ORIGINAL ARTICLE

Improvement in Obstructive Sleep Apnea With Weight Loss is Dependent on Body Position During Sleep

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Study Objectives: Weight loss fails to resolve obstructive sleep apnea (OSA) in most patients; however, it is unknown as to whether weight loss differentially affects OSA in the supine compared with nonsupine sleeping positions. We aimed to determine if weight loss in obese patients with OSA results in a greater reduction in the nonsupine apnea/hypopnea index (AHI) compared with the supine AHI, thus converting participants into supine-predominant OSA.

Methods: Post hoc analysis of data from a randomized controlled trial assessing the effect of weight loss (bariatric surgery vs. medical weight loss) on OSA in 60 participants with obesity (body mass index: >35 and <55) with recently diagnosed (<6 months) OSA and AHI of ≥ 20 events/hour. Patients were randomized to very low calorie diet with regular review (n = 30) or to laproscopic adjustable gastric banding (n = 30) with follow-up sleep study at 2 years.

Results: Eight of 37 (22%) patients demonstrated a normal nonsupine AHI (<5 events/hour) on follow-up compared to 0/37 (0%) patients at baseline (p = .003). These patients were younger (40.0 ± 9.6 years vs. 48.4 ± 6.5 years, p = .007) and lost significantly more weight (percentage weight change −23.0 [−21.0 to −31.6]% vs. −6.9 [1.9 to −17.4], p = .001). The percentage change in nonsupine AHI was greater than the percentage change in supine AHI (−54.0 [−15.4 to −87.9]% vs −33.1 [−1.8 to −69.1]%, p = .05). However, the change in absolute nonsupine AHI was not related to change in absolute supine AHI (p = .23).

Conclusions: Following weight loss, a significant proportion (22%) of patients with obesity have normalization of the nonsupine AHI. For these patients, supine sleep avoidance may cure their OSA.

Keywords: obesity, obstructive sleep apnea, ventilation.

Statement of Significance

Weight loss is an important management strategy for overweight patients with obstructive sleep apnea (OSA). Although weight loss improves OSA severity when assessed using apnea hypopnea index (AHI), it rarely normalizes it. Given that weight loss and lateral positioning are both known to improve the upper airway collapsibility, the combined effect of weight loss and lateral positioning during sleep might be expected to normalize the AHI in a greater number of patients than weight loss alone. This study demonstrates that the effect of weight loss is greater on the lateral AHI compared to the supine AHI. Importantly, 22% of obese patients with OSA in our study displayed normalization of the lateral AHI (compared to 3% using the overall AHI).

INTRODUCTION

Obstructive sleep apnea (OSA) is a common disorder in which repetitive obstruction of the upper airway results in sleep fragmentation and oxygen desaturation. The condition is associated with a number of long-term sequelae including: increased cardiovascular risk, neurocognitive impairment, motor vehicle accidents, and endocrinological abnormalities.[1–5] Although obesity is the strongest risk factor for developing OSA,[6] weight loss does not normalize the apnea/hypopnea index (AHI) for the majority of patients.[7–9] Furthermore, for patients undergoing surgical weight loss, there is no correlation between the percentage weight loss and percentage improvement in AHI.[9]

The supine sleeping position is recognized as a key factor that exacerbates the severity of OSA in many individuals. In sleep clinic populations, approximately 60% of patients have supine-predominant OSA (spOSA), where the frequency of obstructive events is more than twice as common in the supine compared to lateral sleeping positions.[10–12] Furthermore, 25% of patients have supine-isolated OSA (siOSA); that is, OSA that is solely present in the supine body position.[10,13] Like weight loss,[14,15] lateral positioning during sleep improves the passive anatomical collapsibility of the upper airway.[16] Therefore, weight loss may provide additional anatomical improvement in the lateral compared to the supine sleeping position, which may result in a preferential improvement in the lateral AHI, especially for those patients with OSA who have a small/negligible contribution from nonanatomical contributors to OSA.[17]

Unfortunately, weight loss randomized controlled trials (RCTs) have only reported the effect of weight loss on the total AHI—the potential for a differential effect on lateral AHI compared to supine AHI has not been previously explored. It is crucial to know the proportion of patients who have spOSA and siOSA following weight loss as there are efficacious positional treatments that could be used to potentially further improve the AHI in this population.[18,19] We therefore conducted a post hoc analysis of a 2-year RCT involving 60 patients with obesity to determine the relative effects of weight loss interventions on the position dependence of OSA.[9]

