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Maxillomandibular advancement is a successful treatment for obstructive sleep apnoea: a systematic review and meta-analysis

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Le taux de succes de la chirurgie d'avancée bimaxillaire est de 100 % en se référant à l'index d'IAH – apnée hypopnée pour les patients qui présentent une apnée du sommeil obstructive sévère.

Abstract. The primary objective of this review was to establish the effectiveness of maxillomandibular advancement (MMA) as a successful treatment modality in improving airway patency in patients with obstructive sleep apnoea (OSA). A systematic and detailed search was performed using PubMed Central, covering the period January 2000 to December 2015, with well-defined selection criteria. The authors independently conducted the study selection, data extraction, and assessed the risk of bias of the included studies. Twenty studies met the inclusion criteria. The outcome measures studied were the apnoea–hypopnoea index (AHI), respiratory disturbance index (RDI), Epworth Sleepiness Scale (ESS), lowest oxygen saturation (LSAT), and body mass index (BMI). The random-effects model was adopted for meta-analysis as moderate heterogeneity was identified. The analysis revealed significant changes in the outcome measures after the intervention. The results showed that the preoperative severity of OSA based on AHI and RDI significantly influences the outcome of MMA intervention, with a strong positive correlation between the pre MMA AHI values and the percentage change post intervention. The surgical success of MMA in patients with OSA was found to be 100% with respect to AHI and RDI scores. It is concluded that MMA is a successful treatment for OSA.

Key words: obstructive sleep apnoea; obstructive sleep apnoea hypopnoea; maxillomandibular advancement; apnoea–hypopnoea index; respiratory disturbance index; Epworth Sleepiness Scale; lowest oxygen saturation.

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Obstructive sleep apnoea (OSA) is an under-diagnosed breathing disorder and a life-threatening condition, usually associated with a reduction in blood oxygen saturation and repetitive airway collapse during sleep[1]. OSA is characterized by excessive daytime sleepiness, loud snoring, fragmentation of sleep, choking during sleep, and even depression and personality changes affecting quality of life.

Observations of periodic breathing in sleep were first reported in the mid 1850s and in the 1870s. British physicians reported several cases of obstructed apnoea as ''fruitless contractions of the inspiratory and expiratory muscles against glottic obstruction with accompanying cyanosis during sleep''[2]. The clinical picture of OSA was first described in 1918 by William Osler, a physician who coined the term Pickwickian syndrome in reference to a character in Charles Dickens's novel *The Pickwick Papers*. During the latter half of the 19th century, several cases of obese persons with extreme daytime sleepiness were described ($n = 346$) and these subjects were labelled as suffering from the 'Pickwickian syndrome'. Bickelmann et al. published the first description of the syndrome in 1956[3].

The pathology of OSA is the result of a cascade of multiple physiological processes. The factors that play significant roles in the development of OSA are a reduction in the dilating forces of the pharyngeal dilator and abnormal upper airway anatomy[4]. Important physiological contributors to the upper airway include, but are not limited to, ventilatory gain to carbon dioxide, arousal threshold during sleep, linkages of the neuromuscular system including airway reflexes, sensory nerve damage, muscle fibre degeneration and changes in fibre type, and even the physics of airflow and fluid dynamics in the lumen of the upper airway[5]. Arousals that halt respiratory events in OSA are typically associated with quite large hyperventilation because respiratory drive has risen substantially during the respiratory event, causing hypocapnia in at least some patients[2].

From the mid 1990s to the present, a plethora of studies have been conducted to determine the prevalence, pathophysiology, and consequences of OSA, as well as various surgical and non-surgical treatment modalities for this disorder. Overnight polysomnography (PSG) is considered the gold standard in the diagnosis of sleep apnoea. The diagnosis of OSA is confirmed if the number of obstructive events (apnoea, hypopnoea, and respiratory event-related arousals) on PSG is greater than 15 per hour or greater than 5 per hour in a patient who reports any of the following: unintentional sleep episodes during wakefulness, daytime sleepiness, un-refreshing sleep, fatigue, insomnia, waking up breath holding, gasping or choking, or the bed partner describing loud snoring, breathing interruptions, or both during the patient's sleep[6]. The severity of OSA is defined using the apnoea–hypopnoea index (AHI) or respiratory distress index (RDI): mild for values of 5–14, moderate for 15–29, and severe for ≥ 30 (events/h)[7]. The treatment of OSA is a complex undertaking and varies depending upon the classification of the condition and severity of the symptoms.

The definition of surgical success is achieving a greater than 50% reduction in the AHI and/or an AHI of less than 20 events per hour[8]. The surgical success rate is based on PSG results and quality of life. Among the various modalities, maxillomandibular surgery gained popularity in the mid 1980s as an efficacious surgical procedure.

The maxillomandibular surgical technique includes a standard Le Fort I osteotomy in combination with a mandibular sagittal split osteotomy for advancement of the maxilla and mandible, which automatically increases the airway space as it draws the base of the tongue and soft palate forwards, thus reducing upper airway resistance. Maxillomandibular advancement (MMA) has been studied widely and is an accepted treatment modality for OSA.

This systematic review of the literature and meta-analysis of studies was conducted to determine the effectiveness of MMA in OSA.

