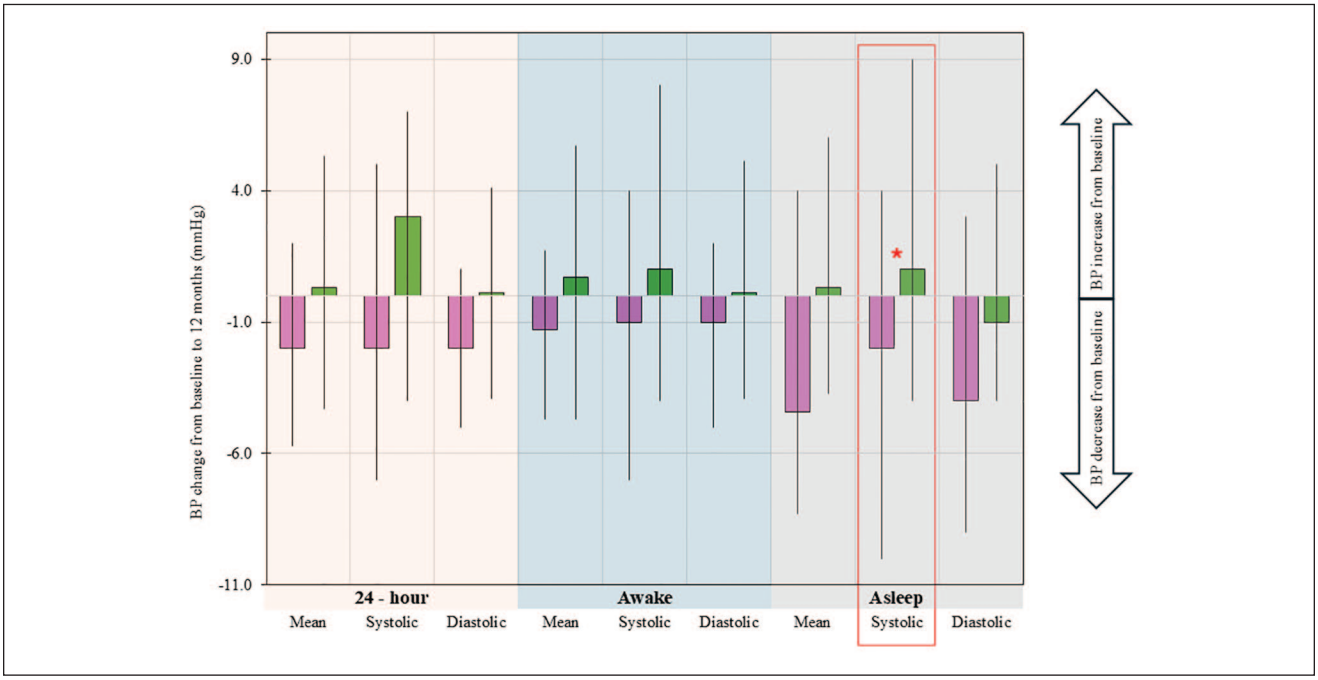

Figure. Blood pressure (BP) changes from baseline to 12-mo follow-up for the mandibular advancement devices (pink) and continuous positive airway pressure (CPAP) (green) groups. The analysis was based on 122 patients with both baseline and 12-mo BP in the mandibular advancement device (MAD) ($n=61$) and CPAP ($n=61$) groups. All BP components of the ambulatory BP (except asleep diastolic BP) increased from baseline to 12 mo in the CPAP arm. On the contrary, all components of the ambulatory BP decreased from baseline to 12 mo in the MAD arm. The between-group difference in asleep mean blood pressure (−3.70 mm Hg, 95% CI −7.40 to 0.00, $P=0.050$) and asleep systolic blood pressure (−4.78 mm Hg, 95% CI: −9.51 to −0.04, $P=0.048$) favored the mandibular advancement devices.

between-group difference in changes in FOSQ was statistically insignificant (Δ −0.92 [−1.95 to 0.10], $P=0.077$). The Sleep Apnea Quality of Life Index (SAQLI) scores improved in both the MAD group (Δ 0.7 [0.3 to 1.2], $P<0.001$) and the CPAP group (Δ 0.8 [0.3 to 1.6], $P<0.001$). The between-group difference in changes in SAQLI favored the MAD group but was statistically insignificant (Δ −0.11 [−0.37 to 0.16], $P=0.415$).

