CLINICAL RESEARCH STUDY

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Effects of Surgical Weight Loss on Measures of Obstructive Sleep Apnea: A Meta-Analysis

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ABSTRACT

OBJECTIVE: Limited evidence suggests bariatric surgery can result in high cure rates for obstructive sleep apnea (OSA) in the morbidly obese. We performed a systematic review and meta-analysis to identify the effects of surgical weight loss on the apnea-hypopnea index.

METHODS: Relevant studies were identified by computerized searches of MEDLINE and EMBASE (from inception to March 17, 2008), and review of bibliographies of selected articles. Included studies reported results of polysomnographies performed before and at least 3 months after bariatric surgery. Data abstracted from each article included patient characteristics, sample size who underwent both preoperative and postoperative polysomnograms, types of bariatric surgery performed, results of preoperative and postoperative measures of OSA and body mass index, publication year, country of origin, trial perspective (prospective vs retrospective), and study quality.

RESULTS: Twelve studies representing 342 patients were identified. The pooled mean body mass index was reduced by 17.9 kg/m^2 (95% confidence interval [CI], 16.5-19.3) from 55.3 kg/m^2 (95% CI, 53.5-57.1) to 37.7 kg/m^2 (95% CI, 36.6-38.9). The random-effects pooled baseline apnea hypopnea index of 54.7 events/hour (95% CI, 49.0-60.3) was reduced by 38.2 events/hour (95% CI, 31.9-44.4) to a final value of 15.8 events/hour (95% CI, 12.6-19.0).

CONCLUSION: Bariatric surgery significantly reduces the apnea hypopnea index. However, the mean apnea hypopnea index after surgical weight loss was consistent with moderately severe OSA. Our data suggest that patients undergoing bariatric surgery should not expect a cure of OSA after surgical weight loss. These patients will likely need continued treatment for OSA to minimize its complications.

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KEYWORDS: Bariatric surgery; Meta-analysis; Obesity; Obstructive sleep apnea

Obesity is an important risk factor for obstructive sleep apnea (OSA).[1-3] The prevalence of OSA among obese individuals is high and correlates with increasing body mass index (BMI).[1,4,5] Among the severely obese, the prevalence of OSA ranges from 55% to 100%.[2,6] In addition, obese individuals often have more severe disease as manifested by a higher apnea-hypopnea index (AHI) and lower nadir on nocturnal pulse oximetry.[1,6,7]

Bariatric surgery is now widely accepted as a mainstay in the treatment of obesity, especially for morbidly obese patients who have failed more conservative approaches or developed comorbidities of their obesity.[8] Bariatric surgery has been found to lower rates of several important clinical outcomes, including death.[9] Cases of weight loss curing OSA have been reported for approximately 2 decades.[10] Even modest weight changes are suggested as an effective approach to the management of OSA.[11] However, the results of the collected series to date examining the effect of bariatric weight loss on sleep apnea have had conflicting results. These published series have been limited by small sample sizes, lack of clear definitions of success, selection

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bias, follow-up bias, and lack of data on postoperative polysomnography findings.

Because sham-controlled studies for bariatric surgery would be unethical, meta-analyses have been performed using existing uncontrolled series of patients with OSA to improve our understanding of the role of surgical weight loss. A 2004 systematic review and meta-analysis on the beneficial effects of bariatric surgery on other health measures reported cures rates of OSA with bariatric surgery of more than 80%.[12] In particular, this review highlighted the dramatic reductions in AHI after bariatric surgery. This review was severely compromised by combining studies of patients with OSA, sleep-disordered breathing, and obesity-hypoventilation syndrome under the label of OSA. Furthermore, information was not provided regarding how the presence of OSA was evaluated after bariatric surgery. Review of the references suggests that most participants did not undergo postoperative polysomnography. Therefore, it is difficult to identify the true effects of bariatric surgery on OSA from this review. Other similar publications overshadow the fact that bariatric weight loss may not resolve OSA and that patients may be left with OSA requiring treatment.[13]