Materials and methods

Search strategy

This systematic review and meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist throughout the whole procedure. The PubMed database was used for the comprehensive electronic search using medical subject heading terms (MeSH); the search covered the period from January 2000 to December 2015. The search used a combination of controlled vocabulary and free text terms such as 'obstructive sleep apnoea', 'obstructive sleep apnoea hypopnoea', and 'maxillomandibular advancement'. Table 1 describes the full electronic search strategy used in PubMed, including the key words and numbers of results.

Inclusion and exclusion criteria

Randomized controlled trials, case series, and cohort studies were included in the systematic review. The criteria for selection included studies (1) of patients of all ages and sexes undergoing MMA or modified MMA for OSA, (2) published after the year 2000, and (3) with pre MMA and post MMA data provided. The studies excluded were those with a sample size of less than 10 patients, studies using animal models, studies not reported in the English language, and studies with patients who had undergone previous surgery to the upper airway or craniofacial surgery not related to OSA or adjunctive pharyngeal surgery done along with MMA.

Data collection

The search strategy obtained 103 articles after searching and filtering. The titles and articles were assessed independently by the review authors to determine whether they met the inclusion criteria. The following data were extracted from the studies included: first author, year of publication, study design, number of subjects, sex, mean age, pre and post MMA data for the apnoea–hypopnoea index (AHI), respiratory disturbance index (RDI), Epworth Sleepiness Scale (ESS), lowest oxygen saturation (LSAT), and body mass index (BMI).

Methodological quality of included studies

The quality of all studies that were considered eligible for the review was assessed. Taking into account the additional information provided by the authors of the trials, studies were grouped into the following categories: (1) low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met, (2) unclear risk of bias (plausible bias that raises some doubt about the results) if one or more criteria were assessed as unclear, and (3) high risk of bias (plausible bias that seriously weakens confidence in the results) if one or more criteria were not met.

Statistical analysis

A meta-analysis of the studies was performed to assess heterogeneity and the overall effect of MMA on OSA. Heterogeneity of the studies was assessed by reviewing the I^2 statistic as well as the Cochran Q statistic, with a cut-off of $P < 0.10$. The individual studies were classified based on the I^2 statistic as showing minimal heterogeneity ($I^2 = 0$–40%), moderate heterogeneity ($I^2 = 30$–60%), substantial heterogeneity ($I^2 = 50$–90%), or considerable heterogeneity ($I^2 = 75$–100%). A fixed-effects model was adopted when the homogeneity hypothesis was not rejected, assuming that the estimated effect sizes only differ by sampling error.

Table 1. PubMed search strategy.

Sl. No.	Search strategy including key words	Time taken	No. of studies
#7	''Search ((OBSTRUCTIVE SLEEP APNEA) OR OBSTRUCTIVE SLEEP APNEA HYPOPNEA) AND MAXILLOMANDIBULAR ADVANCEMENT. Filters: Publication date from 2000/01/01 to 2015/12/01; Humans; English''	03:19:40	103
#6	''Search ((OBSTRUCTIVE SLEEP APNEA) OR OBSTRUCTIVE SLEEP APNEA HYPOPNEA) AND MAXILLOMANDIBULAR ADVANCEMENT. Filters: Publication date from 2000/01/01 to 2015/12/01; Humans''	03:17:54	116
#5	''Search ((OBSTRUCTIVE SLEEP APNEA) OR OBSTRUCTIVE SLEEP APNEA HYPOPNEA) AND MAXILLOMANDIBULAR ADVANCEMENT. Filters: Publication date from 2000/01/01 to 2015/12/01''	03:17:48	143
#4	''Search ((OBSTRUCTIVE SLEEP APNEA) OR OBSTRUCTIVE SLEEP APNEA HYPOPNEA) AND MAXILLOMANDIBULAR ADVANCEMENT''	03:16:57	165
#3	''Search MAXILLOMANDIBULAR ADVANCEMENT''	03:12:52	272
#2	''Search OBSTRUCTIVE SLEEP APNEA HYPOPNEA''	03:12:23	5092
#1	''Search OBSTRUCTIVE SLEEP APNEA''	03:12:12	22,778

A random-effects model was adopted for studies with moderate to considerable heterogeneity. Funnel plot analysis was done to analyze publication bias, and the Spearman rank correlation test was used to measure the degree of association between two variables. The mean differences (Δ) of the outcome measures were calculated by subtracting pre MMA values from post MMA values. The percentage change was calculated using the formula:

$$\%\ \text{change} = \frac{\text{Post MMA value} - \text{Pre MMA value}}{\text{Pre MMA value}} \times 100$$

Surgical success was defined as a greater than 50% reduction in the outcome measure or fewer than 20 events/h after MMA. Surgical cure was defined as a post MMA value of fewer than 5 events/h. Surgical success and cure were analysed for both the AHI and RDI outcome measures.

Results

The search initially identified 103 publications, from which 16 studies were excluded after a review of the titles. Eighty-seven articles were retrieved for further detailed evaluation, and 67 articles were then excluded as they did not fulfil the required study criteria. Thus 20 studies were considered potentially appropriate for this systematic review[9–28]. Figure 1 depicts the PRISMA flow diagram of the study selection process. Table 2 summarizes the characteristics of the selected studies, including demographic data and the outcome measures provided. Table 3 summarizes the pre MMA and post MMA characteristics of the studies for the outcome measures.