Cardiac MRI

A subgroup of participants underwent cardiac MRI. In total, 39.7% (29/73) of the MAD group and 53.5% (38/71) of the CPAP group were included. Baseline demographics were well-balanced between groups. The ejection fraction, end-diastolic volume, end-systolic volume, and stroke volume of both the

Table 4. Between-Group Difference in Quality-of-Life Questionnaire Changes from Baseline to 12-mo Follow-up in Severe OSA Patients.

	MAD ($n=62$)		CPAP ($n=60$)			
	Changes from Baseline to 12 mo	*P* Value	Changes from Baseline to 12 mo	*P* Value	Difference (95% CI) in QoL Changes	*P* Value ANOVA
ESS	−3.0 (−7.0 to −1.0)	<0.001	−4.0 (−7.5 to −1.0)	<0.001	1.63 (0.45 to 2.81)	0.007
FOSQ	0.6 (−0.5 to 1.6)	0.010	0.9 (−0.1 to 3.6)	<0.001	−0.92 (−1.95 to 0.10)	0.077
SAQLI						
Total	0.7 (0.3 to 1.2)	<0.001	0.8 (0.3 to 1.6)	<0.001	−0.11 (−0.37 to 0.16)	0.415
DF	0.5 (0.1 to 1.1)	<0.001	0.5 (0.0 to 1.7)	<0.001	−0.06 (−0.35 to 0.23)	0.663
EF	0.5 (0.0 to 1.2)	<0.001	0.7 (0.2 to 1.3)	<0.001	−0.23 (−0.48 to 0.03)	0.080
SI	0.2 (0.0 to 1.0)	<0.001	0.4 (0.0 to 1.1)	<0.001	−0.08 (−0.37 to 0.22)	0.603
SY	1.6 (0.8 to 2.4)	<0.001	1.6 (0.6 to 2.5)	<0.001	−0.06 (−0.50 to 0.38)	0.786

ANOVA, analysis of variance; CI, confidence interval; CPAP, continuous positive airway pressure; ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcomes of Sleep Questionnaire; MAD, mandibular advancement device; SAQLI, Sleep Apnea Quality of Life Index. SAQLI subgroups: DF, daily functioning; EF, emotional functioning; SI, social interactions; SY, symptoms.

left and right ventricles remained within the normal range at baseline and after 12 mo in both groups.

Details of cardiac MRI measurements for the MAD and CPAP group at baseline and 12-mo follow-up are shown in Appendix Table 2. Although some changes were observed within the MAD group (baseline to 12 mo), within the CPAP group (baseline to 12 mo), and differences between the 2 groups, the magnitude of the changes were small and not clinically significant.

Ambulatory ECG Monitoring

At baseline, 94.5% (69/73) from the MAD group and 91.5% (65/71) from the CPAP group had valid ambulatory ECG monitoring results. The median duration of ambulatory ECG monitoring for the MAD and CPAP groups was 3.5 (2.9 to 3.8) d and 3.5 (3.1 to 4.6) d, respectively. At 12-mo follow-up, 90.2% (55/61) of the MAD group and 85.2% (52/61) of the CPAP group had valid ambulatory ECG monitoring results. The median duration for the MAD and CPAP groups was 3.0 (2.3 to 3.4) d and 2.0 (1.5 to 3.1) d, respectively.

Between baseline and 12-mo follow-up, there were no differences in the median heart rate for the MAD group (71 [65 to 79] versus 70 [64 to 79] beats per minute, $P=0.348$) and the CPAP group (74 [68 to 84] versus 74 [68 to 78], $P=0.08$). The between-group difference was 1.36 (−0.84 to 3.56, $P=0.223$). The incidences of all the predefined clinically relevant arrhythmia (sinus arrest, high-grade atrioventricular block, supraventricular tachycardia, atrial fibrillation, or flutter, ventricular tachycardia or fibrillation) were less than 0.01% and similar between the 2 groups.