Achieving an improved AHI is not sufficient in view of the associated risk for comorbid illnesses. According to the American Academy of Sleep Medicine, OSA is said to be present when individuals average at least 5 apneic or hypopneic events per hour. Severity of OSA is considered mild if the AHI is 5 to 14 events per hour, moderate if the AHI is 15 to 29 events per hour, and severe if the AHI is 30 or more events per hour.[14,15] Two high-quality population-based cohort studies confirm that untreated OSA is an independent risk factor for death.[16,17] Evidence suggests that even mild OSA is strongly associated with an increased risk for cardiovascular disease.[5] Treatment of mild OSA with continuous positive airway pressure (CPAP) may lower rates of cardiovascular disease morbidity.[18] To avoid the risks of OSA, treatment goals must be more ambitious than simply lowering the AHI. Therapeutic goals should aim for resolution of sleep-disordered breathing both to treat associated symptoms and to limit medical sequelae.

We sought to clarify the impact of surgical weight loss on the diagnosis and severity of OSA by performing a meta-analysis of available studies. In particular, we were interested in determining the mean AHI after maximal weight loss from bariatric surgery.

CLINICAL SIGNIFICANCE

- Bariatric surgery results in dramatic reductions in body mass index and apnea-hypopnea index.
- Many patients who undergo bariatric surgery will have residual OSA despite dramatic weight loss.
- The average apnea-hypopnea index after surgical weight loss is consistent with moderately severe OSA.
- Patients with OSA diagnosed preoperatively should undergo repeat polysomnography after surgical weight loss even if they lack symptoms of excessive sleepiness.

MATERIALS AND METHODS

Search Strategy

With the assistance of a reference librarian, we performed an online search of the MEDLINE and EMBASE databases to identify potentially relevant studies. Search terms included *obstructive sleep apnea, obstructive sleep apnoea, sleep-disordered breathing, bariatric surgery, surgical weight loss, gastric bypass,* and *obesity*. All databases were searched from inception to March 17, 2008. The search was limited to case series reporting data on patients who underwent a clinical assessment and polysomnography before bariatric surgery and at least 3 months after bariatric surgery to allow sufficient time for weight loss to occur. Bibliographies of previously published articles, reviews, and meta-analyses were also searched.[12,19]

Study Selection

All investigators participated in the search process to determine eligibility for inclusion in our analysis and independently abstracted data. Disputes were resolved by consensus discussion. To be eligible for inclusion in our analysis, articles had to report both preoperative and postoperative measures of polysomnographically measured parameters of sleep apnea. Acceptable terms for sleep apnea measures included the apnea index, AHI, and respiratory-disturbance index. To be acceptable for inclusion, it was necessary that polysomnography be performed in accordance with recommendations of the American Academy of Sleep Medicine, including measures of electroencephalography for sleep staging and measures of airflow.

Data Abstraction

For each of the included studies, all authors independently abstracted data. The main data recorded included the sample size who underwent both preoperative and postoperative polysomnography, results of preoperative and postoperative sleep apnea measures, and results of the preoperative and postoperative BMI measures. Additional information that was abstracted for each article included country of origin, year of publication, time from bariatric surgery to the postoperative polysomnogram, and patient demographics, such as mean age and gender distribution, weight change, and study perspective (prospective vs retrospective). Studies were assessed in an unblinded fashion.[20] Where data had been published multiple times, we abstracted data from the most recent publications with the longest follow-up period. Because all identified studies were observational, we assessed study quality using a variation of criteria published by Downs and Black.[21]

Data Synthesis

The potential for publication bias was assessed using funnel plots and the statistical tests described by Begg and Berlin[22] and Egger et al.[23] Statistical heterogeneity was assessed using the chi-square statistic and the I^2 statistic, with I^2 greater than 50% indicating at least moderate heterogeneity. Preoperative and postoperative BMI, changes in BMI, and measures of sleep apnea were pooled using random-effects models of DerSimonian and Laird.[24] To assess the potential effect of trial quality on the outcomes, a component approach was used with a modified checklist of those by Downs and Black.[21] Potential explanations for heterogeneity were explored by separately pooling studies by publication year (before and after 2003) and country of origin. Meta-regression was used to examine potential sources of heterogeneity where continuous variables (sample size, gender distribution, age, and baseline AHI and BMI) were involved. All analyses were conducted using Stata 9.2 (StataCorp, College Station, Tex).