METHODS

A detailed description of the methods can be found in our previous paper.[9] Briefly, patients with obesity were recruited from seven sleep clinics across Melbourne, Australia, between September 2006 and March 2009. Ethics approval was obtained through Monash University and the participating hospitals. Patients were included in the original study if aged 18–60 years with a body mass index (BMI) of 35–55 kg/m^2, AHI of 20 events/hour or more with the diagnosis having been made within 6 months of entry to the study, with a clinical recommendation to commence continuous positive airways pressure

(CPAP) treatment and with three prior attempts to lose weight. In addition, for inclusion in the current analysis, patients were required to have a baseline sleep study and a follow-up sleep study demonstrating greater than 20 minutes of sleep in both the supine and nonsupine positions (with nonsupine taken as the sum of left lateral, right lateral, and prone times). The cutoff of 20 minutes was chosen in light of recent evidence suggesting that cutoffs between 15–30 minutes are comparable with regard to proportional effects on patients classified with positional OSA.[20] To account for the possible effect of sleep stage (nonrapid eye movement sleep [NREM] vs. rapid eye movement sleep [REM]), we conducted an additional analysis based on NREM values alone.

Patients were excluded if they had previous bariatric surgery, any contraindications to bariatric surgery (cognitive impairment; alcohol or drug dependence; significant neurological, vascular, cardiopulmonary, gastrointestinal, or malignant disease), or if they had obesity hypoventilation requiring bilevel ventilation. If included in the study, participants were then randomized to either the medical program or the surgical program (see below for description).

Polysomnogram

Overnight in-laboratory polysomnographies (PSGs) were performed at various hospitals in Melbourne, Australia. Sleep studies were staged and scored according to American Academy of Sleep Medicine criteria.[21] At all laboratories, body position was recorded with a body position sensor (part number 7000-0104-02, Compumedics, Abbotsford, Australia) placed over the sternum and attached to the thoracic inductance band with Velcro and tape and verified with video monitoring, with manual correction as appropriate. The sensor uses a series of gravity-referenced switches to output a signal indicating one of four possible positions—supine, left lateral, right lateral, or prone.

Medical Program

Patients were enrolled in best practice education, treatment, and follow-up for the issues of obesity and OSA with behavioral, physical, and dietary programs individualized to the patient. Dietary advice included a planned daily deficit of 500 kcal from the estimated energy requirements and was derived from the Dietary Guidelines for Australian Adults and the Australian Guide to Healthy Eating.[22,23] An intensive very low energy diet (VLED) (Optifast, Nestle, Australia) was offered initially to all patients. The meal replacements were provided and were available throughout the study for further use. Physical activity was encouraged with 200 minutes/week of structured activity including resistance exercise and moderate-intensity aerobic activity.

Surgical Program

At the outset, patients had 2 weeks of VLED prior to the insertion of a LAGB (LAP-BAND System, Allergan Health) via the pars flaccida pathway by one of three experienced surgeons. The surgery was performed within 1 month of randomization, and adjustments to the band were made using standard criteria.[24]

Patients in both intervention arms were reviewed every 4–6 weeks over the 2-year study, and the management of OSA was common to both groups. The primary outcome measure of the original study was change in AHI from baseline to 2-year follow-up. For the purpose of our post hoc analysis, the primary outcome measures are change in supine AHI and change in nonsupine AHI. A standard PSG montage was employed with electroencephalogram, submental and leg electromyogram, arterial oxygen saturation, electrocardiogram, and nasal pressure cannula. PSGs were staged and scored according to standard criteria.[21] Typical anthropomorphic measurements were made including waist, hip, and neck circumference.

Statistical comparisons were made using paired *t* tests and Wilcoxon signed-rank test, and correlations were performed with Pearson's R (r) and Spearman's Rho (r_s) as appropriate (SPSS; New York, USA). Values are presented as means ± SD or medians (interquartile range) as appropriate. A p value less than .05 was considered significant. A locally weighted smoothing (Loess) curve was generated using SPSS (New York, USA) and was used to indicate nonlinear trends in scatter plots. Mediation regression analysis was performed to explore the relationship between intervention type, weight loss, and change in nonsupine AHI.

RESULTS

Thirty-seven of the 60 patients enrolled in the original RCT were included in the current analyses (Figure 1).

Baseline characteristics of the 37 included patients and a comparison with 2-year follow-up data are presented in Table 1. There were no significant differences between medical and surgical groups in any of the baseline characteristics.