Cardiovascular Biomarkers

The plasma levels of high-sensitivity C-reactive protein, N-terminal pro B-type natriuretic peptide, and high-sensitivity cardiac troponin T for both the MAD and CPAP groups with severe OSA were not elevated at baseline or 12 mo. There were no between-group differences in the changes in these biomarkers from baseline to 12 mo ($P=0.366$, 0.851, and 0.928, respectively) (Appendix Table 3).

Treatment-Related Side Effects

At the 12-mo follow-up, common side effects reported in the MAD group included dry mouth (27.9%, 17/61), jaw pain (14.8%, 9/61), teeth discomfort (8.2%, 5/61), sleep disturbances (3.3%, 2/61), and hypersalivation (3.3%, 2/61). In the CPAP group, common side effects at 12 mo included dry mouth (50.8%, 31/61), air leakage (29.5%, 18/61), nasal congestion or runny nose (23.0%, 14/61), headache or body ache (18.0%, 11/61), facial rash (11.5%, 7/61), sleep disturbances (8.2%, 5/61), mask discomfort (4.9%, 3/61), eye irritation (3.3%, 2/61), and partner complaints (3.3%, 2/61).

Discussion

We reported the outcomes of 144 participants with hypertension, high cardiovascular risk, and severe OSA who were randomized to either MADs or CPAP for 12 mo. Key findings include better treatment adherence with MADs compared with CPAP, with twice as many participants achieving an adherence of ≥6 h per night in the MAD group. Although MADs were less effective than CPAP in reducing the AHI, they led to greater improvements in asleep BP and comparable enhancements in sleep-related quality of life. The improvement in asleep BP is clinically significant, as recent evidence suggests that asleep BP is a stronger predictor of cardiovascular outcomes than 24-hour and daytime BP (Hermida et al. 2018; Yang et al. 2019). To the best of our knowledge, this study represents the largest randomized clinical trial comparing MADs and CPAP in patients with severe OSA.

Severe OSA leads to adverse myocardial remodeling, cardiovascular events, and health care utilization (Kryger et al. 1996; Cloward et al. 2003; Lee et al. 2011). Several studies have evaluated MAD in patients with severe OSA, particularly those unable to tolerate CPAP. One study reported that in patients with very severe OSA (AHI >50 events per hour),

MAD treatment reduced the median AHI from 60 to 15 events per hour, with 95.5% of patients achieving a ≥50% reduction in AHI and 72.7% experiencing symptom improvement (Leibovitz et al. 2025). In the ORCADES study, 158 patients with severe OSA were treated with MAD; after 3 mo, 60% achieved an AHI of <15 events per hour and 38% had complete symptom resolution (Vecchierini et al. 2016). At 5 y, 63% maintained treatment success (defined as a >50% reduction in AHI), and 91% of patients continued to use MAD for ≥6 h per night, with sustained improvements in symptoms and quality of life (Vecchierini et al. 2021). In a nonrandomized study comparing MAD versus CPAP in patients with different degrees of OSA severity, 14 patients were treated with MAD (selection guided by drug-induced sleep endoscopy) and 19 with CPAP, MAD reduced AHI from 51.0 ± 12.3 to 6.5 ± 7.5 events per hour, whereas CPAP reduced AHI from 42.0 ± 8.6 to 2.6 ± 2.8 events per hour (Gogou et al. 2024).

Our study extended these findings and demonstrated that MADs are effective in improving BP control and sleep-related quality of life. Compared with daytime BPs, asleep BPs are better predictors of death and adverse cardiovascular outcomes (Yang et al. 2019). In this regard, it is encouraging that our study showed MAD has greater effectiveness in reducing asleep BP than CPAP does. This study challenges the prevailing view that CPAP is the only effective treatment for severe OSA. These findings pave the way for future pivotal clinical trials to fully assess the safety and efficacy of MAD in patients with severe OSA.

