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CLINICAL REVIEW

Maxillomandibular advancement for the treatment of obstructive sleep apnea: A systematic review and meta-analysis

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SUMMARY

The reported efficacy of maxillomandibular advancement (MMA) for the treatment of obstructive sleep apnea (OSA) is uncertain. We performed a meta-analysis and systematic review to estimate the clinical efficacy and safety of MMA in treating OSA. We searched Medline and bibliographies of retrieved articles, with no language restriction. We used meta-analytic methods to pool surgical outcomes. Fifty-three reports describing 22 unique patient populations (627 adults with OSA) met inclusion criteria. Additionally, 27 reports provided individual data on 320 OSA subjects. The mean apnea–hypopnea index (AHI) decreased from 63.9/h to 9.5/h ($p < 0.001$) following surgery. Using a random-effects model, the pooled surgical success and cure (AHI <5) rates were 86.0% and 43.2%, respectively. Younger age, lower preoperative weight and AHI, and greater degree of maxillary advancement were predictive of increased surgical success. The major and minor complication rates were 1.0% and 3.1%, respectively. No post-operative deaths were reported. Most subjects reported satisfaction after MMA with improvements in quality of life measures and most OSA symptomatology. We conclude that MMA is a safe and highly effective treatment for OSA.

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Introduction

Obstructive sleep apnea (OSA) is characterized by repetitive episodes of pharyngeal collapse with increased airflow resistance during sleep.[1] Risk factors include obesity, male gender, advancing age and an anatomically smaller upper-airway (i.e., maxillary or mandibular insufficiency).[2] Up to 25% of adults have OSA (i.e., an apnea–hypopnea index (AHI) ≥5/h) and roughly 10% of all adults have moderate to severe disease (i.e., an AHI ≥15/h).[3,4] OSA is associated with higher rates of cardiovascular and cerebrovascular morbidity and mortality as well as excessive daytime sleepiness, fatigue and neurocognitive deficits.[2] When left untreated, the mortality rate for severe OSA approaches 30% at 15 years.[3]

Conventional OSA therapy entails the use of indefinite nocturnal positive airway pressure (either continuous [CPAP] or bilevel) that pneumatically stents open the upper-airway.[5] Unfortunately, adherence rates are poor with more than 50% of patients intolerant of CPAP, with many rejecting therapy within the first few months after initiation.[6,7] Patients who are nonadherent to CPAP therapy (compared with adherent subjects) have a 10% absolute increased mortality risk at 5 years.[8] Several soft-tissue surgical procedures are now available to increase the posterior airspace and treat OSA in patients intolerant to CPAP. However, the reported surgical success rate for these procedures is approximately 40–60%.[9–11] The limited efficacy for these procedures is primarily because clinically significant airflow restriction during sleep is due to multiple concurrent pharyngeal abnormalities.[12–14] In the early 1980s several studies reported improvement in polysomnographic parameters in patients treated with mandibular osteotomy with advancement.[15–18] However, by the mid 1980s combined maxillomandibular advancement (MMA) was championed over mandibular osteotomy alone to treat nonsyndromic OSA patients in order to preserve the maxilla–mandibular relationship and due to the recognition that the physiologic etiology of OSA is often from concomitant mandibular and maxillary deficiency.[19,20]

MMA enlarges the pharyngeal space by expanding the skeletal framework that the soft-tissue pharyngeal structures and tongue attach to resulting in reduced pharyngeal collapsibility during negative-pressure inspiration.[14,21] MMA is currently the most effective craniofacial surgical technique for the treatment of OSA in adults.[22,23] However, some have questioned the widespread suitability of MMA because of a perceived lack of multicenter data and the potential for increased morbidity.[24–26] Thus, we performed

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a systematic review of interventional studies of MMA to evaluate the polysomnographic effectiveness of MMA in treating OSA and alleviating daytime sleepiness, the effects of patient factors (e.g., age, gender) and therapeutic factors (e.g., degree of maxillary and mandibular advancement) on OSA improvement and the long-term effects and morbidity of MMA on OSA.

Methods

We used systematic methods to identify relevant studies, apply inclusion and exclusion criteria, and summarize the clinical efficacy of MMA for the treatment of OSA.

Literature sources and study identification

We searched Medline (January 1950 to May 2009) to identify interventional studies of MMA for the treatment of OSA. Details of the computerized search strategy are available from the authors by request. In addition, we manually searched reference lists of retrieved bibliographies.

Study selection

We included studies that provided both pre- and post-MMA outcomes in subjects with OSA (pre- and post-MMA polysomnogram data) and reported a full methods section (i.e., not an abstract). All studies regardless of language were considered. OSA was defined as an apnea–hypopnea index (AHI; or respiratory disturbance index) ≥5/h.[1,2] MMA was defined as a Le Fort-one maxillary and bilateral sagittal ramus split mandibular osteomies with subsequent maxillomandibular advancement and rigid fixation.[19,22,23]

Data abstraction

We searched potentially relevant articles to determine whether they met inclusion criteria and scanned bibliographies and review articles for additional potentially relevant studies. If two or more studies presented the same data from a single patient population, we included these data only once in our analyses. We identified studies that reported individual patient data and abstracted these data separately (from study level data).

For each included study, we abstracted data regarding patient demographics (e.g., age, gender); pre-MMA surgery clinical factors (e.g., weight, sleep study data, cephalometrics); MMA surgery factors (e.g., degree of MMA advancement); and post-MMA surgery clinical factors (e.g., sleep study data, weight loss, cephalometrics, complications). Similar to previous reviews of OSA surgery,[9,11] we defined surgical success as an AHI <20 and a ≥50% reduction in AHI post MMA.[23] We defined surgical cure as an AHI <5.[27]

Statistical analyses

We programmed all biostatistical models with Excel 2007 for Windows (Microsoft Corporation, Redmond, Washington, USA). We used a random-effects model (inverse variance weighted) to pool surgical success rate and the percent of subjects with an AHI <5, <10 or <15/h after MMA.[28] When pooling mean patient (i.e., age, body mass index [BMI]), polysomnographic (i.e., AHI) or cephalometric variables we utilized analysis of variance (ANOVA).[29] When pooling study level data, we excluded studies with less than two subjects in the calculations. All regressions were programmed in SPSS software version 17.0 (SPSS Inc., Chicago, Illinois, USA). We compared categorical variables with Fisher's exact test and continuous variables with an unpaired *t*-test (or a one-way ANOVA) as appropriate. The normality assumption for the ANOVA was assessed via the Kolmogorov–Smirnov test and a nonparametric test used for *p*-value calculations, as appropriate. Welch's *T*-test (degrees of freedom calculated via the Welch–Satterthwaite equation) was used for statistical comparisons between pooled estimates.[30] This *T*-test does not assume equal population variances. A two-tailed p-value <0.05 was considered statistically significant. If range (and not variance) was provided for a mean value, the standard deviation was estimated assuming a normal distribution using a z-score $= 4.0$. The variance for percent change ([pre-MMA measurement − post-MMA measurement]/pre-MMA variable) was calculated using the following equation:[31]

$$\text{Variance}\left(\frac{w_1 - w_2}{w_1}\right) = \text{var}\left(1 - \frac{w_2}{w_1}\right) = \text{var}\left(\frac{w_2}{w_1}\right) = \frac{w_2^2}{w_1^4} \times v_1 + \frac{1}{w_1^2} \times v_2 - 2 \times \frac{w_2}{w_1^2} \times v_{1,2}$$

When the covariance $(v_{1,2})$ was not provided, we arbitrarily chose $v_{1,2} = 0.3$. In sensitivity analysis, we varied the covariance between 0 and 0.5 and found no effect on the statistical significance or direction of effect for any of the included results.