Individual Patient Data Analysis

Individual patient data were abstracted from studies when they were provided. Descriptive measures of means were analyzed using *t* tests for continuous variables, and the Mann–Whitney *U* test for nonparametric data was used. Paired data were analyzed using the Student paired *t* test and Kruskall–Wallis's rank sum test when appropriate. To identify independent predictors of OSA cure (AHI < 5) we used logistic regression models. To assist in identifying the most parsimonious model, we used the log-likelihood test. Goodness of fit of models was assessed using area under receiver operating characteristic curves.

RESULTS

A total of 2309 references were retrieved by the search. The flow of studies is shown in Figure 1. Review of the titles allowed for exclusion of 2249 publications. We reviewed the abstracts for 60 publications. Of the abstracts reviewed, 22 articles were reviewed. After excluding duplicate studies and studies that did not meet the inclusion criteria, we identified 12 studies representing 342 patients for inclusion.

The characteristics of the included studies are shown in Table 1. Most studies were performed in the United States, although 5 studies were from Mexico, Australia, Brazil, and Israel. The average study included 28.5 patients. Only 1 study included at least 50 subjects.[25] With the exception of 1 article that evaluated adolescents,[13] all other studies focused on adults. Although early studies tended to be retrospective, 5 studies were performed prospectively.[25-28]

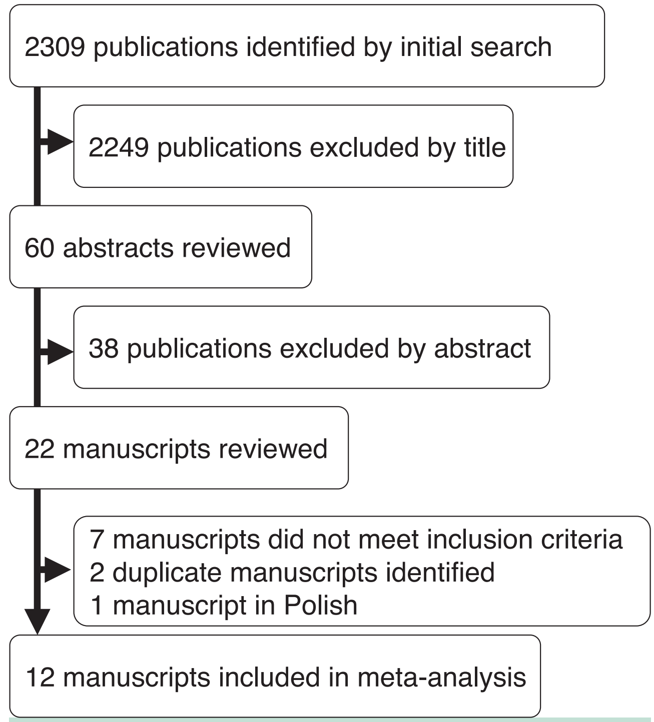

Figure 1 Flow of studies into the meta-analysis.

Overall Effect of Bariatric Surgery on Obstructive Sleep Apnea and Body Mass Index

There was evidence of a high degree of between-study heterogeneity ($\chi^2 < 0.001$; I^2 statistic = 74.1%).[29] There was no evidence of publication bias on the results of the postsurgical AHI by visual inspection of the funnel plot or assessment using Egger's (bias = 0.057, $P = .48$) or Begg's ($P = .22$) statistics. The random-effects pooled mean BMI decreased by 17.9 kg/m^2 (95% confidence interval [CI], 16.5-19.3) from 55.3 kg/m^2 (95% CI, 53.5-57.1) to 37.7 kg/m^2 (95% CI, 36.6-38.9). The random-effects pooled mean AHI decreased by 38.2 events/hour (95% CI, 31.9-44.4) from 54.7 events/hour (95% CI, 49.0-60.3) to 15.8 events/hour (95% CI, 12.6-19.0). Forrest plots of baseline and follow-up AHI and BMI are presented in Figures 2 and 3, respectively.