The 23 excluded patients were not significantly different from the included 37 patients in terms of age, gender, BMI, or AHI (see online data supplement Table E1).

For all patients (n = 37), the percentage change in nonsupine AHI was greater than the percentage change in supine AHI

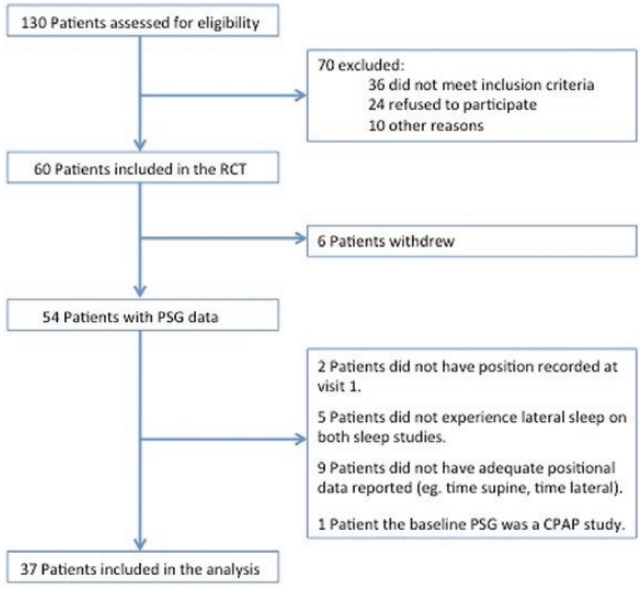

Figure 1—Flow diagram demonstrating patients included in the study. CPAP = continuous positive airways pressure; PSG = polysomnography; RCT = randomized controlled trial.

Table 1—Baseline Characteristics of Included Patients and Comparison With Follow-up Measurements.

N = 37	Baseline	Follow-up	*p* value
Age (years)	47.7 (41.9, 52.8)		
Sex	16F 21M		
Comorbid hypertension	18/37, 49%		
Comorbid diabetes	14/37, 38%		
Weight (kg)	131.0 ± 21.4	113.3 ± 24.0	<.0005
BMI (kg/m^2)	45.5 ± 5.7	39.2 ± 6.3	<.0005
Total AHI (events/hour)	52.4 (34.7 79.5)	27.7 (13.1, 50.9)	<.0005*
Supine AHI (events/hour)	61.1 (38.4, 89.7)	36.0 (22.8, 78.5)	.002*
Nonsupine AHI (events/hour)	44.8 (27.1, 85.2)	24.3 (6.1, 36.9)	<.0005*
Percentage time supine	27.5 (14.3, 54.3)	26.0 (14.0, 54.0)	.79*
Percentage time nonsupine	72.5 (45.8, 86.0)	74.0 (46.0, 86.0)	.71*
spOSA (*n*, %)	8/37, 22%	17/37, 46%	.03★
siOSA (*n*, %)	0/37, 0%	8/37, 22%	.003★

Mean are expressed ± standard deviation, medians are expressed with interquartile range in parentheses.
AHI = apnea/hypopnea index, BMI = body mass index, F = female, M = male, siOSA = supine-isolated obstructive sleep apnea (where at least twice as many respiratory events are seen in the supine position and the lateral AHI is less than 5 events/hour); spOSA = supine-predominant obstructive sleep apnea (where at least twice as many respiratory events are recorded in the supine position).
*Wilcoxon signed-rank test was applied.
★Chi-squared test was applied.

(−54.0 [−15.4 to −87.9]% vs. −33.1 [−1.8 to −69.1]%, p = .05). However, the absolute change (in the number of events per hour) in nonsupine AHI was not significantly different to the change in absolute supine AHI.

Effect of Weight Loss on OSA Severity

A within-group analysis of the pre- and post-intervention PSG characteristics as well as a between-group comparison of the change in weight and PSG characteristics over the follow-up period is displayed in Table 2.

Associations With Weight Loss

Figure 2 demonstrates that the percentage weight loss for all patients was significantly correlated with percentage change in both total AHI (p = .0004) and the nonsupine AHI (p < .0001) but with a weaker positive relationship to percentage change in supine AHI (p = .052). Similar results were observed in the medical group, whereas in the surgical group the percentage weight change was only correlated with percentage change in nonsupine AHI (r_s = 0.48 [95% CI = 0.03 to 0.77] p = .03).