We used multivariate analysis of variance (MANOVA) to assess sources of heterogeneity in surgical success rates between studies.[32,33] We used a multivariate logistic regression model to examine the association between the following variables and surgical success (or cure) on individual patient data: age (continuous variable); gender; pre-MMA BMI (continuous variable); pre-MMA AHI (continuous variable); degree of maxillary advancement (continuous variable); degree of mandibular advancement (continuous variable); concomitant phase-I (uvulopalatopharyngoplasty; UPPP) surgery (categorical variable); and change in BMI between pre- and post-MMA assessment (continuous variable). We assessed each variable by stepwise backward regression using a p-value cutoff ≤ 0.1.

Results

We identified 914 titles of potentially relevant articles from our computerized search strategy and 97 additional references from our manual search of the bibliographies of retrieved articles. Of the 1011 potentially relevant articles, 59 reports met our inclusion criteria (Fig. 1). This included 53 reports (45 English[14,19,21–23,34–73] and eight non-English[74–81] language) describing 22 unique MMA patient populations (Table 1). Additionally, 27 reports provided individual data on 320 subjects.[14,19,34,37–42,45,46,49,58–60,66,69,71,74,75,77,82–87] Thirteen studies of OSA patients undergoing MMA were excluded for not providing polysomnographic data pre- or post-surgery.[88–100] Two studies were excluded for not providing pre- or post-MMA outcomes separately from patients undergoing other surgical procedures for OSA.[101,102] One case report was excluded that described a patient who underwent sequential bimaxillary transverse distraction osteogenesis with MMA.[103]

Characteristics and efficacy of MMA

Study level data. Twenty-two studies describing 627 adults undergoing MMA to treat OSA were included (Table 1). Most subjects were obese (mean BMI 30.4 ± 5.5 kg/m^2) men (88%) with a mean age of 44.4 ± 9.4 years. Sixty-seven percent of subjects had previous or concurrent phase-I surgery. Most subjects had maxillary (mean SNA angle 79.9 ± 4.4°) or mandibular (mean SNB angle 75.9 ± 4.3°) insufficiency prior to surgery (Table 2).

A statistically and clinically significant reduction in the AHI (63.9 ± 26.7/h vs. 9.5 ± 10.7/h; $p < 0.001$) and improvement in the

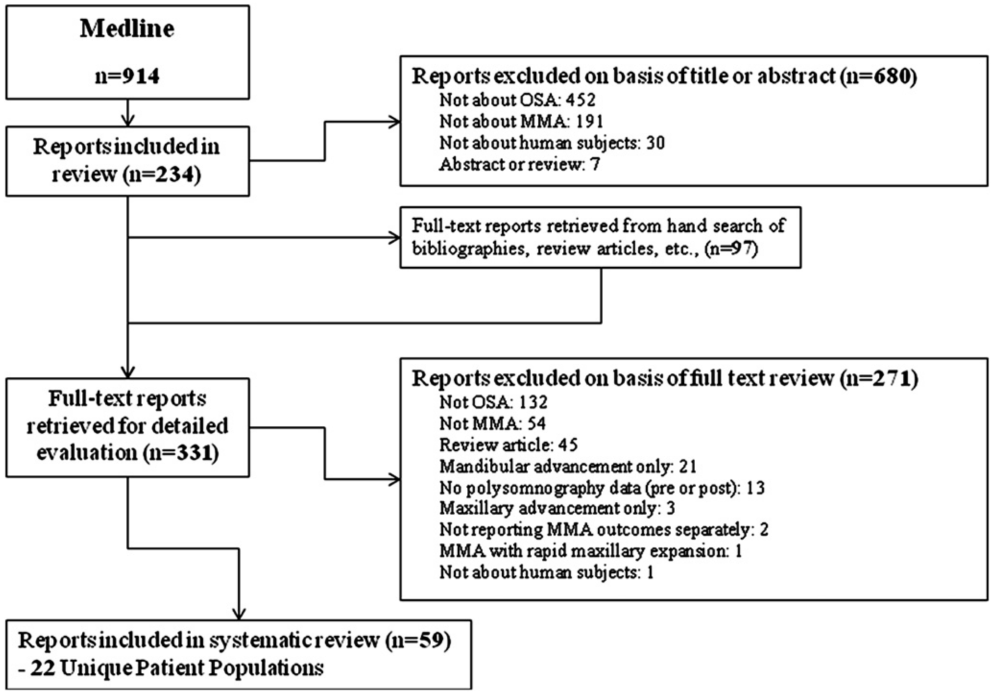

Fig. 1. Literature search and selection. Studies could meet one or more exclusion criteria. For simplicity, only one primary exclusion criterion per study is shown.

lowest nocturnal oxyhemoglobin saturation ($71.9 \pm 14.8\%$ vs. $87.7 \pm 4.8\%$; $p < 0.001$) was observed at a mean follow-up of 5.3 months after MMA (Tables 1 and 2). Improvements were noted in most polysomnographic measures (Table 2) as well as a statistically and clinically significant reduction in reported daytime sleepiness (Epworth sleepiness scale 13.2 ± 5.5 vs. 5.1 ± 3.6; $p < 0.001$) after MMA. The observed improvement in OSA was not explained by a clinically relevant weight change following surgery (pre- and post-BMI 30.4 ± 5.5 kg/m^2 vs. 29.4 ± 5.3 kg/m^2; $p = 0.023$). The pooled (random effects) surgical success rate was 86.0% (Table 1, Fig. 2). The percent of subjects with an AHI <15, <10 and <5/h after MMA was 77.6%, 63.4% and 43.2%, respectively.

Three studies reported long-term follow-up (≥24 months) in 56 OSA subjects after MMA.[50,68,75] At a mean follow-up of 43.7 ± 29.5 months, 89% of patients were considered a surgical success with a significant reduction in the AHI (66.2 ± 26.0/h vs. 7.9 ± 6.4/h; $p < 0.001$) and improvement in the lowest nocturnal oxyhemoglobin saturation ($67.5 \pm 14.8\%$ vs. 86.3 ± 3.9; $p < 0.001$). There was no significant difference between the short-term (3–6 months) and long-term postoperative AHI (8.1 ± 5.8/h vs. 7.9 ± 6.4/h; $p = 0.882$). The BMI increased from 30.6 ± 6.1 kg/m^2 preoperatively to 32.2 ± 6.3 kg/m^2 (longest follow-up) ($p = 0.584$) without apparent clinical effect on OSA. One study ($n = 6$) with 24-month polysomnographic follow-up was not included in the pooled analysis because the variance for the pre-MMA AHI was not reported.[38] This study noted a reduction in AHI from 46.6/h to 7.6/h six months after MMA, but had risen to 15.2 ± 8.6/h 24 months after surgery.

No randomized trials of MMA were identified and all included studies had a before and after case series design. Five cohort studies compared the preoperative AHI on continuous positive airway pressure (CPAP) therapy versus the post-MMA AHI.[56,61,65,66,71] In 207 subjects, no statistically significant difference in AHI was noted between CPAP and MMA therapies (pre-MMA AHI on CPAP 6.1 ± 6.2/h vs. post-MMA AHI 6.1 ± 6.6/h; $p = 0.999$). Studies that did not report pre-MMA AHI on CPAP ($n = 20$; 315 patients) enrolled subjects who were older (45.5 ± 7.7 vs. 43.2 ± 10.2 years; $p = 0.003$) had higher post-MMA AHIs (12.6 ± 12.5/h vs. 6.4 ± 6.6/h; $p < 0.001$) and reported a lower surgical success rate ($88.8 \pm 6.1\%$ vs. $98.3 \pm 1.9\%$; $p < 0.001$).