Study characteristics

There were 13 retrospective cohort studies, one retrospective review, and five prospective cohort studies, of which one was a prospective randomized controlled trial. A single case series was also included in this meta-analysis, thus making a total of 20 studies. The median minimum follow-up period reported by the studies was 6 months.

Demographic data

The details of 462 patients were extracted from the 20 studies that met the study criteria. The male to female ratio was 5.8:1 (394 male, 85.3%; 68 female, 14.7%). The mean age of the patients was 43.22 years. Twelve studies (251 patients) provided data on AHI changes following MMA[9–14,17–20,22,27]; only six studies documented changes in RDI with MMA (163 patients)[21,23–26,28]. Seven studies (118 patients) reported the ESS[9–11,13,17,18,21], and 16 studies (397 patients) showed LSAT changes with MMA[9,11,13–17,19,20,22–28]. A total of 11 studies (217 patients) provided BMI changes with MMA[9,10,13,17–20,22,23,27,28].

Meta-analysis

Statistically significant moderate to high heterogeneity was found among the 20 studies included in the meta-analysis. Therefore the random-effects model was adopted for the meta-analysis, except for BMI ($I^2 = 0\%$, $P = 0.94$) for which the fixed-effects model was used. Figures 2–6 show the forest plots depicting the effect estimates of the individual studies (with 95% confidence intervals) with the pooled result for AHI, RDI, ESS, LSAT, and BMI, respectively.

Apnoea–hypopnoea index (AHI)

The mean pre MMA AHI score was 54.55 events/h and the mean post MMA AHI score was 9.78 events/h. The mean difference between the pre and post MMA values (ΔAHI) was −44.76. A negative value for the mean difference represents a net reduction in postoperative value for the outcome, thus denoting an improvement in symptoms post MMA. There was an average 82.63% change in outcome after the intervention, ranging between 73.17% and 87.95% within individual studies. A change of more than 80% was reported for 129 out of the 251 patients under consideration. OSA was graded according to AHI values as normal (0–4 events/h), mild (5–14 events/h), moderate (15–29 events/h), or severe ($\geq$30 events/h). After the MMA intervention, 12 patients (4.8%) were found to be normal (<5 events/h) and thus were considered surgically cured. Two hundred and nineteen patients had mild OSA following surgery. All of the studies reviewed showed a reduction in AHI of more than 50% with <20 events/h after MMA. Thus the surgical success was said to be 100%.

A random-effects model was assumed in order to control for the moderate heterogeneity demonstrated ($I^2 = 56\%$). Forest plot analysis (Fig. 2) showed that the individual effect estimates and pooled result lay on the side of an effect favouring MMA. The outcomes were desirable and statistical significance was demonstrated ($P < 0.05$) both at the individual study level and at the meta-analysis level ($P < 0.00001$).

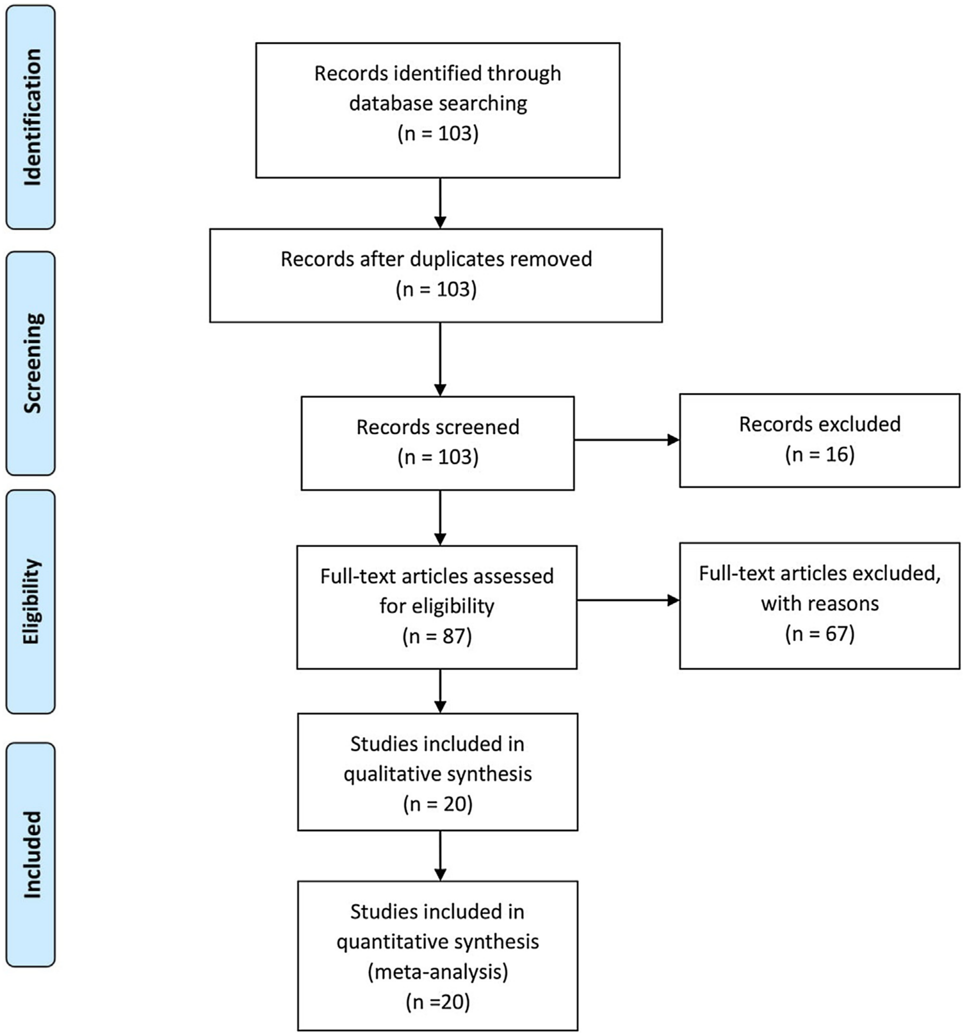


Fig. 1. PRISMA flow diagram of the study selection process.