Mediation Analysis

Because two interventions are being tested or included in this analysis (medical vs. surgical weight loss), it raises the possibility that these interventions did not have an equivalent effect on reducing nonsupine OSA severity. In order to address this issue and to explore the hypothesis that it is the degree of weight loss that causes improvement in the nonsupine AHI, we performed a mediation regression analysis.[25] Results indicated that weight loss intervention was a significant predictor of percentage weight loss (b = −0.689, $t(35)$ = −4.20, p = .002), and the percentage weight loss was a significant predictor of reduction in nonsupine AHI (b = 153.7, $t(34)$ = 3.82, p=.0005). Moreover, weight loss intervention was no longer a significant predictor of reduction in nonsupine AHI after controlling for percentage weight loss (b = 2.41, $t(34)$ = 0.21, p = .8382) indicating that percentage weight loss fully mediated the reduction in the nonsupine AHI. Approximately 38% of the variance in reduction in nonsupine AHI was accounted for by the predictors ($F(2,34)$ = 10.33, p = .0003, R^2 = 0.38). The Sobel test (normal theory test) was significant (Z = −2.79, p = .0054).

Multiple linear regression was performed in order to assess which of age, sex, change in supine AHI, percentage weight change, and medical versus surgical intervention was associated with the change in nonsupine AHI. The model significantly predicted the nonsupine AHI ($F(5,31)$ = 5.686, p = .001, R^2 = 0.478). This analysis demonstrated that only percentage weight loss contributed significantly to the prediction (p = .004).

Patients "Converted" to Predominantly Supine OSA

OSA was resolved (total AHI <5 events/hour) in 1/37 (3%) patients over the follow-up period. By contrast, if OSA resolution was judged using the criteria of nonsupine AHI less than 5 events/hour, then this number increased significantly to 8/37 (22%) chi-squared p = .01. There was a significant increase in the number of patients classified as spOSA and siOSA over the study period (Table 1). Patients who converted to siOSA were younger (40.0 ± 9.6 years vs. 48.4 ± 6.5 years, p = .007) and lost significantly more weight (percentage weight change −23.0 [−21.0 to −31.6]% vs. −6.9 [1.9 to −17.4], p = .001).

Table 2—Comparison of Weight Loss and Sleep Study Parameters Within Treatment Groups and Between Treatment Groups.

	Medical group (*N* = 17)		Surgical group (*N* = 20)	
	Baseline	**Follow-up**	**Baseline**	**Follow-up**
Weight (kg)	130.5 ± 18.9	125.4 ± 21.4	131.4 ± 23.8	103.0 ± 21.5»
BMI (kg/m^2)	44.5 ± 5.5	42.7 ± 5.7	46.4 ± 5.8	36.3 ± 5.2»
Total AHI (events/hour)	44.0 (32.8, 67.9)	30.7 (16.3, 50.9)	54.4 (38.4, 91.6)	25.1 (12.9, 51.9)»*
Supine AHI (events/hour)	61.1 (35.1, 75.4)	36 (21.3, 72.9)	64.9 (43.0, 106.7)	37.3 (23.4, 81.2)»*
Nonsupine AHI (events/hour)	41.8 (25.6, 73.0)	29.6 (8.3, 48.5)»*	61.2 (29.0, 90.7)	17.8 (5.1, 32.3)»*
Δ Weight (kg)	−5.1 ± 13.5		−28.4 ± 21.0‡	
Δ Weight (% baseline)	0.9 (4.0 to −10.0)		−19.5 (−10.3 to −30.8)‡*	
Δ BMI (kg/m^2)	0.4 (1.6 to −5.0)		−9.0 (−4.4 to −16.3)‡*	
Δ BMI (% baseline)	0.9 (4.0 to −10.0)		−19.5 (−10.3 to −30.8)‡*	
Δ Total AHI (events/hour)	−14.7 ± 33.0		−28.9 ± 27.9	
Δ Supine AHI	−15.8 ± 32.2		−22.7 ± 39.1	
Δ Nonsupine AHI	−16.7 ± 29.8		−40.4 ± 37.4†	
Δ Total AHI (% baseline)	−28.8 (10.5 to −57.7)		−47.4 (−25.7 to −73.8)	
Δ Supine AHI (% baseline)	−23.1 (22.1 to −71.9)		−34.8 (−3.8 to −68.4)	
Δ Nonsupine AHI (% baseline)	−39.1 (−5.6 to −73.0)		−73.4 (−41.4 to −88.6)	
Increase in spOSA	3/17		5/20	
Increase in siOSA	3/17		5/20	

Means are expressed ± standard deviation, medians are expressed with interquartile range in parentheses.
For within-group analysis, a paired *t* test is applied, for between-group analyses an independent samples *t* test is applied.
AHI = apnea/hypopnea index measured in events/hour; *N* = number.
Δ = change calculated as baseline minus follow-up value.
›*p* value less than .05 for within-group analysis.
»*p* value less than .005 for within-group analysis.
†*p* value less than .05 for between-group analysis.
‡*p* value less than .005 for between-group analysis.
*Mann-Whitney *U* test was applied.