Sensitivity Analysis and Potential Sources of Heterogeneity

We assessed for differences in measures of effect between retrospective[30-36] and prospective[25-28,37] studies. There was a trend for retrospective studies to report slightly lower AHIs at follow-up: 13.5 (95% CI, 8.5-18.6) versus 18.9 (95% CI, 14.2-23.7). Only 1 study evaluated the effects of surgical weight loss on the AHI in adolescents.[30] When this study was excluded, the follow-up AHI in adults was 16.8 (95% CI, 13.6-20.0). We did not detect any effect of the year of publication (before vs since 2003), type of surgery performed, or country on follow-up AHI. With the exception of 2 studies,[27,37] all the other studies were subject to selection bias because of the inability to determine whether study participants represented the sampled population. Those studies subject to selection bias reported a lower follow-up AHI (14.6, 95% CI, 11.3-18.0) than the studies without this bias (24.3; 95% CI, 17.9-30.7). Eight studies

Table 1 Description of Included Studies

First Author	Year	Country	Sample Size	Surgery	Preoperative BMI	Preoperative Weight (kg)	Preoperative AHI	Postoperative BMI	Postoperative Weight (kg)	Postoperative AHI	Difference BMI	Difference Weight (kg)	Difference AHI	Notes
Charuzi	1992	Israel	47	Various		139 (24.6)	60.8 (35.5)			8.0 (11.8)			52.8	Retrospective. Follow-up data reported at 1 and 7 y. Most (92%) of those with OSA returned for follow-up PSG. Sample consisted of 7 women and 44 men.
Sugerman	1992	USA	40	Various	58 (13.0)	166 (35)	61.1 (39.0)	39.0 (8.0)	110.0 (23.0)	26.0 (26.0)	19	56	38	Retrospective. Inclusion criteria unclear. Potential for follow-up bias because only 34% of patients with preoperative OSA had postoperative PSG. Numbers of men and women not reported.
Pillar	1994	Israel	14	Various	45 (7.2)	131 (22.5)	40 (28.8)	35.0 (6.0)		24.0 (23.0)	10		16	Retrospective. Inclusion criteria unclear. Population sampled unclear. Sample consisted of 3 women and 11 men.
Scheuller	2001	USA	15	Biliopancreatic bypass or gastroplasty		160 (26.6)	96.9 (44.3)		105.0 (21.2)	11.3 (15.0)		54.6	85.6	Retrospective. Population sampled unclear. No criteria for postoperative PSG. Wide variation in follow-up times (1-12 y). Sample consisted of 5 women and 10 men.