Table 2. Characteristics of the included studies.

First author and year	Type of study	Number of patients	Age in years, mean ± SD	Sex		Outcome measures
				Male	Female	
Liu 2015[9]	Retrospective cohort	16	47 ± 10.9	15	1	AHI, ESS, LSAT, BMI
Butterfield 2015[10]	Retrospective cohort	15	42.2 ± 11.7	13	2	AHI, ESS, BMI
Liao 2015[11]	Prospective cohort	20	33.4 ± 6.5	17	3	AHI, ESS, LSAT
Schendel 2014[12]	Retrospective cohort	10	46.4 ± 9.7	8	2	AHI
Cohen-Levy 2013[13]	Retrospective cohort	15	42 ± 9.75	15	0	AHI, ESS, LSAT, BMI
Boyd 2013[14]	Retrospective cohort	37	44.2 ± 9	27	10	AHI, LSAT
Serra 2012[15]	Retrospective cohort	37	35 ± 7.25	36	1	LSAT
Abramson 2011[16]	Retrospective cohort	11	39 ± 12.9	9	2	LSAT
Lin 2011[17]	Prospective cohort	12	33 ± 7.71	9	3	AHI, ESS, LSAT, BMI
Vicini 2010[18]	Prospective RCT	25	49.1 ± 9.1	23	2	AHI, ESS, BMI
Blumen 2009[19]	Case series	50	46.4 ± 9	49	1	AHI, LSAT, BMI
Fairburn 2007[20]	Retrospective cohort	20	47.55 ± 10.03	13	7	AHI, LSAT, BMI
Dattilo 2004[21]	Retrospective cohort	15	44.2 ± 7.11	12	3	RDI, ESS
Goh 2003[22]	Prospective cohort	11	42.8 ± 8.19	11	0	AHI, LSAT, BMI
Li 2002[23]	Retrospective cohort	12	47.3 ± 9.8	9	3	RDI, LSAT, BMI
Li 2001[24]	Retrospective cohort	52	46.6 ± 6.7	43	9	RDI, LSAT
Li 2001[25]	Retrospective cohort	44	46.5 ± 6.5	39	5	RDI, LSAT
Li 2000[26]	Retrospective cohort	19	45.3 ± 6.6	15	4	RDI, LSAT
Bettega 2000[27]	Prospective cohort	20	44 ± 12	18	2	AHI, LSAT, BMI
Li 2000[28]	Retrospective review	21	42.6 ± 7.9	13	8	RDI, LSAT, BMI

AHI, apnoea–hypopnoea index; BMI, body mass index; ESS, Epworth Sleepiness Scale; LSAT, lowest oxygen saturation; RCT, randomized controlled trial; RDI, respiratory disturbance index; SD, standard deviation.

Table 3. Pre and post MMA mean (SD) values of the outcome measures from the included studies.