Given MADs' efficacy in severe cases, closer collaboration between dentists and sleep specialists could enhance treatment outcomes. A multidisciplinary approach involving sleep physicians, dentists, and cardiologists may facilitate more personalized care for OSA patients with high cardiovascular risk. Optimizing MAD therapy through customized titration, such as incremental mandibular advancement based on airway anatomy, could further improve both adherence and cardiovascular outcomes. Future research should focus on developing standardized craniofacial screening tools to refine patient selection.

Limitations

Several limitations of this study should be considered. First, the MAD used in this study was custom made, removable, 2-piece, and adjustable (SomnoDent Flex, SomnoMed). As a result, the findings may not be generalizable to simpler, over-the-counter MADs. Second, repeat polysomnography was not performed at the follow-ups in response to the COVID-19 pandemic. Although the CRESCENT trial began recruitment in October 2019, the emergence of COVID-19 in Singapore in early 2020 prompted the study team to take necessary precautions to reduce hospital-based procedures. Therefore, we opted to use home-based WatchPAT sleep studies for participants in the MAD group. For those in the CPAP group, we relied on residual AHI data recorded by the built-in CPAP device. Therefore, interpretation and comparability of the OSA data may be affected as the data from different types of sleep study may not be directly comparable. Third, the study population was primarily recruited from internal medicine and cardiology clinics, resulting in fewer patients with excessive daytime sleepiness compared with those in typical sleep clinic populations. In addition, all participants were of Chinese ethnicity, which may limit applicability to other ethnic groups. Although Chinese craniofacial features increase the propensity for developing severe OSA (Hnin et al. 2018), and it is possible that Chinese ethnicity is associated with better MAD response and BP outcomes, there is no biological reason to suggest that these results cannot be generalized to Caucasian populations. During the trial visits, the dentist addressed patient-reported symptoms, and all were mild and self-limiting, requiring no intervention. However, occlusal or temporomandibular joint–related side effects were not systematically captured. Finally, while the 12-mo follow-up provides valuable insights, longer-term studies are needed to assess the durability of MAD therapy, particularly regarding long-term device adherence and cardiovascular outcomes.

Conclusion

Treatment of severe OSA with MADs resulted in better BP control and comparable improvements in sleep-related quality of life compared with CPAP. These benefits, along with higher adherence and fewer side effects, underscore the potential of MADs as a first-line treatment option for severe OSA.

Acknowledgments

The CRESCENT trial was supported by the Clinician Scientist Award (CSASI18may-0005) and Collaborative Centre Grant (NMRC/CG2/001b/2021) from the National Medical Research Council, Ministry of Health, Singapore, and the USyd-NUS Partnership Collaboration Award, a joint award from the National University of Singapore and the University of Sydney. We thank Miss Venesa Loh and Miss Junping Liu from the National University Hospital for administrative support for the CRESCENT trial.

Author Contributions

J.T. Colpani, Y.-H. Ou, H.H. Tan, P.A. Cistulli, C.-H. Lee, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; A.M. Kosasih, contributed to conception, data analysis and interpretation, drafted and critically revised the manuscript; F.K.F. Lee, contributed to conception, design, data acquisition and interpretation, drafted and critically revised the manuscript; S.-P. Chan, R.C.W. Wong, contributed to conception, data interpretation, drafted and critically revised the manuscript; C.W. Chin, contributed to design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

Declaration of Conflicting Interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: P.A. Cistulli has an appointment as an endowed Academic Chair at the University of Sydney that was created from ResMed

funding; he receives no personal fees, and an Oversight Committee of the University manages this relationship. In addition, he has received research support from ResMed and SomnoMed and is a consultant/adviser to SomnoMed, ResMed, Sunrise Medical, and Eli Lilly. He also has a pecuniary interest in SomnoMed related to a previous role in R&D (2004). C.-H. Lee has received an honorarium from ResMed (2022) and a research grant from the Boston Scientific Corporation. The remaining authors have nothing to disclose.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported by a Clinician Scientist Award from the National Medical Research Council of Singapore (grant CSASI18may-0001) and the USyd-NUS Partnership Collaboration Award, a joint award from the National University of Singapore and the University of Sydney.