Guardiano	2003	USA	8	Roux-en-Y	49 (12.0)		55.0 (31.0)	34.0 (12.0)	105 (22.0)	14.0 (17.0)	15		41	Retrospective. Small sample size. Potential for follow-up bias because only 24% of patients with preoperative OSA had postoperative PSG. Excluded patients who were not compliant with CPAP. Sample consisted of 7 women and 1 man.
Rasheid	2003	USA	11	Gastric bypass	62 (3.0)		56.0 (13.0)	40.0 (2.0)		23.0 (7.0)	22		33	Prospective. Small sample size. Potential for selection bias because only 12% of patients with preoperative OSA had postoperative PSG. Numbers of men and women not reported.
Valencia-Flores	2004	Mexico	28	Various	56.7 (2.3)	56.5 (12.3)	51.7 (19.6)	39.2 (1.6)		13.4 (12.8)	17		33	Retrospective. Potential for follow-up bias because only 45% of patients with preoperative OSA had postoperative PSG. Sample consisted of 16 women and 13 men. Results only reported by presence or absence of OSA at follow-up.
Dixon	2005	Australia	25	Lapascopic gastric banding	53 (9.5)	154 (35.0)	61.6 (31.9)	37.2 (7.2)	105 (22.0)	13.4 (13.0)	15.5	49	48.2	Prospective. Evidence of selection bias because only 51% of patients with preoperative OSA had postoperative PSG. Sample consisted of 8 women and 17 men.
Kalra	2006	USA	17	Gastric bypass	58 (7.2)	163 (30.3)	22.2 (33.6)	43.8 (8.2)		5.6 (11.0)	14.5		16.6	Retrospective. Small sample limited to adolescents. Potential for follow-up bias because only 50% of patients with OSA had follow-up PSG. Numbers of women and men not reported.
Haines	2007	USA	101	Roux-en-Y	56 (1.0)		51.0 (4.0)	38.0 (1.0)		15.0 (2.0)	18		36	Prospective study with clear inclusion criteria. Potential for follow-up bias because only 35% of patients with OSA had follow-up PSG. Numbers of men and women not reported.
Fritscher	2007	Brazil	12	Roux-en-Y	55.5 (10.1)	151.9 (22.6)	66 (33.4)	34.1 (8.1)	100.7 (18.9)	23.7 (24.3)	21	50.2	42.3	Prospective study with clear inclusion criteria. Only 1 patient did not return for follow-up PSG. Sample consisted of 9 men and 3 women.
Lettieri	2008	USA	24	Lapascopic gastric banding	51 (10.4)	147 (29.0)	47.8 (33.8)	24.5 (18.1)	93.0 (18.5)	24.5 (18.1)	18.9	54	23.3	Prospective study with clear inclusion criteria. All patients who survived perioperative period returned for follow-up PSG. Sample consisted of 18 women and 6 men.