Individual patient data. Individual pre- and post-MMA data were available for 330 subjects (mean age 44.1 ± 9.0 years; 86% male). Preoperatively, the mean BMI was 33.6 ± 8.2 kg/m^2, the mean AHI was 64.2 ± 26.9/h and the mean lowest nocturnal oxyhemoglobin saturation was $67.3 \pm 16.4\%$. At a mean follow-up of 5.4 ± 1.9 months, the AHI had decreased to 10.4 ± 12.0/h ($p < 0.001$) and lowest nocturnal oxyhemoglobin saturation had increased to $86.2 \pm 6.0\%$ ($p < 0.001$). Individuals with lower pre-MMA AHIs were generally less heavy, less likely to have had previous phase-I surgery and have a lower AHI after MMA (Table 3). Surgical success was obtained in 84.0% of individuals after MMA, but only 38.9% had an AHI <5/h. The AHI for the 194 individuals not obtaining post-MMA cure went from 68.3 ± 27.5/h pre-MMA to 15.9 ± 12.5/h post-MMA ($p < 0.001$). Of these 194 individuals, 73.8% were considered a surgical success and 88.7% had an AHI <30/h after surgery.

Predictors of OSA improvement

Study level data. The degree of reported surgical success between studies varied widely (range 0–100%; median 86.7%) (Table 1, Fig. 2). In univariate analysis, the only preoperative characteristic predictive of surgical success was younger age ($p = 0.013$) (Table 4). Degree of maxillary, but not mandibular advancement was suggestive of surgical success. Studies with a surgical success rate less than 80% ($n = 4$) had a diminutive mean maxillary advancement (8.4 ± 2.8 mm vs. 9.9 ± 1.3 mm; $p < 0.001$) compared with studies with higher success ($n = 10$). Postoperative BMI (or degree of weight change) and most post-MMA cephalometric measurements (except posterior airspace (PAS)) were not predictive of surgical success. The only statistically significant univariate predictors of surgical cure (AHI <5/h) were greater degree of maxillary advancement (31.4% less than vs. 63.7% greater than or

Table 1
Characteristics of studies in the meta-analysis.[a]

Study	Year[m]	Num	Age (yrs)	Male	Phase-I[d]	Follow-up (mo)	BMI (kg/m^2)[b]		AHI[b]		SpO2 Nadir[c]		Cure[e]	Success[e]
							Pre-MMA	Post-MMA	Pre-MMA	Post-MMA	Pre-MMA	Post-MMA		
Yu et al.,[34]	2009	2	36.5 ± 9.2	100%	0%	6.0	28.9 ± 3.7	25.4 ± 3.1	79.0 ± 5.7	27.0 ± 4.9	48.7 ± 13.2%	85.8 ± 1.1%	0%	0%
Lye et al.,[35,36]	2005-2007	15	47.9 ± 5.5	87%	80%	6.0	32.1 ± 2.3	31.5 ± 2.2	69.1 ± 11.7	13.9 ± 6.4	76.5 ± 5.7%	85.0 ± 4.1		87%
Lu et al.,[74]	2005-2006	9	47.8 ± 9.7	100%	100%	7.7	35.3 ± 2.5		88.7 ± 6.7	2.1 ± 1.1	52.2 ± 9.3%	81.8 ± 9.3%	100%	100%
Fairburn et al.,[14]	2000-2003	20	47.6 ± 10.0	65%	75%	4.5	33.9 ± 8.5	34.7 ± 9.2	69.2 ± 35.8	18.6 ± 16.3	80.5 ± 10.5%	87.8 ± 5.6%	10%	65%
Dekeister et al.,[75]	1998-2004	25	48.0 ± 7.0	100%	16%	3.0	28.0 ± 3.4	26.0 ± 3.0	45.0 ± 15.0	7.0 ± 7.0			48%	84%
Hoekema et al.,[37]	1999-2003	4	50.3 ± 5.7	100%	50%	6.0	29.5 ± 4.2		49.5 ± 24.0	1.5 ± 1.3	75.0 ± 17.5%	85.5 ± 5.9%	100%	100%
Smatt and Ferri[38]	2005	18	46.1 ± 6.1	83%	100%	6.0	29.9 ± 4.1	28.4 ± 3.7	54.0 ± 20.7	9.7 ± 6.7			33%	94%
Dattilo and Drooger[39]	2004	15	44.2 ± 7.1	80%	0%				76.2 ± 45.7	12.6 ± 12.1			40%	87%
Goh and Lim[40,41]	2000-2001	11	42.3 ± 8.2	100%	27%	7.7	29.4 ± 4.5	27.2 ± 3.3	64.7 ± 18.8	11.4 ± 7.4	58.5 ± 12.3%	83.5 ± 8.0%	27%	82%
Li et al.,[21]	2002	12	47.3 ± 9.8	75%		6.0	33.5 ± 6.2	32.3 ± 4.1	75.3 ± 26.4	10.4 ± 10.8	74.2 ± 12.0%	86.9 ± 6.7%		83%
Hendler et al.,[42]	2001	7	47.0 ± 6.2	86%	0%	6.0	36.3[h]		90.1 ± 31.6	16.5 ± 23.6	64.9 ± 16.8%	88.2 ± 5.1%	57%	57%
Li et al.,[43–46]	2001	52	46.6 ± 6.7	83%	100%	6.0	32.0 ± 6.0		61.6 ± 23.9	9.2 ± 8.0	75.9 ± 10.6%	87.5 ± 4.7%	29%	90%
Bettega et al.,[47,76]	1994-1997	20	44.4 ± 10.6	90%	65%	6.0	26.9 ± 4.4	25.4 ± 3.3	59.3 ± 29.0	11.1 ± 8.9	82.0 ± 11.0%	90.0 ± 7.0%		75%
Gregg et al.,[48]	2000	35	41.0 ± 6.3	89%		4.5			50.5 ± 15.2	17.2 ± 4.8	83.2 ± 3.9%	90.8 ± 1.8%		94%[i]
Wagner et al.,[77,78]	1993-1997	17[j]	45.8 ± 10.0	95%	57%	3.0	29.5 ± 4.0	28.8 ± 3.9	70.7 ± 23.3	16.9 ± 13.9	73.5 ± 8.8%	86.0 ± 4.0%	24%	71%
Li et al.,[23,49–59]	1988-1995	175	43.5 ± 11.5	83%	94%	6.0			72.3 ± 26.7	7.2 ± 7.5	63.2 ± 17.5%	86.6 ± 3.4%	29%	95%
Lee et al.,[60]	1990-1995	3	42.7 ± 4.0	100%	100%				74.0 ± 29.6	5.0 ± 3.0			33%	100%
Prinsell[61–64]	1999	50	42.7 ± 9.3	88%	72%	5.2	30.7 ± 4.5	28.6 ± 3.9	59.2 ± 28.4	4.7 ± 5.9	72.7 ± 13.6%	88.6 ± 3.9%		100%[k]
Conradt et al.,[65,79]	1993-1996	24	42.7 ± 10.7	100%	0%	3.0	26.7 ± 2.9		59.4 ± 24.1	5.6 ± 9.6	80.6 ± 9.7%	90.7 ± 1.9%		
Hochban et al.,[66–68,80]	1989-1992	38	42.8 ± 10.5	95%	5%	3.0	27.0 ± 3.2	27.1 ± 3.4	45.2 ± 17.1	2.5 ± 3.9	78.0 ± 8.1%	91.9 ± 2.5%	79%	97%
Waite et al.,[22,69,70,81]	1989	50	45.0 ± 3.6	91%	79%				60.0 ± 27.6	16.2 ± 19.8			28%	65%
Riley et al.,[19,71–73]	1985-1987	25	43.8 ± 5.6	88%	84%	6.0	31.3 ± 4.9	30.8 ± 4.7	67.8 ± 15.8	9.3 ± 6.4	65.9 ± 14.3%	87.2 ± 3.2%	32%	88%
Overall		627	44.4 ± 9.4	88%	67%	5.3[l]	30.4 ± 5.5	29.4 ± 5.3[f]	63.9 ± 26.7	9.5 ± 10.7[f]	71.9 ± 14.8%	87.7 ± 4.8%[f]	43.2 ± 117.7%[g]	86.0 ± 30.9%[g]