ORCID iDs

R.C.W. Wong https://orcid.org/0000-0002-8877-1584
C.-H. Lee https://orcid.org/0000-0001-8777-2705

References

Bratton DJ, Gaisl T, Schlatzer C, Kohler M. 2015. Comparison of the effects of continuous positive airway pressure and mandibular advancement devices on sleepiness in patients with obstructive sleep apnoea: a network meta-analysis. Lancet Respir Med. 3(11):869–878.

Cloward TV, Walker JM, Farney RJ, Anderson JL. 2003. Left ventricular hypertrophy is a common echocardiographic abnormality in severe obstructive sleep apnea and reverses with nasal continuous positive airway pressure. Chest. 124(2):594–601.

Colpani JT, Ou YH, Thakumar AV, Cheong CS, Loke W, Sia CH, Teo YH, Chan SP, Chin CW, Kojodjojo P, et al. 2025. Patient-reported quality of life outcomes with mandibular advancement versus CPAP: insights from the CRESCENT Trial. Sleep [epub ahead of print 31 Jan 2025]. doi:10.1093/sleep/zsaf022

Dissanayake HU, Colpani JT, Sutherland K, Loke W, Mohammadieh A, Ou YH, de Chazal P, Cistulli PA, Lee CH. 2021. Obstructive sleep apnea therapy for cardiovascular risk reduction-time for a rethink? Clin Cardiol. 44(12):1729–1738.

Flemons WW, Reimer MA. 1998. Development of a disease-specific health-related quality of life questionnaire for sleep apnea. Am J Respir Cri Care Med. 158(2):494–503.

Gogou ES, Psarras V, Giannakopoulos NN, Minaritzoglou A, Tsolakis IA, Margaritis V, Tzakis MG. 2024. Comparing efficacy of the mandibular advancement device after drug-induced sleep endoscopy and continuous positive airway pressure in patients with obstructive sleep apnea. Sleep Breath. 28(2):773–788.

Hermida RC, Crespo JJ, Otero A, Domínguez-Sardiña M, Moyá A, Ríos MT, Castiñeira MC, Callejas PA, Pousa L, Sineiro E, et al. 2018. Asleep blood pressure: significant prognostic marker of vascular risk and therapeutic target for prevention. Eur Heart J. 39(47):4159–4171.

Hnin K, Mukherjee S, Antic NA, Catcheside P, Chai-Coetzer CL, McEvoy D, Vakulin A. 2018. The impact of ethnicity on the prevalence and severity of obstructive sleep apnea. Sleep Med Rev. 41:78–86.

Johns MW. 1993. Daytime sleepiness, snoring, and obstructive sleep apnea. The Epworth Sleepiness Scale. Chest. 103(1):30–36.

Kryger MH, Roos L, Delaive K, Walld R, Horrocks J. 1996. Utilization of health care services in patients with severe obstructive sleep apnea. Sleep. 19(9 suppl):S111–S116.

Lavigne GJ, Herrero Babiloni A, Beetz G, Dal Fabbro C, Sutherland K, Huynh N, Cistulli PA. 2020. Critical issues in dental and medical management of obstructive sleep apnea. J Dent Res. 99(1):26–35.

Lee CH, Khoo SM, Chan MY, Wong HB, Low AF, Phua QH, Richards AM, Tan HC, Yeo TC. 2011. Severe obstructive sleep apnea and outcomes following myocardial infarction. J Clin Sleep Med. 7(6):616–621.

Leibovitz S, Levi S, Hanut A, Yanko R, Sharav Y, Haviv Y. 2025. Evaluating the effectiveness of mandibular advancement devices in treating very severe obstructive sleep apnea: a retrospective cohort study. Sleep Breath. 29(1):84. doi:10.1007/s11325-025-03249-8

Mohammadieh AM, Sutherland K, Chan ASL, Cistulli PA. 2022. Mandibular advancement splint therapy. Adv Exp Med Biol. 1384:373–385.