BMI = body mass index; AHI = apnea-hypopnea index; OSA = obstructive sleep apnea; PSG = polysomnogram. Values are presented as mean (standard deviation).

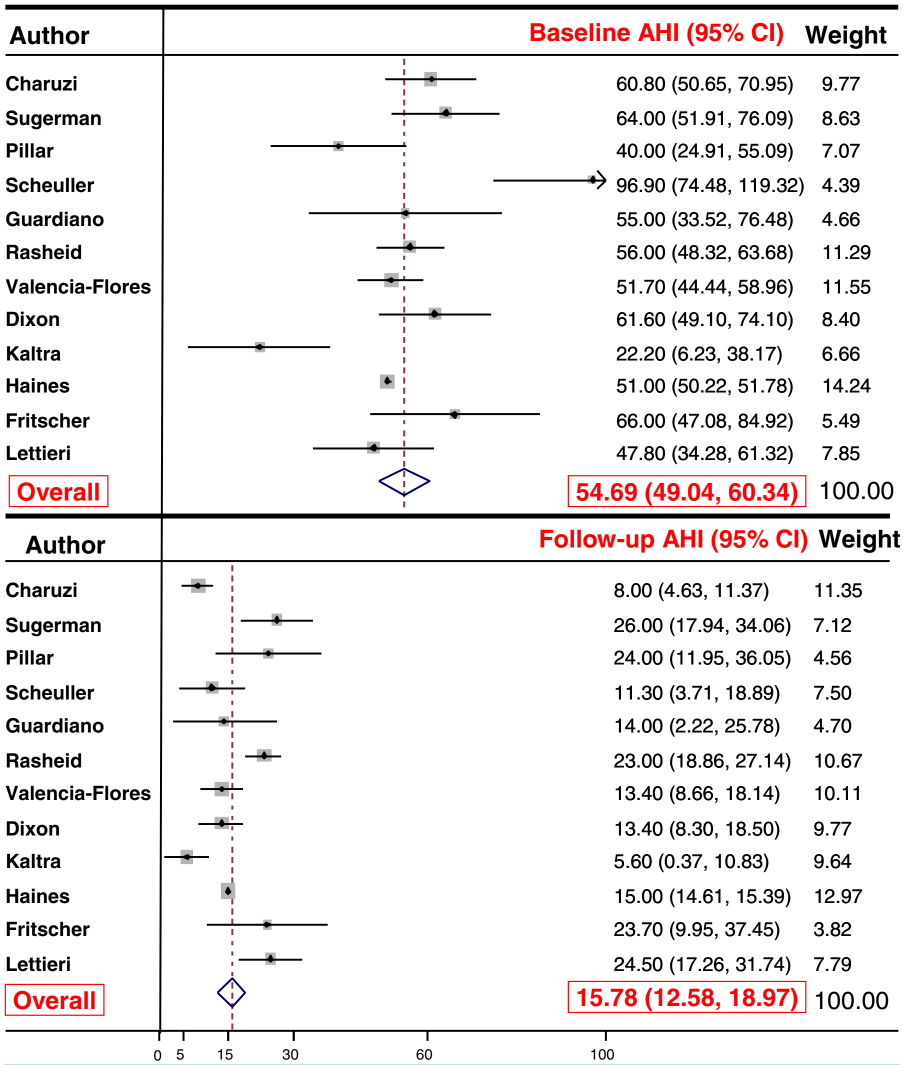

Figure 2 AHI at baseline and after bariatric surgery. AHI = apnea-hypopnea index; CI = confidence interval.

provided information on the distribution of included patients by gender. Analysis by meta-regression did not reveal an effect on the follow-up AHI by age or gender distribution.

Individual Patient Data Analysis

Six studies[27,31,33,36,37,38] provided individual patient level data (n = 80). Data from these patients were pooled to evaluate the distribution and predictors of the AHI after surgical weight loss. The available individual patient data represent 23% of the patients included in the summary measures meta-analysis. The characteristics of patients included in individual patient data analysis are described in Table 2. After surgical weight loss, the average AHI improved by 49.4 events per hour from 67.8 ± 40.2 to 18.4 ± 18.4 events per minute, whereas the BMI improved from 49.7 ± 10.1 to 32.8 ± 6.7 kg/m^2. Those cured of OSA were lighter and younger than those who had residual OSA after bariatric surgery (102.7 ± 20.2 kg vs 173.3 ± 60.4 kg; $P < .001$) and (38.9 ± 9.8 years vs 46.5 ± 9.2 years; $P = .005$). There was no difference in OSA cure rates by sex or baseline AHI. Of the 9 patients aged less than 35 years for whom individual patient data were available, 7 (78%) were cured of OSA and the remaining 2 had only mild OSA after surgical weight loss. Of the 15 patients who weighed less than 100 kg at follow-up, 10 (67%) and 13 (87%) were cured or had mild OSA or better at follow-up, respectively. In logistic regression models, both age (odds ratio 1.08; 95% CI, 1.01-1.16) and follow-up weight less than 100 kg (odds ratio 0.18; 95% CI, 0.46-0.72) independently predicted OSA cure. The fit of this model was good with an area under the receiver operating characteristic curve of 0.788.

DISCUSSION

The results of our meta-analysis corroborate previously reported improvements in AHI after bariatric surgery. The