First author	AHI		RDI		ESS		LSAT		BMI		Surgical success[a]
	Pre MMA	Post MMA	Pre MMA	Post MMA	Pre MMA	Post MMA	Pre MMA	Post MMA	Pre MMA	Post MMA	
Liu 2015[9]	59.8 (25.6)	9.3 (7.1)	–	–	19.5 (2.9)	7.1 (2.6)	80.8 (7.6)	88.9 (3.4)	29.4 (5.1)	29.6 (4.1)	93
Butterfield 2015[10]	45.54 (27.6)	7.71 (6)	–	–	13.15 (4.14)	6.14 (3.13)	–	–	30.33 (4.18)	30.05 (3.78)	73.33
Liao 2015[11]	41.6 (19.2)	5.3 (4)	–	–	11.9 (7.3)	7 (3)	80.2 (9.7)	88.9 (5)	–	–	100[b]
Schendel 2014[12]	42.91 (21.17)	5.17 (8.34)	–	–	–	–	–	–	–	–	90
Cohen-Levy 2013[13]	51.07 (15.21)	10.3 (7.24)	–	–	12.3 (5)	3.9 (2.8)	79.5 (13)	82.2 (5.4)	27.41 (3.5)	25 (2.6)	80[b]
Boyd 2013[14]	56.3 (22.6)	11.4 (9.8)	–	–	–	–	74.2 (13.8)	83.6 (10.5)	–	–	–
Serra 2012[15]	–	–	–	–	–	–	85 (6.8)	86 (7)	–	–	81
Abramson 2011[16]	–	–	–	–	–	–	80.5 (11.4)	90 (2.68)	–	–	–
Lin 2011[17]	35.9 (17.95)	4.6 (4.03)	–	–	12.4 (4.5)	6 (2.3)	83 (7.2)	90.6 (3.6)	22.4 (2.73)	21.6 (2.35)	–
Vicini 2010[18]	56.8 (16.5)	8.1 (7)	–	–	11.6 (2.8)	7.7 (1.3)	–	–	32.7 (5.8)	31.4 (6.5)	84
Blumen 2009[19]	65.5 (26.7)	14.4 (14.5)	–	–	–	–	70.7 (19.2)	84.2 (7.4)	28.9 (4.6)	28.4 (4.2)	80
Fairburn 2007[20]	69.22 (35.8)	18.57 (16.29)	–	–	–	–	80.45 (10.49)	87.8 (5.58)	33.85 (8.54)	34.65 (9.16)	–
Dattilo 2004[21]	–	–	76.15 (45.71)	12.59 (12.11)	17.86 (3.76)	4.73 (2.6)	–	–	–	–	95[c]
Goh 2003[22]	70.7 (15.9)	11.4 (7.4)	–	–	–	–	58.6 (12.3)	83.9 (8.8)	29.4 (4.6)	27.2 (3.3)	–
Li 2002[23]	–	–	75.3 (26.4)	10.4 (10.8)	–	–	74.2 (12)	86.9 (6.7)	33.5 (6.2)	32.3 (4.1)	83.3
Li 2001[24]	–	–	61.6 (23.9)	9.2 (8)	–	–	75.9 (10.6)	87.5 (4.7)	–	–	90[d]
Li 2001[25]	–	–	60.3 (22.2)	10.8 (9.4)	–	–	75.8 (12.4)	86.7 (6.1)	–	–	88.63[d]
Li 2000[26]	–	–	63.6 (20.8)	8.1 (5.9)	–	–	73.3 (13.2)	88.1 (4.1)	–	–	94.73[d]
Bettega 2000[27]	59.3 (29)	11.1 (8.9)	–	–	–	–	82 (11)	90 (7)	26.9 (4.3)	25.4 (3.3)	75[b]
Li 2000[28]	–	–	83 (30.1)	10.6 (10.8)	–	–	63.9 (17.7)	86 (7.9)	45 (5.4)	43 (4.3)	81[d]

AHI, apnoea–hypopnoea index (events/h); BMI, body mass index (kg/m^2); ESS, Epworth Sleepiness Scale; LSAT, lowest oxygen saturation (%); MMA, maxillomandibular advancement; RDI, respiratory disturbance index (events/h); SD, standard deviation.

[a] Surgical success defined as the percentage of subjects with an AHI <20/h and $\geq 50\%$ reduction post MMA.

[b] The authors defined surgical success as an AHI <15/h and $\geq 50\%$ reduction post MMA.

[c] The authors defined surgical success as an RDI <15/h and $\geq 50\%$ reduction post MMA.

[d] The authors defined surgical success as an RDI <20/h and $\geq 50\%$ reduction post MMA.

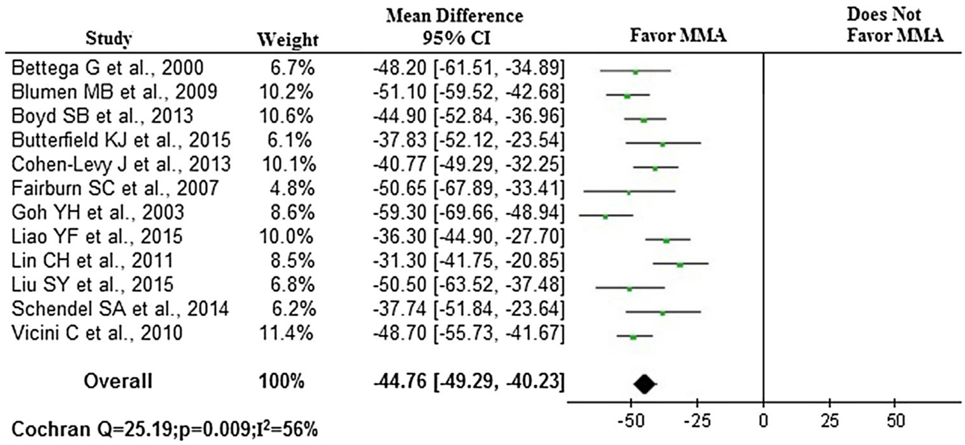


Fig. 2. Forest plot for apnoea–hypopnoea index (AHI).

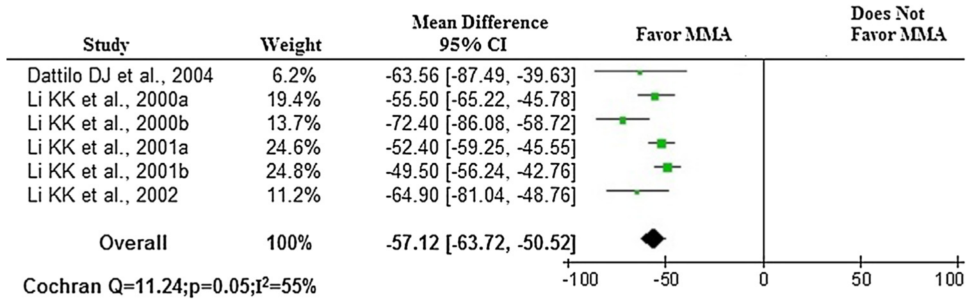


Fig. 3. Forest plot for respiratory disturbance index (RDI).