[a] This table includes all studies with two or more patients undergoing MMA. Plus-minus values are mean (or percent) ± Standard deviation. A "." denotes not reported. ***Abbreviations:*** AHI, apnea-hypopnea index; BMI, body mass index; MMA, maxillomandibular advancement; Num, number; RDI, respiratory disturbance index; SpO2, pulse oximeter oxygen saturation; UPPP, uvulopalatopharyngoplasty.

[b] The apnea-hypopnea index (AHI) is the average number of apneas and hypopneas per hour during sleep.

[c] The SpO2 nadir is the lowest oxyhemoglobin saturation measured during sleep.

[d] Percent of subjects who underwent uvulopalatopharyngoplasty (phase-I surgery, UPPP) prior to or concurrent with MMA.

[e] Surgical success defined as the percent of subjects with an AHI <20/h and a $\geq 50\%$ reduction in the AHI post-MMA. Surgical cure defined as an AHI <5/h after MMA.

[f] P-value $=0.023$ for comparison between pre and post-MMA mean BMIs. Statistical analysis of BMIs compared only patients ($n=327$) with both pre and post-MMA BMI measurements (pre-BMI 30.3 ± 5.5 vs. post-BMI 29.4 ± 5.3 kg/m^2). p-value <0.001 for comparisons between pre and post-MMA mean AHI and SpO2 nadir.

[g] Percent of subjects obtaining surgical success ($n=582$) or cure ($n=312$) calculated via a random-effects model.[28]

[h] No variance provided by the reporting authors.

[i] This study defined surgical success as a reduction in RDI $\geq 50\%$ after MMA. Most patients (89%) had a post-MMA RDI <10/h.

[j] Seventeen patients had pre and post-MMA polysomnographic data. Age, gender and percent having previous phase-I surgery were provided on 21 patients with pre-MMA polysomnographic data (4 patients did not have a post-MMA sleep study).

[k] This study defined surgical success as an AHI <15/h, an SpO2 nadir $>80\%$ and an apnea index <5/h, or a $>60\%$ reduction in AHI (or apnea index) after MMA.

[l] Most studies did not report a variance for the mean follow-up. The overall follow-up was calculated by weighting each individual mean value by the number of enrolled patients.

[m] Year of study enrollment initiation and completion. If enrollment was not provided, year of publication is shown.

Table 2
Pre- and post-MMA study level data.[a]

	Pre-MMA	Post-MMA	*p*-Value
Polysomography			
AHI (events/h) ($n = 627$)	63.9 ± 26.7	9.5 ± 10.7	<0.001
Apnea Index (events/h) ($n = 111$)	34.7 ± 26.2	1.6 ± 2.4	<0.001
Sleep efficiency (%) ($n = 89$)	83.5 ± 11.1	86.4 ± 9.4	0.053
Sleep stages[b]			
REM (%) ($n = 260$)	12.1 ± 7.4	18.9 ± 7.0	<0.001
Stage III or IV (%) ($n = 260$)	6.0 ± 8.7	11.5 ± 10.9	<0.001
SpO2 nadir (%)[c] ($n = 402$)	71.9 ± 14.8	87.7 ± 4.8	<0.001
SpO2 <90% (%) ($n = 120$)	15.4 ± 19.8	2.3 ± 7.1	<0.001
Epworth sleepiness scale[d] ($n = 44$)	13.2 ± 5.5	5.1 ± 3.6	<0.001
Cephalometrics			
SNA (degrees) ($n = 226$)	79.9 ± 4.4	86.0 ± 4.8	<0.001
SNB (degrees) ($n = 226$)	75.9 ± 4.3	81.4 ± 4.5	<0.001
PAS (mm) ($n = 230$)	5.5 ± 2.7	11.5 ± 3.6	<0.001
MPH (mm) ($n = 184$)	25.9 ± 7.1	20.0 ± 6.3	<0.001

[a] This table includes all studies with two or more patients undergoing MMA. ± Values are mean (or percent) ± standard deviation. Values in parenthesis are the number of patients evaluated. **Abbreviations**: AHI, the apnea–hypopnea index; MPH, distance of hyoid bone to mandibular plane; PAS, posterior airway space – base of tongue; REM, rapid eye movement; SNA, sella-nasion-Point A angle; SNB, sella-nasion-Point B angle; SpO2, pulse oximeter oxygen saturation.

[b] Reported as a percent of total sleep time.

[c] The SpO2 nadir is the lowest oxyhemoglobin saturation measured during sleep. The SpO2 <90% is the percent of sleep time that the oxyhemoglobin saturation was below 90%.

[d] The Epworth sleepiness scale is an eight-item questionnaire that measures daytime sleepiness (scores 0–24) with scores >10 considered as excessive.[110]

equal to median of 8.3 mm; $p = 0.019$) and increased post-MMA PAS (29.6% less than vs. 81.0% greater than or equal to median of 14.0 mm; $p < 0.001$) (data not shown).

We assessed potential sources of heterogeneity with a multivariate ANOVA comparing percent surgical success rate with respect to median age (<45.0 vs. ≥45.0 years), median preoperative AHI (<67.8 vs. ≥67.8/h) and median maxillary advancement (<10.7 vs. ≥10.7 mm). Surgical success rate was higher in studies with a lower mean age (difference = 6.7%; 95%CI, 5.5–8.0%), lower mean preoperative AHI (difference = 1.6%; 95%CI, 0.7–2.4%), and greater maxillary advancement (difference = 5.6%; 95%CI, 4.1–7.2%).

Individual patient data. Univariate predictors of surgical success included female gender, lower pre-MMA AHI and greater degree of maxillary advancement (Table 5). Of the six subjects age <30 years, 100% achieved surgical success compared with 77% age ≥50. However, this was not statistically significant ($p = 0.278$). Limiting the assessment to those with a baseline AHI ≥90/h found that subjects age <30 years experienced a 100% surgical success compared with 88% for those age 30–49.9 and 40% for those age ≥50 ($p = 0.049$). Both a lower pre-MMA AHI and absence of previous phase-I surgery were predictive of an AHI <5 after surgery. Subjects with previous phase-I surgery ($n = 84$) were heavier (pre-MMA BMI 33.9 ± 6.0 kg/m^2 vs. 28.6 ± 6.3 kg/m^2; $p < 0.001$), had more severe OSA (pre-MMA AHI 67.4 ± 22.0/h vs. 57.9 ± 30.9/h; $p = 0.019$), and were less likely to achieve surgical cure (AHI <5) (27.4% vs. 47.1%; $p = 0.006$) compared with the 102 subjects without previous or concurrent UPPP surgery. No pre- or post-cephalometric measurements were predictive of either surgical success or cure except postoperative PAS (data not shown).