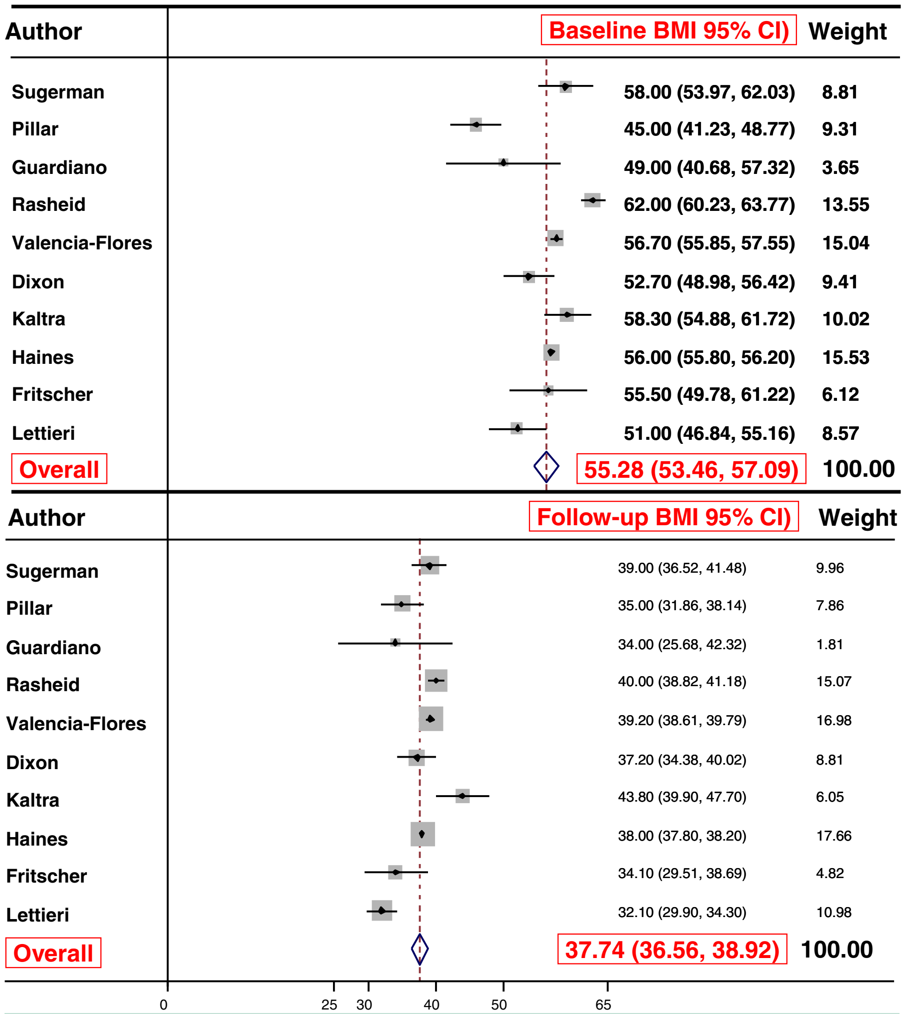

Figure 3 BMI at baseline and after bariatric surgery. BMI = body mass index; CI = confidence interval.

overall effect size of the pooled, weighted data shows a reduction of 38.2 events per hour in the combined study results, a combined reduction in AHI of 71%. This is a substantial improvement for obese patients with sleep apnea. However, residual disease is seen in the majority of patients (62%) after bariatric surgery with a mean residual AHI of more than 15 events per hour. A disease severity of 15 events per hour reflects moderate disease severity[14] and may contribute to adverse medical sequelae, such as hypertension, heart disease, stroke, and difficulty with weight control. Patients newly diagnosed with OSAS at a severity of 15 events per hour are encouraged to pursue treatment, both to alleviate symptoms and to lessen other consequences of the illness. Improvement from a worse index of severity, when significant disease remains, does not relieve the provider of the responsibility or the patient of the benefit of pursuing continued, effective treatment.

It is especially revealing that of the 342 patients identified by the studies who met inclusion criteria for this meta-analysis, few patients achieved an AHI consistent with being cured of OSA. For the 6 studies in which individual patient data were reported, only 25% were shown to attain an AHI of less than 5 events per hour, and less than half (44%) attained an AHI of less than 10 events per hour.