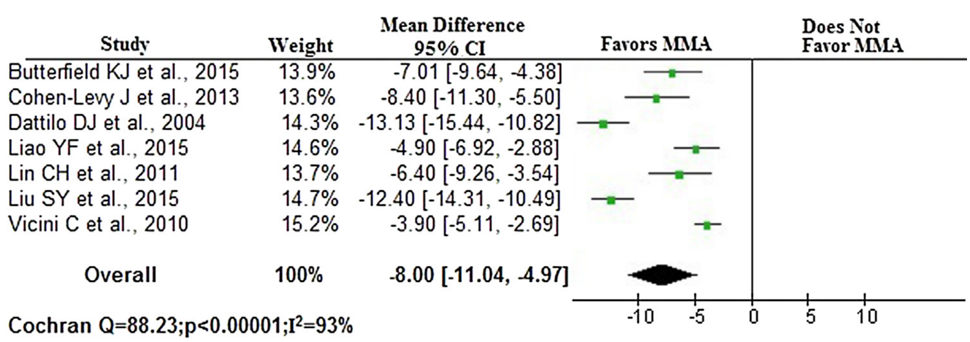


Fig. 4. Forest plot for Epworth Sleepiness Scale (ESS).

Respiratory disturbance index (RDI)

From the six studies that reported changes in RDI, the mean pre MMA score was 69.99 events/h and the mean post MMA score was 10.28 events/h. The mean difference (ΔRDI) calculated was −59.71. Data from the 163 patients were analyzed, and all of them showed a change of more than 80%. The severity of the OSA based on the RDI improved from severe OSA (>30 events/h) to mild OSA (5–14 events/h). The studies showed 100% surgical success but failed to demonstrate surgical cure.

Moderate heterogeneity ($I^2 = 55\%$) was present between the studies, thus the random-effects model was adopted. Forest plot analysis (Fig. 3) showed that the individual effect estimates and pooled result lay on the side of an effect favouring MMA. The forest plot demonstrated statistical significance at the meta-analysis level ($P < 0.00001$).

Epworth Sleepiness Scale (ESS)

The mean pre MMA ESS score was 14.10 and the mean post MMA score was 6.08 (ΔESS = −8.02). Of the 118 patients included in this analysis, 73 showed a change of more than 50% (61.9%). Considerable heterogeneity was present between the studies ($I^2 = 93\%$), thus the random-effects model was considered for analysis. Analysis of the forest plot (Fig. 4) showed that individual effect estimates and pooled results lay on the side of an effect favouring MMA ($P < 0.00001$).

Lowest oxygen saturation (LSAT)

Sixteen studies provided the details regarding pre and post MMA LSAT values, which were 76.13% and 86.95%, respectively (ΔLSAT = 10.83%). Changes in LSAT were minimal in most of the studies, with

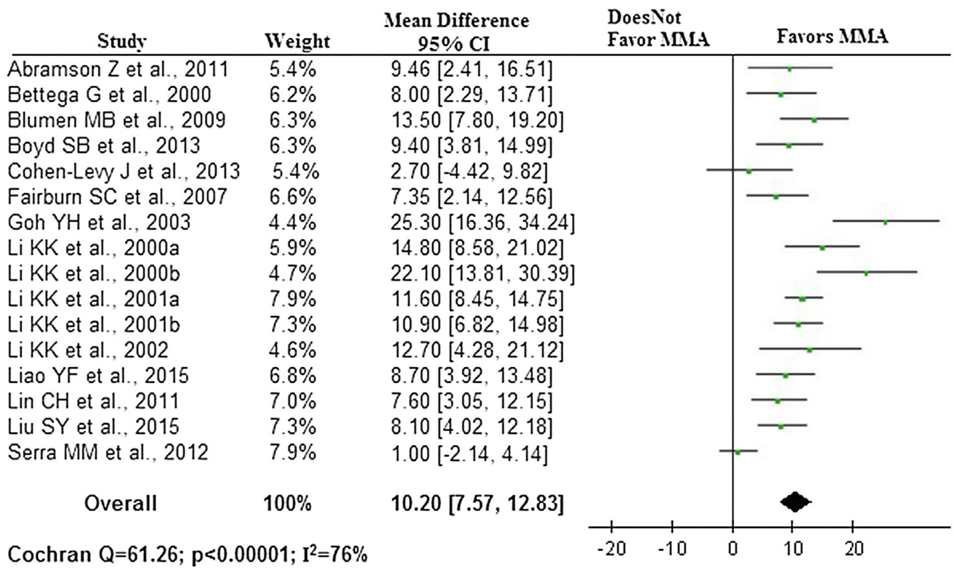


Fig. 5. Forest plot for lowest oxygen saturation (LSAT).