Analysis Accounting for Sleep Stage (NREM vs. REM)

To account for the possible confound of sleep state on body position, we analyzed our data using NREM-specific data. Such information was available for 23 out of 37 patients. The complete analysis is contained in the online data supplement. There were no important differences in (1) pre and post weight loss analysis, (2) between-group and within-group analysis, or (3) in the number of patients converted to supine OSA. In a parallel analysis of the section above "Associations With Weight Loss," the percentage weight loss for all 23 patients with NREM data was only significantly correlated with percentage change in the NREM nonsupine AHI ($p < .01$) and was not significantly correlated with percentage change in total NREM AHI or supine NREM AHI. A breakdown of this data by treatment group can also be found in the online supplement. The regression analysis, run with the same parameters, reflected the results observed in the overall analysis with a trend to significance ($F(5,17) = 2.471$, $p = .074$, $R^2 = 0.421$); however, because of the small numbers included (and therefore reduced power), this finding must be interpreted with caution.

DISCUSSION

The major findings of our study are, first, that a significant proportion of patients who undergo weight loss treatment for OSA are converted from nonpositional OSA to supine predominant and siOSA. Second, we have demonstrated that in 37 patients undergoing weight loss, the percentage change in weight appears more closely related to the change in nonsupine AHI compared to the change in supine AHI. Finally, surgical weight loss has a greater effect on the nonsupine AHI than medical weight loss, which appears to be driven by the greater weight loss observed in the surgical treatment group in our cohort.

Given that both weight loss[14] and lateral positioning[16] improve passive pharyngeal anatomy/collapsibility, we speculate that the improvement in lateral AHI relates to a "double hit" improvement in passive airway collapsibility. Weight loss of a similar degree to our cohort has been demonstrated to reduce the volume of the lateral pharyngeal walls and parapharyngeal fat pads, and this may contribute to the improvement in AHI in the lateral position.[26] In the current analysis, we report a linear relationship between percentage weight loss