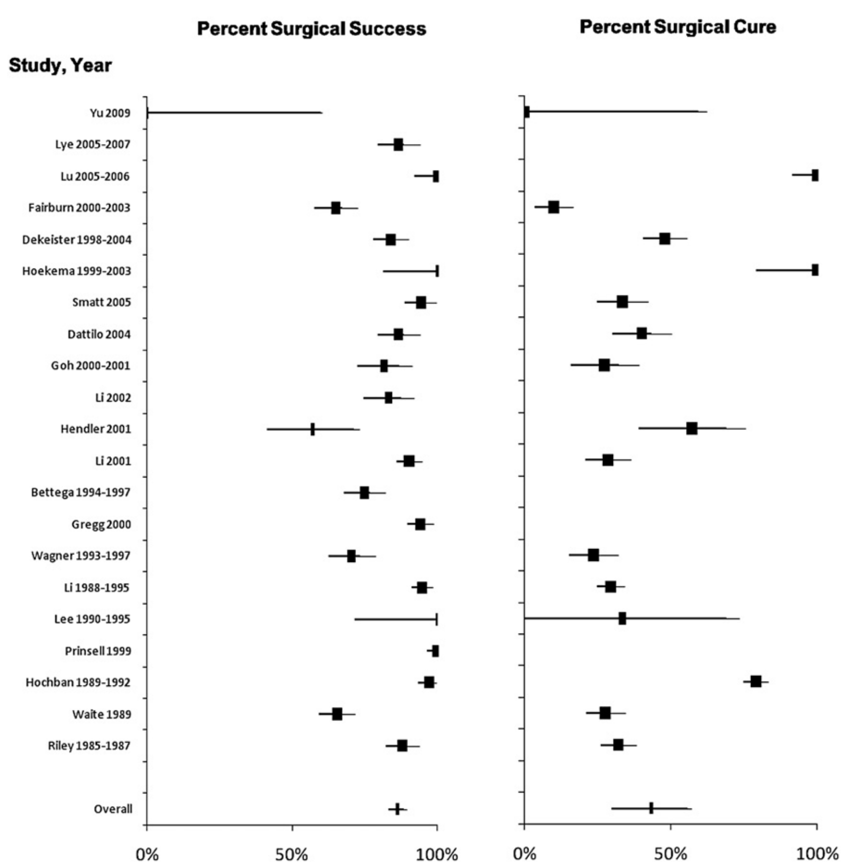

Fig. 2. Individual study estimates of surgical success and surgical cure rates. Summary point estimates and corresponding 95% CI's (error bars) are shown and were calculated using a random-effects model. The width of the point estimate reflects the weight of the individual study in calculating the pooled estimate. Surgical success defined as the percent of subjects with an AHI <20/h and a ≥50% reduction in the AHI post-MMA. Surgical cure defined as an AHI <5/h.

Table 3
Individual patient characteristics stratified by pre-surgical AHI.[a]

Characteristic	Pre-MMA AHI				*p*-Value[c]
	<30/h	30–59.9/h	60–89.9/h	≥90/h	
Pre-MMA					
Age (years)	43.6 ± 8.9 (15)	44.3 ± 9.7 (60)	45.2 ± 7.2 (50)	41.8 ± 10.6 (25)	0.5
Male (%)	86.7 (15)	91.3 (80)	86.7 (60)	70.0 (30)	0.042
BMI (kg/m^2)	27.7 ± 4.8 (11)	31.4 ± 7.6 (50)	34.5 ± 7.9 (54)	39.9 ± 8.2 (20)	<0.001
AHI (events/h)	23.5 ± 5.1 (21)	44.6 ± 8.8 (130)	74.3 ± 8.6 (117)	107.6 ± 19.6 (51)	<0.001
Previous phase-I surgery (%)[b]	20.0 (20)	29.9 (87)	54.0 (76)	33.3 (39)	0.003
Surgery					
Maxillary advancement (mm)	8.8 ± 2.6 (12)	9.3 ± 2.4 (44)	9.3 ± 2.7 (27)	9.6 ± 3.1 (14)	0.879
Mandibular advancement (mm)	10.5 ± 1.6 (12)	11.2 ± 2.6 (44)	11.4 ± 3.2 (27)	12.2 ± 2.1 (14)	0.392
Concurrent phase-I surgery (%)[b]	0.0 (21)	10.0 (130)	12.0 (117)	17.7 (51)	0.172
Post-MMA					
BMI (kg/m^2)	27.5 ± 4.9 (8)	30.8 ± 7.3 (30)	34.5 ± 9.0 (28)	41.6 ± 7.0 (14)	<0.001
Percent change in BMI (%)	0.8 ± 5.7 (8)	−1.0 ± 4.2 (30)	−5.3 ± 7.7 (28)	0.1 ± 3.3 (14)	0.005
AHI (events/h)	6.9 ± 10.2 (21)	8.2 ± 9.5 (130)	11.8 ± 11.9 (117)	14.5 ± 16.4 (51)	0.003
Percent AHI <5 (%)	66.7 (21)	46.2 (130)	30.8 (117)	27.5 (51)	0.001
Percent surgical success (%)	81.0 (21)	88.5 (130)	81.2 (117)	80.4 (51)	0.355

[a] Mean (or percent) ± standard deviation. The number of patients is shown in parentheses.
[b] Percentage of patients who underwent uvulopalatopharyngoplasty (phase-I surgery) prior to or concurrently with MMA.
[c] *P*-Value assesses whether mean differences between the groups are statistically significant. Levene's test was not statistically significant ($p > 0.05$) for each one-way ANOVA comparison, suggesting the variances are not homogenous.

In multivariate logistic regression analysis, independent predictors of surgical success included a lower pre-MMA BMI (OR 0.84 per one BMI unit increase; 95%CI, 0.71–0.98; $p = 0.029$) and a greater degree of maxillary advancement (OR 1.97 per 1 mm advancement; 95%CI 1.13–3.44; $p = 0.016$). Age, gender, AHI, weight change, concurrent UPPP, or degree of mandibular advancement were not predictive of surgical success in multivariate analysis. Similarly, a lower pre-MMA BMI (OR 0.83 per one BMI unit increase; 95%CI, 0.68–0.99; $p = 0.046$) and greater degree of maxillary advancement (OR 2.01 per 1 mm advancement; 95%CI 1.14–3.56; $p = 0.017$) were also predictive of a post-AHI <5 (surgical cure) in multivariate analysis.