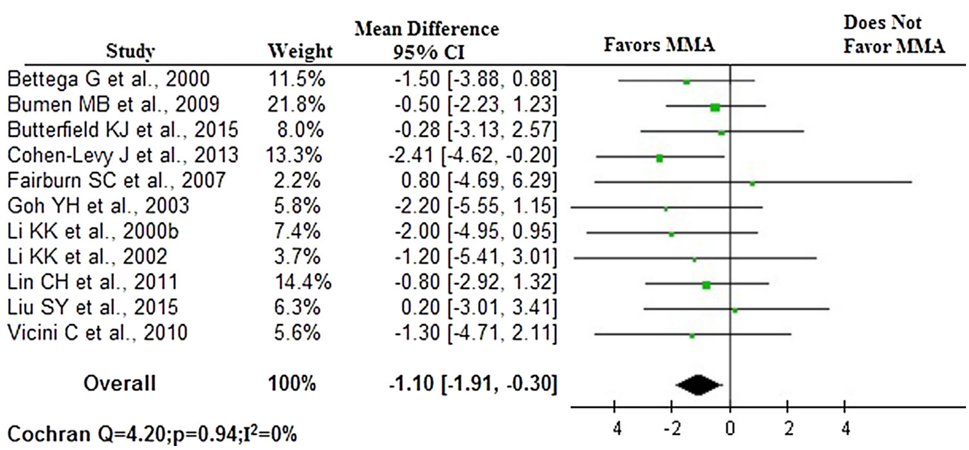


Fig. 6. Forest plot for body mass index (BMI).

changes of less than 10% seen in 26.2% of the patients. Considerable heterogeneity was present ($I^2 = 76\%$) between the studies and the random-effects model was considered for analysis. Forest plot analysis (Fig. 5) showed that the confidence interval crossed the line of no effect for two individual studies[13,15], representing no statistical significance at the study level; however, the pooled result demonstrated a statistical significance at the meta-analysis level ($P < 0.00001$).

Body mass index (BMI)

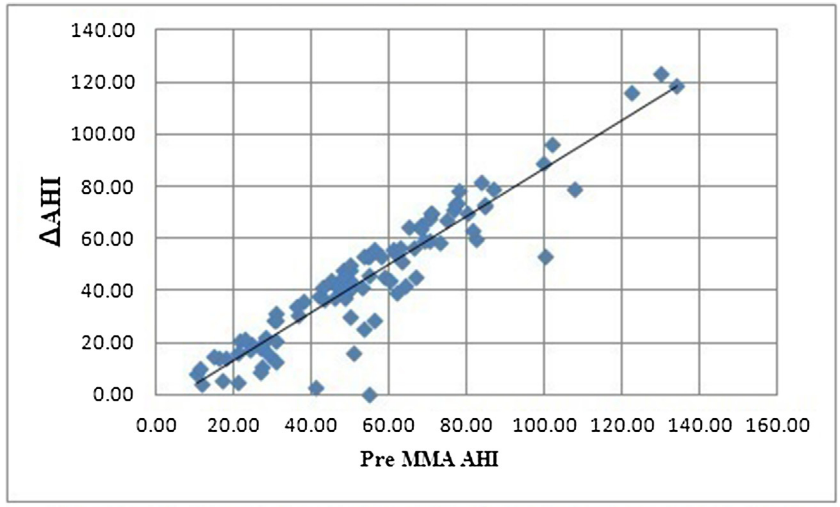
Data for BMI were available for 217 patients from 11 studies. The mean pre MMA value was 30.89 kg/m^2 and the mean post MMA value was 29.88 kg/m^2 (ΔBMI = -1.02 kg/m^2). The studies showed minimal changes in BMI values, with a maximum change of 8.79% (in 6.9% of patients)[13]. The studies maintained homogeneity ($I^2 = 0\%$), thus the fixed-effects model was adopted for analysis. On analyzing the forest plot (Fig. 6), the confidence interval of all except one study[13] crossed the line of no effect, with effect estimates to the side favouring MMA. The pooled result favoured MMA. Thus there was no statistical significance at the study level, but significance was demonstrated at the meta-analysis level ($P = 0.007$).

Risk of bias

The risk of bias was assessed individually for the studies included. No study reported allocation or sequence generation or information about blinding. Individual patient data were provided in eight studies[10,12,16–18,20–22]. Information on loss to follow-up and drop-outs was provided in few studies. The retrospective cohort studies demonstrated a low risk of bias for selection, information, loss to follow-up, non-response, and confounding. The study by Dattilo and Drooger showed a high risk of information bias[21], and other studies were unclear on selection bias (Cohen-Levy et al.[13], Abramson et al.[16], Li et al.[23,25,28]). All prospective cohorts showed a low risk of bias in most aspects[11,17,18,22,27]. Meta-analysis of the studies by graphically analyzing funnel plots showed symmetric inverted funnel shapes, consistent with minimal publication bias.