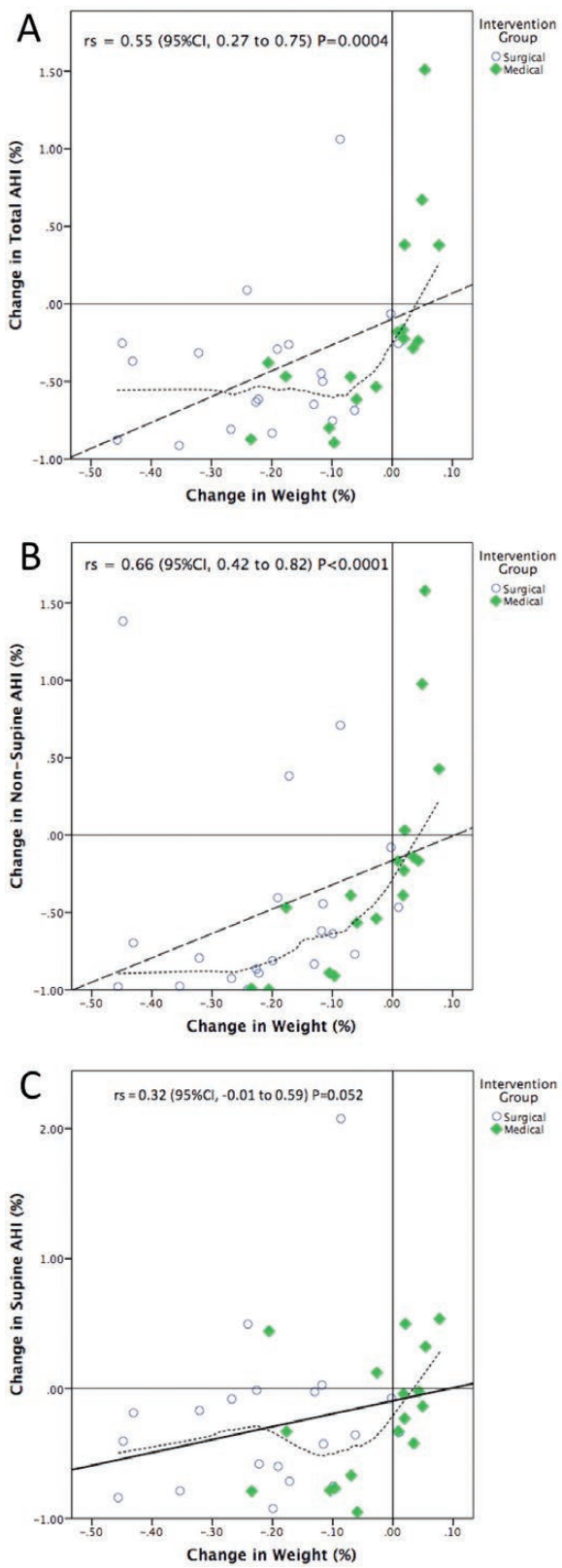

Figure 2—Correlation between percent weight reduction and percent reduction in (A) total AHI, (B) nonsupine AHI, and (C) Supine AHI. Linear regression lines are displayed with a straight dashed line, and locally weighted smoothing curve is used to demonstrate nonlinear trends with 50% proportion. AHI = apnea/hypopnea index; CI = confidence interval.

and percentage improvement in nonsupine and supine AHI over a weight loss range up to 10% (Figure 2). Beyond this range, there is a plateau of effect on AHI. It may be that there is a limit to the improvement in OSA severity in some patients that can be achieved with weight loss alone. This is certainly the case for anatomically based treatments such as mandibular advancement devices.[27] When anatomically based treatments fail to resolve OSA, either the magnitude of effect of the treatment is insufficient to overcome the baseline deficit or there is significant contribution to OSA from one of a number of possible nonanatomical pathophysiological processes that are unaffected by anatomical treatments such as ventilatory control instability (ie, elevated loop gain), low arousal threshold, or poor upper airway dilator muscle effectiveness. We do not currently understand how weight loss affects nonanatomical OSA factors such as elevated loop gain, and future research aimed at measuring the pathophysiological traits of OSA before and after weight loss is crucial to confirm the exact mechanisms at play.

In obese patients, weight loss has a number of important metabolic and cardiovascular benefits; however, remission of OSA with weight loss is unusual.[7] Indeed, in our study, only one patient had a normalization of total AHI. We report that 22% of patients had normalization of the nonsupine AHI, which has important implications for the ongoing treatment of OSA in these patients. In such patients, the combination of weight loss and supine sleep avoidance has the potential to normalize the total AHI and "cure" their OSA, which is a major improvement compared to weight loss alone.[7] For example, an RCT of the effectiveness of CPAP versus positional therapy for patients with siOSA, demonstrated that positional therapy was noninferior to CPAP on measures of quality of life, mood, vigilance, and sleep latency on maintenance of wakefulness testing.[18] Notwithstanding that the trial by Jokic et al. only utilized CPAP and positional modification treatment for 2 weeks in a crossover fashion, this evidence suggests that significant improvements across a number of neurocognitive domains equivalent to CPAP could be achieved for up to 22% of obese patients with OSA who have undergone weight loss simply by preventing them from sleeping on their back.

CONCLUSIONS

In conclusion, we have demonstrated that weight loss appears more closely related to the nonsupine AHI compared with the supine AHI. This leads to a clinically significant proportion of obese patients being converted from nonpositional OSA to siOSA. This opens up simple treatment options for patients with OSA who have lost weight and highlights the importance of measuring body position when performing PSG in these OSA patients.

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SUPPLEMENTARY MATERIAL

Supplementary material is available at *SLEEP* online.

FUNDING

The National Health and Medical Research Council (NHMRC) funded the study through a project grant 436728. Shane A. Landry is supported by the NHMRC Centre of Research Excellence, NeuroSleep. Bradley A. Edwards is supported by the NHMRC of Australia's CJ Martin Overseas Biomedical Fellowship (1035115). John B. Dixon is supported by an NHMRC Senior Research Fellowship. ACTRN 12605000161628.

ACKNOWLEDGMENTS

Conception and design: JD, MN, JKK, SAJ, GSH, and BAE; Acquisition, analysis, and interpretation: SAJ, SL, JKK, BAE, GSH, and JD; Drafting the manuscript for important intellectual content: SAJ, GSH, JD, JKK, SL, BAE, and MN.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication October, 2016
Submitted in final revised form December, 2016
Accepted for publication February, 2017
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DISCLOSURE STATEMENT

None declared.