Table 4
Predictors of surgical success (study level data).[a]

Characteristic	%Surgical success		
	<Median	≥Median	*p*-Value
Pre-MMA			
Age (median 45.0 years)	90.9 ± 27.0	81.6 ± 49.8	0.013
BMI (median 30.1 kg/m^2)	84.2 ± 46.6	89.2 ± 31.6	0.246
AHI (median 67.8 events/h)	87.9 ± 38.3	82.1 ± 60.4	0.166
SNA (median 79.8°)	95.3 ± 29.3	89.4 ± 27.0	0.071
SNB (median 76.3°)	95.3 ± 29.3	89.4 ± 27.0	0.071
PAS (median 5.1 mm)	93.9 ± 38.4	92.0 ± 30.9	0.593
Surgery			
Maxillary advancement (median 8.7 mm)	81.2 ± 55.2	88.9 ± 29.2	0.148
Mandibular advancement (median 10.7 mm)	86.9 ± 24.5	84.8 ± 44.7	0.524
Post-MMA			
BMI (median 28.6 kg/m^2)	85.4 ± 43.3	85.3 ± 33.4	0.983
% Change in BMI (median −2.7%)	84.9 ± 36.5	85.1 ± 51.2	0.965
SNA (median 86.2°)	91.5 ± 25.7	93.7 ± 39.2	0.577
% Change in SNA (median 7.3%)	94.7 ± 20.1	89.7 ± 45.8	0.226
SNB (median 81.3°)	91.5 ± 25.7	93.7 ± 39.2	0.577
% Change in SNB (median 7.4%)	93.9 ± 23.9	90.8 ± 43.2	0.436
PAS (median 11.6 mm)	89.9 ± 31.5	95.5 ± 21.3	0.041
% Change in PAS (median 86.3 %)	90.2 ± 44.2	94.4 ± 31.7	0.422

[a] This table includes all studies with two or more patients undergoing MMA. ± Values are mean (or percent) ± standard deviation. This table shows the random-effects calculated percent surgical success rate for studies having a given characteristic below or above the median value (shown in parenthesis). Surgical success defined as the percent of patients with an AHI <20/h and a ≥50% reduction in the AHI post MMA. **Abbreviations**: AHI, apnea–hypopnea index; BMI, body mass index; PAS, posterior airway space – base of tongue; SNA, sella-nasion-Point A angle; SNB, sella-nasion-Point B angle.

Surgical morbidity and mortality

After surgery, subjects required 3.5 ± 3.5 days (range 1.7 ± 0.5–11.8 ± 4.7) of hospitalization. In 455 consecutive patients, no deaths were reported.[14,21,34,37,38,40,42,47,50,60,61,65,67,71,74,75,77] Only four major complications (1.0%; two cardiac arrests, one dysrhythmia and one mandibular fracture) were reported.[69,75] Facial paresthesia was common (100%), but resolved in 85.8% of patients at 12 months postoperative. One study reported malocclusion easily treated with prosthetics or minor occlusional equilibration in 44% of 29 patients after MMA.[69] However, the largest single center experience ($n = 175$) reported no major skeletal relapse and only mild malocclusion (in some patients) successfully treated with dental adjustment.[50] Another study reported a trend for poor bone healing and foreign-body reactions after surgery.[48] Excluding facial paresthesias and malocclusion, the minor complication rate was 3.1% (12 reporting studies of 390 patients) consisting mostly of minor hemorrhages or local infections cured with antibiotics.[34,40,42,43,47,50,60,61,71,74,75,77] One study reported an association between increasing age (especially ≥45 years) and an increased surgical complication rate.[47]

Li and colleagues reported subtle subjective changes in speech (24%) and swallowing (12%) in 42 subjects (all received sequential phase-I and phase-II surgery) following MMA.[45] Forty of these patients (95%) reported satisfaction with their results. The two subjects not reporting satisfaction had residual moderate–severe OSA and excessive daytime sleepiness after MMA, and one complained of clinically significant dysphagia thought secondary to pharyngeal wall scarring and stricture from previous laser-assisted uvulopalatoplasty. The same authors evaluated 52 patients undergoing sequential UPPP followed by MMA and found only five patients (10%) to have symptoms of velopharyngeal insufficiency (i.e., nasal regurgitation).[43] Two of the five developed symptoms after UPPP (not exacerbated by MMA), all reported symptoms as occasional or rare, and all (100%) had complete resolution of symptoms 12 months after MMA. In another study of seven patients, none reported velopharyngeal insufficiency after MMA.[42] However, Bettega and colleagues reported that all patients ($n = 13$) with previous phase-I (UPPP) surgery experienced velopharyngeal insufficiency after MMA (primarily a phonetic deficit without

Table 5
Predictors of post-MMA success (individual patient data).[a]

Predictor	Post-MMA			Post-MMA		
	Surgical cure (AHI <5)	No cure (AHI ≥5)	*p*-Value	Surgical success[b]	No success	*p*-Value
	(*n* = 124; 39%)	(*n* = 195; 61%)		(*n* = 268; 84%)	(*n* = 51; 16%)	
Pre-MMA						
Age (years)	43.6 ± 9.2 (66)	44.5 ± 8.9 (84)	0.556	43.6 ± 8.9 (125)	46.6 ± 9.5 (25)	0.139
Male (%)	87.4 (87)	84.7 (98)	0.603	83.3 (156)	100.0 (29)	0.018
BMI (kg/m^2)	33.0 ± 8.3 (48)	33.9 ± 8.2 (87)	0.553	33.7 ± 8.3 (116)	32.8 ± 7.7 (19)	0.659
AHI (events/h)	57.7 ± 24.9 (123)	68.3 ± 27.5 (195)	<0.001	62.7 ± 25.8 (268)	71.8 ± 31.6 (51)	0.027
SpO2 nadir (%)	65.4 ± 16.2 (50)	68.3 ± 16.5 (91)	0.313	66.7 ± 16.3 (116)	69.9 ± 16.7 (25)	0.379
Previous phase-I surgery[c] (%)	24.7 (89)	46.2 (132)	0.002	37.6 (186)	37.1 (35)	0.926
Surgery						
Maxillary advancement (mm)	9.5 ± 2.4 (51)	9.0 ± 2.7 (46)	0.303	9.5 ± 2.5 (82)	7.9 ± 2.8 (15)	0.029
Mandibular advancement (mm)	10.8 ± 2.4 (51)	11.8 ± 2.8 (46)	0.068	11.3 ± 2.5 (82)	11.1 ± 3.5 (15)	0.808
Concurrent phase-I surgery[c] (%)	15.3 (124)	8.7 (195)	0.069	11.6 (268)	9.8 (51)	0.715
Post-MMA						
BMI (kg/m^2)	32.2 ± 8.1 (29)	34.5 ± 9.0 (51)	0.257	34.2 ± 8.9 (63)	31.6 ± 7.8 (17)	0.275
% Change in BMI (%)	−2.6 ± 5.6 (29)	−1.9 ± 6.4 (51)	0.604	−1.9 ± 6.1 (63)	−3.1 ± 6.2 (17)	0.463
AHI (events/h)	1.8 ± 1.4 (124)	15.9 ± 12.5 (195)	<0.001	6.3 ± 5.2 (268)	32.1 ± 13.9 (51)	<0.001
% Change in AHI (%)	−96.3 ± 3.9 (124)	−73.4 ± 25.1 (195)	<0.001	−89.1 ± 9.7 (268)	−47.0 ± 35.4 (51)	<0.001
SpO2 nadir (%)	87.2 ± 6.4 (50)	85.7 ± 5.8 (91)	0.171	87.1 ± 5.5 (116)	82.4 ± 6.8 (25)	<0.001
% Change in SpO2 nadir (%)	47.8 ± 75.5 (50)	38.8 ± 82.9 (91)	0.525	45.4 ± 86.1 (116)	26.1 ± 41.0 (25)	0.275

[a] Mean (or percent) ± standard deviation. The total number of patients is shown in parentheses.
[b] Surgical success defined as the percent of subjects with an AHI <20/h and a ≥50% reduction in the AHI post-MMA.
[c] Percent of patients who underwent uvulopalatopharyngoplasty (phase-I surgery) prior to or concurrently with MMA.