Knowledge of the likelihood of residual disease takes on greater importance when coupled with the insight that patients experiencing the benefits of bariatric weight loss may feel subjectively that they are well and do not have OSA.[16] Salutary effects of bariatric surgery are many, including improved mobility, agility, and physical endurance. It is understandable that patients enjoying these improvements might be reluctant to accept the notion that their OSA and its risks remain, and that they should remain compliant with therapy. Patients and providers alike must be aware that symptoms of OSA might not correlate with severity of OSA as measured using polysomnographic criteria[39] and that lack of subjective sleepiness does not confer protection from the untreated OSA.[16,39] To align patient expectations with realistic outcomes, practitioners counseling patients on the risks and benefits of bariatric surgery should communicate that OSA may not be cured by postsurgical weight loss. Because of the substantial risk of residual sleep-disordered

Table 2 Description of Individual Patient Data Available from Five Studies

	Baseline			Follow-up		
	n	Mean (SD)	Range	n	Mean (SD)	Range
Male (%)	62	31 (50%)				
Age	62	43.6 (10.0)	20-65			
Follow-up days[a]	32	523 (342)	181-1811			
Weight (kg)	54	227.8 (98.9)	92-47	54	147.1 (60.0)	66-282
BMI	47	49.7 (10.1)	32-73	47	32.8 (6.7)	24-63
AHI	80	67.8 (40.2)	5-190	80	18.4 (19.2)	0-87
CPAP[b]	32	10.9 (3.3)	7-20	28	6.8 (3.7)	0-12

BMI = body mass index; AHI = apnea-hypopnea index; CPAP = continuous positive airway pressure; SD = standard deviation.
[a]Mean days from bariatric surgery to follow-up polysomnography.
[b]Measurement refers to CPAP pressures in millimeters of mercury required to ablate apneic events.

breathing, diagnostic sleep testing with repeat polysomnography should be pursued when attaining a goal weight or stable weight. Only follow-up polysomnography can identify those who have achieved freedom from the risks accompanying untreated OSA. An additional benefit of pursuing follow-up polysomnography for all patients undergoing bariatric surgery is that many patients will experience a reduction in positive airway pressures required to ablate apneic events. Repeat polysomnography allows for retitration of CPAP and may translate into improved mask fit and higher CPAP therapy compliance.[11]

The AHI is not a comprehensive parameter for determination of severity of illness in patients with OSA. Unfortunately, other potential severity parameters (eg, oxygen saturation, arousal indices) and subjective assessments (eg, the Epworth Sleepiness Scale) were infrequently reported in the studies surveyed, making these additional parameters unavailable for meta-analysis. These assessment indices do not necessarily parallel the AHI.[39] We can speculate that changes in these parameters in response to weight loss may have provided insight into the physiological mechanisms underlying improvements in sleep apnea.

Meta-analysis is used when it is not possible to perform a randomized controlled trial, when a number of studies show disparate results, or when a more precise effect estimate is desired. Bariatric weight loss as a treatment for OSA presents all these circumstances, and meta-analysis is an appropriate and attractive option. Our study has the limitation inherent in any meta-analysis, specifically that the data to be analyzed are limited to those reported in publications. Many well-designed studies must be excluded from analysis when certain data points are not reported, thus limiting the pool of patients to be included. We were further limited by lack of clear inclusion criteria and substantial heterogeneity between studies. We believe that prior meta-analytic reviews have correctly shown dramatic improvements in OSA resulting from bariatric surgery. However, these prior reviews missed the mark in not demonstrating and underscoring the infrequency of cure.

CONCLUSIONS

Given the limitations of the pooled studies and the finding that the mean follow-up BMIs of patients in both aggregate and individual patient data analyses were still in the obese range, additional larger, prospective studies are needed to better define patients for whom follow-up polysomnograms are warranted. The high prevalence of clinically unsuspected OSA identified in patients before bariatric surgery has led some bariatric surgical centers to universally screen all patients with baseline polysomnograms. We suspect that additional research in this area will reveal similarly high levels of residual OSA after surgical weight loss. Until further studies are performed, clinicians should have low thresholds for evaluating postsurgical patients with repeat polysomnograms. In particular, concern for residual OSA should remain high in patients with other independent risk factors of OSA, such as male sex, older age, severe OSA at baseline, or residual obesity. These individuals remain at high risk for OSA and its complications.

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