Ou YH, Colpani JT, Chan SP, Loke W, Cheong CS, Kong W, Chin CW, Kojodjojo P, Wong P, Cistulli P, et al. 2023. Mandibular advancement device versus CPAP in lowering 24-hour blood pressure in patients with obstructive sleep apnoea and hypertension: the CRESCENT trial protocol. BMJ Open. 13(5):e072853. doi:10.1136/bmjopen-2023-072853

Ou YH, Colpani JT, Cheong CS, Loke W, Thant AT, Shih EC, Lee F, Chan SP, Sia CH, Koo CY, et al. 2024. Mandibular advancement vs CPAP for blood pressure reduction in patients with obstructive sleep apnea. J Am Coll Cardiol. 83(18):1760–1772.

Pengo MF, Schwarz EI, Barbé F, Cistulli PA, Drager LF, Fava C, Fuchs FD, Ip MSM, Loffler KA, Lui MM, et al. 2024. Effect of CPAP therapy on BP in patients with OSA a worldwide individual patient data meta-analysis. Eur Respir J. 65:2400837. doi:10.1183/13993003.00837-2024

Phillips CL, Grunstein RR, Darendeliler MA, Mihailidou AS, Srinivasan VK, Yee BJ, Marks GB, Cistulli PA. 2013. Health outcomes of continuous positive airway pressure versus oral appliance treatment for obstructive sleep apnea: a randomized controlled trial. Am J Respir Crit Care Med. 187(8):879–887.

Ramar K, Dort LC, Katz SG, Lettieri CJ, Harrod CG, Thomas SM, Chervin RD. 2015. Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: an update for 2015. J Clin Sleep Med. 11(7):773-827.

Trzepizur W, Cistulli PA, Glos M, Vielle B, Sutherland K, Wijkstra PJ, Hoekema A, Gagnadoux F. 2021. Health outcomes of continuous positive airway pressure versus mandibular advancement device for the treatment of severe obstructive sleep apnea: an individual participant data meta-analysis. Sleep. 44(7):zsab015. doi:10.1093/sleep/zsab015

Vecchierini MF, Attali V, Collet JM, d'Ortho MP, El Chater P, Kerbrat JB, Leger D, Monaca C, Monteyrol PJ, Morin L. 2016. A custom-made mandibular repositioning device for obstructive sleep apnoea-hypopnoea syndrome: the ORCADES study. Sleep Med. 19:131–140.

Vecchierini MF, Attali V, Collet JM, d'Ortho MP, Goutorbe F, Kerbrat JB, Leger D, Lavergne F, Monaca C, Monteyrol PJ, et al. 2021. Mandibular advancement device use in obstructive sleep apnea: ORCADES study 5-year follow-up data. J Clin Sleep Med. 17(8):1695–1705.

Walia HK, Li H, Rueschman M, Bhatt DL, Patel SR, Quan SF, Gottlieb DJ, Punjabi NM, Redline S, Mehra R. 2014. Association of severe obstructive sleep apnea and elevated blood pressure despite antihypertensive medication use. J Clin Sleep Med. 10(8):835–843.

Weaver TE, Laizner AM, Evans LK, Maislin G, Chugh DK, Lyon K, Smith PL, Schwartz AR, Redline S, Pack AI, et al. 1997. An instrument to measure functional status outcomes for disorders of excessive sleepiness. Sleep. 20(10):835–843.

Xu PH, Fong DYT, Lui MMS, Lam DCL, Ip MSM. 2023. Cardiovascular outcomes in obstructive sleep apnoea and implications of clinical phenotyping on effect of CPAP treatment. Thorax. 78(1):76–84.

Yang WY, Melgarejo JD, Thijs L, Zhang ZY, Boggia J, Wei FF, Hansen TW, Asayama K, Ohkubo T, Jeppesen J, et al. 2019. Association of office and ambulatory blood pressure with mortality and cardiovascular outcomes. JAMA. 322(5):409–420.