regurgitation) that resolved with speech therapy.[47] Smatt and Ferri reported that no patient ($n = 18$) experienced speech problems after MMA.[38]

In patients ($n = 42$) who completed sequential phase-I (UPPP) and phase-II (MMA) surgery, the perceived pain after MMA was not statistically significantly different from the pain encountered after phase-I surgery.[45] Interestingly, Bettega and colleagues noted that patients undergoing sequential phase-I and phase-II surgery reported less pain after MMA compared with phase-I surgery.[47] Most patients were able to return to full-work within two to ten weeks after surgery.[47,61]

Quality of life and other outcomes

One study ($n = 15$) noted a statistically significant improvement in all domains of the functional outcomes of sleep questionnaire (FOSQ) after surgery (summary score 14.4 pre-MMA vs. 18.9 post-MMA; $p < 0.001$).[35] Another study ($n = 50$) observed a 72% absolute reduction in reported symptoms of depression or irritability.[61] Improvements in excessive daytime sleepiness, morning headaches, memory loss and impaired concentration were reported by most patients after MMA.[37,38,50,61,65,67,72,75,77,79] Additionally, statistically and clinically relevant improvements in blood pressure were also noted following surgery (mean systolic blood pressure went from 138.9 mmHg preoperatively to 123.9 mmHg after MMA; $p = 0.001$).[40,61]

Six months after surgery, 50% ($n = 42$) of MMA patients reported a younger facial appearance, 36% reported a more attractive facial appearance, and 9% reported a less attractive facial appearance.[44,46] All patients (100%) in this study reported satisfaction with the surgical outcome. Studies by both Smatt and Ferri ($n = 18$) and Wagner et al. ($n = 17$) reported that no patients were bothered by aesthetics.[38,77] Another study ($n = 9$) reported no aesthetic, occlusion, swallowing or pronunciation problems after MMA.[74] However, Dekeister and colleagues observed that only 64% ($n = 25$) of patients at 12 months post MMA reported overall satisfaction.[75] Patients in this study experienced a relatively high complication rate and lower surgical success compared with other studies.

Discussion

Our systematic review and meta-analysis of 22 studies of MMA describing 627 adult OSA subjects revealed four key findings. First, we found that MMA is highly effective at treating OSA. The mean AHI decreased from 63.9/h to 9.5/h ($p < 0.001$) with a pooled surgical success rate of 86.0%. Overall, 43.2% of subjects were cured (AHI <5/h) with an increased cure rate (66.7%) for those with a preoperative AHI <30/h. Long-term surgical success was maintained at a mean follow-up of 44 months. Second, univariate predictors of surgical success included younger age ($p = 0.013$), lower preoperative AHI ($p = 0.027$), and greater degree of maxillary advancement ($p = 0.029$). Multivariate predictors of surgical success included lower mean age (study level data), lower mean preoperative AHI (study level data), lower preoperative BMI (individual level data), and greater degree of maxillary advancement (both study and individual level data). The degree of mandibular advancement was not predictive of surgical success with univariate or multivariate analysis. Third, MMA was generally safe with a reported major surgical complication rate of 1.0%, minor complication rate of 3.1% and no reported deaths. Persistent facial paresthesias (14.2% at one year) and malocclusion (up to 44%) were also reported. Finally, most subjects reported satisfaction with the surgical outcome with few noting aesthetic complaints. Statistically significant improvements in quality of life measures, OSA symptomatology (i.e., excessive daytime sleepiness), and blood pressure control were noted after MMA.

Early reports of OSA reported an association between mandibular and maxillary insufficiency and nocturnal breathing abnormalities.[1,104] Additionally, subjects with OSA often have multiple pharyngeal abnormalities,[12,13] with primary collapse in the lateral dimension.[105,106] Two studies using computed tomography scanning noted that improvement in pharyngeal restriction following MMA occurred along the entire airway, in both the lateral and anterioposterior dimensions.[14,34] The observed superiority of MMA over UPPP (surgical success rate of 86% vs. ~50%)[9–11] in treating OSA is likely because MMA expands the skeletal framework that all pharyngeal soft-tissue structures (including the tongue) attach to.[88] Candidates for MMA include adolescents (once ossification of the cranial sutures is complete) and adults with OSA who have failed other therapeutic interventions or who have maxillomandibular hypoplasia.[22,23] As shown by our analysis, MMA can be successfully performed in individuals who are either obese or have severe OSA.

Although we observed an overall surgical success rate of 86.0%, the surgical cure rate (AHI <5/h) was only 43.2%. However, because most MMA subjects in the included studies had very severe OSA (mean pre-MMA AHI 63.9 ± 26.7/h and mean SpO2 nadir 71.9 ± 14.8%) and were intolerant of conventional CPAP therapy, the overall reduction in the AHI post MMA to 9.5 ± 10.7/h is likely clinically relevant. Campos-Rodriguez and colleagues observed a 10% absolute increased mortality rate at five years in OSA persons intolerant of CPAP (compared with tolerant subjects; $p < 0.001$).[8] Young and colleagues in a population survey of 1546 persons found that the mortality rate in those with severe OSA (AHI ≥30/h) was 19% compared with 4% in those without OSA (AHI <5/h) ($p < 0.001$) at a mean follow-up of 13.8 years.[3] The adjusted hazards ratios for subjects with untreated OSA were 1.4, 1.7 and 3.8 for mild, moderate and severe disease (p-trend = 0.004). We found that subjects who did not obtain surgical cure had a statistically and clinically relevant decrease in their AHI from 68.3 ± 27.5/h pre-MMA to 15.9 ± 12.5/h post-MMA ($p < 0.001$) and that 88.7% had a post-MMA AHI <30/h. Furthermore, several studies have consistently shown a mortality benefit in CPAP intolerant patients treated with uvulopalatopharyngoplasty (compared with no treatment), even though most surgical patients did not obtain surgical cure (e.g., AHI ≥5/h).[107–109] Thus, MMA is likely to confer a mortality benefit, even in subjects who are not cured.

Additionally, we also observed a statistically significant and clinically relevant reduction in the Epworth sleepiness scale in all subjects from 13.2 ± 5.5 before to 5.1 ± 3.6 after MMA ($p < 0.001$). Although subjects obtaining a surgical cure had a statistically significant lower Epworth sleepiness scale (2.2 ± 2.1) compared with those without surgical cure (6.3 ± 2.1; $p < 0.001$), this finding is unlikely to have clinical relevance.[110]

Patient characteristics and clinical factors predictive of surgical success in our analysis included younger age and lower preoperative BMI and AHI. Others have also reported lower preoperative BMI as predictive of success after MMA.[38,78] No pre- or post-MMA cephalometric measurements other than a wider PAS after surgery were predictive of surgical success or cure. In an analysis of pre-MMA cephalometrics ($n = 18$), Teitelbaum and colleagues found the only measure predictive of surgical success was a smaller baseline hypopharyngeal airway measured at the velum or below the base of tongue.[76] Because too few studies reported these cephalometric measures, we were unable to confirm this finding. Similar to our own findings, Teitelbaum and colleagues found the preoperative posterior airspace (PAS; measured at the base of tongue) was not predictive of surgical success ($p = 0.10$).

Maxillary advancement pulls forward the velum and velopharyngeal muscles[111] while mandibular advancement advances the tongue and suprahyoid muscles.[112] We found that OSA subjects obtaining surgical success had a mean maxillary advancement of 9.5 mm compared with 7.9 mm ($p = 0.029$) for those without success. Subjects with surgical success were more likely to have the maxilla advanced ≥10 mm (67%) compared with those without surgical success (27%; $p = 0.003$). Lye and colleagues found a statistically significant correlation between the degree of maxillary advancement and reduction in AHI ($p = 0.036$, $n = 15$).[35] However, others have reported no association between the degree of maxillary (or mandibular advancement) and improvement in AHI after MMA.[38]

During MMA, the maxilla is generally advanced first (maximally) with the mandible advanced into occlusion. Because many MMA patients have retrognathia (class II malocclusion), the mandible is generally advanced more than the maxilla. We found that the degree of mandibular advancement was not predictive of surgical success (study level data, 11.3 mm with success vs. 11.1 mm without success; $p = 0.808$). This finding likely reflects that mandibular advancement (study level data, median 10.6 mm) was generally sufficient in most patients. However, Farole and colleagues noted that in non-OSA patients undergoing mandibular advancement surgery, the increase in the posterior airspace was quite variable and was not predicted by the degree of mandibular advancement.[113] They argue that the base of the tongue is relatively far from its attachment with the genial tubercles resulting in a variable posterior airway response to mandibular advancement. Additionally, Gale and colleagues noted that the vertical position of the hyoid was also quite variable after mandibular advancement.[114] Maxillary advancement alone in non-OSA patients is known to increase both the nasopharyngeal and hypopharyngeal spaces.[115,116] Additionally, maxillary advancement increases alar width with concomitant decrease in nasal airway resistance.[117,118] Increased nasal resistance is a known major contributor to nocturnal pharyngeal collapse.[119] Clearly, the degree of maxillary advancement is important.

Wagner and colleagues noted that two-thirds of their MMA surgical failures had a previous UPPP (phase-I surgery).[77] Some have recommended MMA as the primary surgical therapy for cephalometrically selected OSA patients, with UPPP (and other soft-tissue surgeries) as a secondary procedure in those with residual OSA.[68] The American Sleep Disorders Association in a review of OSA surgery noted that a lack of reported preoperative patient and treatment characteristics limited the assessment of staged (UPPP followed by MMA) versus primary MMA therapy for OSA.[11] They did note that subjects treated with the staged approach tended to be heavier with more severe disease. In our review we also noted that subjects with a higher pre-MMA AHI were more likely to have had previous phase-I surgery. Additionally, individuals with previous phase-I surgery were less likely to obtain surgical cure after MMA (25% vs. 45%; $p = 0.002$) compared with those without previous surgery. Whether this represents an inherent adverse effect of phase-I surgery on the success of subsequent MMA or a confounding by other patient and treatment factors is unknown. We did observe that individuals with prior phase-I surgery were heavier and had more severe OSA compared with those without previous or concurrent UPPP. Clearly, further research is needed to identify preoperative patient and clinical characteristics to select those patients who would benefit most from a staged versus primary MMA surgical approach. Some have advocated a favorable response to mandibular repositioning by oral appliance (an AHI reduction ≥50%) as a predictor for MMA success.[37,120] However, this recommendation needs to be confirmed in larger trials of MMA. Additionally, preoperative pharyngeal anatomy and patient preference (e.g., recovery time, prolonged facial paresthesias, and malocclusion) are other contributing factors influencing the surgical decision.

Major complications (i.e., ischemic necrosis) following Le Fort-one segmental osteotomy in non-OSA patients are rare.[121] We noted a major complication rate of 1.0% for MMA comprising mostly of cardiac etiology. This may reflect that OSA subjects undergoing MMA are likely older (mean age 44.4 years) with more medical comorbidity. Because many OSA patients undergoing MMA are obese (mean BMI 30.2 kg/m^2) with compromised airways, careful postoperative care is warranted including postoperative evaluation by nasopharyngolaryngoscopy.[21,89,93]

In non-OSA patients, mandibular relapse (slippage of the mandibular advancement due to muscular pull or progressive condylar resorption) has been reported.[122–124] A 10–20% surgical relapse occurs in up to 15% of OSA patients after MMA, but without associated symptoms or apparent worsening of the AHI.[58,98]

Furthermore, surgical relapse is not associated with the magnitude of mandibular advancement.[97,98,100] At a follow-up of 12–36 months after MMA, Hendler and colleagues reported no clinically relevant relapse in seven OSA patients.[42] In our meta-analysis of MMA, the most common (100%) complication after MMA was facial paresthesia caused by neurosensory deficits to the inferior alveolar nerve. Fortunately, most cases of paresthesia resolve (86%) by 12 months after surgery. In non-OSA patients undergoing mandibular advancement, advanced age but not the degree of advancement was associated with protracted facial paresthesia after surgery.[125]

Although the potential for maxillary advancement to worsen speech (i.e., hypernasality) is known in patients with cleft palates,[126,127] no included study in our systematic review reported any substantial adverse effect on speech after MMA. Although one study did report subtle clinically insignificant speech changes in 24% of patients, this finding may be confounded because all included patients had undergone prior UPPP.[45] Few studies of MMA reported swallowing problems after surgery with one study noting that only 12% of OSA patients reported dysphagia and only one patient (2%) complained of clinically relevant dysphagia after MMA.[45] In contrast, up to 30% of patients complain of persistent dysphagia after UPPP, albeit usually mild.[128–131] Patient perception of facial aesthetics was generally positive after MMA. Modified MMA techniques particularly using counter-clockwise rotation and pre- or post-surgical orthodontics have been developed to prevent maxillary protrusion and improve facial aesthetics in certain ethnic populations.[40,41,82] Overall, most individuals reported satisfaction (~90%) with their MMA results,[44,75] compared with only ~70% of patients after UPPP.[132,133]

Our analysis has several potential limitations. First, because we did not have access to the original medical records, our analyses depended on the completeness and accuracy of the reporting physicians. Second, most studies did not define their criteria for scoring apneas and hypopneas, thus included studies may be highly heterogeneous with respect to OSA severity. Furthermore, included reports of surgical success and cure were highly heterogenous, thus our findings may be attributed to patient characteristics, surgical techniques or other confounding factors that we could not assess or control for. Third, despite an exhaustive search, we may not have identified all cases of OSA undergoing MMA, especially since our computerized search strategy was limited to a single database. Finally, because of the limited number of individual cases that reported full patient, clinical and surgical characteristics, we could not include all potential interaction terms in our regression models.

In conclusion, MMA appears safe and highly effective treatment for OSA. Further research is needed to assess clinical outcomes (e.g., quality of life, patient satisfaction, morbidity and mortality) of MMA more thoroughly in long-term cohort studies and to identify which OSA patients would benefit most from maxillomandibular advancement.

Practice points

1. Maxillomandibular advancement is generally safe and highly effective treatment for obstructive sleep apnea.
2. Younger age, lower preoperative weight, and greater maxillary advancement are all predictive of greater surgical success.
3. Most patients report satisfaction after MMA with observed improvements in quality of life measures and most OSA symptomatology.

Research agenda

1. Long-term cohort studies of MMA (compared with conventional medical (CPAP) and other surgical (UPPP) therapies) are needed to more thoroughly assess clinical outcomes (e.g., quality of life, patient satisfaction, medical morbidity and mortality) and confirm the long-term effectiveness of MMA for the treatment of OSA.
2. Large, multicenter assessments of patient, clinical and surgical characteristics using multivariate regression analysis are needed to definitively identify what factors predict surgical success.
3. Further research is needed to identify key preoperative patient and clinical characteristics to determine which patients would benefit most from a staged versus primary MMA surgical approach.

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