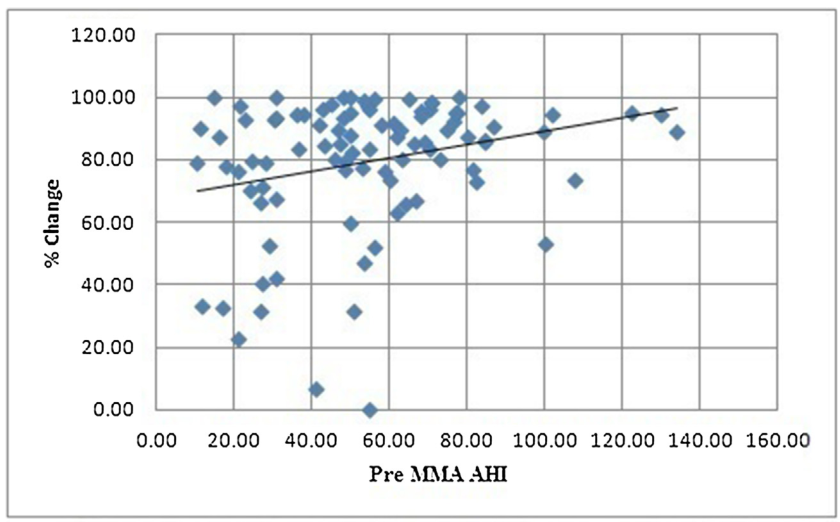
Individual patient data

Out of the eight studies that provided individual patient data, six reported individual pre and post MMA AHI values, accounting for 93 patients. The mean pre MMA AHI value was 54.66 events/h, whereas the mean post MMA AHI value was 9.94 events/h. Seventy-seven of the 93 patients were obese (82.8%) according to the pre MMA BMI values, of whom eight were extremely obese (class III, BMI $\geq$40 kg/m^2). Thirty-three patients showed surgical cure (35.5%) with a post MMA AHI value of <5 events/h. The surgical success rate in these patients was 80.6%, with 75 patients showing a >50% change after MMA and a post MMA AHI value of less than 20 events/h. A significant relationship was identified between the pre MMA AHI values and the difference between the pre and post MMA AHI values (ΔAHI) for the available individual data. The post MMA AHI values were always lower than the pre MMA values. Hence the absolute value of the mean differences was taken for the correlation analysis. A strong positive linear correlation was found to be present between the pre MMA AHI values and ΔAHI (Spearman's $r = 0.916$, $P = 0.0001$) (Fig. 7). A significant positive linear correlation was also found between the pre MMA AHI values and the percentage change in AHI (Spearman's $r = 0.230$, $P = 0.026$) for the available individual data (Fig. 8).



Spearman's r = 0.916 (p = 0.0001), significant positive correlation present (p < 0.05)

Fig. 7. Relationship between pre MMA AHI and the change in AHI (ΔAHI); MMA, maxillomandibular advancement; AHI, apnoea–hypopnoea index.



Spearman's r = 0.230 (p = 0.026), significant positive correlation present (p < 0.05)

Fig. 8. Relationship between the pre MMA AHI and the percentage change in AHI; MMA, maxillomandibular advancement; AHI, apnoea–hypopnoea index.

Discussion

This systematic review and meta-analysis studied the data from a total of 462 patients. Substantial improvements were seen for the outcome measures AHI, RDI, ESS, and LSAT in the interventional studies included.

AHI improved from 54.55 events/h to 9.78 events/h post MMA. The maximum change in AHI was noticed in the study by Goh and Lim[22], in which a change in AHI from 70.17 events/h to 11.4 events/h was recorded; the minimum change was seen in the study by Lin et al.[17], which documented a change from 35.9 events/h to 4.6 events/h. The studies demonstrated 100% surgical success according to the AHI. A positive correlation was found between the pre MMA AHI values and the percentage change in AHI, as well as between the pre MMA AHI values and ΔAHI when the individual data of 93 patients were analyzed. This showed that the patients with high AHI values prior to MMA experienced a greater improvement than those with low pre MMA AHI values. The chance of complete surgical cure following MMA was also found to increase with higher AHI values prior to the intervention. These results are similar to those of the study by Zaghi et al.[29], in which those with a higher severity of disease showed a greater magnitude of improvement. With regard to the RDI (data from six studies reporting 163 patients), the mean pre MMA score was 69.99 events/h and post MMA score was 10.28 events/h. All studies showed an RDI value of less than 15 events/h post MMA, which was graded as mild; however, surgical success was 100%.

Surgical cure is defined as a post MMA AHI of fewer than 5 events/h. In the articles included, the study by Lin et al. demonstrated a mean post MMA AHI value of 4.6, thus showing surgical cure[17]. Of the 251 patients assessed for AHI who underwent MMA, 12 were considered normal following surgery, whereas 219 continued with mild OSA and 20 with moderate OSA. For the 93 patients with individual data available, the surgical success rate was 80.6% and the cure rate was 35.5%. A prior meta-analysis by Zaghi et al. demonstrated surgical cure of 38.5% on evaluation of 455 patients[29]. Although the surgical success rate was found to be high for MMA, the rate of surgical cure was found to be lower. Surgical success does not determine the resolution of chronic disease. The low cure rates in these studies indicate residual disease. The postsurgical follow-up in the articles under review ranged from 2 to 66 months. Longer follow-up periods are required to evaluate surgical cure for OSA.

The subjective evaluation of patients diagnosed with OSA by quantifying excessive day time sleepiness was demonstrated by the ESS. The pre MMA ESS score of all patients (118 patients from seven studies) exhibited a high level of excessive day time sleepiness. The change in mean ESS score from 14.10 to 6.08 suggested that all patients had an ESS score of less than 8 and an improvement in their symptoms. Among the 16 studies (397 patients) recording LSAT, the mean LSAT was 76.13% pre MMA and 86.95% post MMA. The Pre MMA data showed severe oxygen desaturation ($\leq$80%), and an improvement in LSAT was noticed in the post MMA mean values ranging from 82.2% to 90.6%.

It was found that the majority of subjects undergoing MMA for OSA management were obese (mean 30.89 kg/m^2). The post MMA measure of BMI showed only a small change of 1.02 kg/m^2 with a post MMA mean of 29.88 kg/m^2. This is in accordance with the results of the meta-analysis performed by Holty and Guilleminault in 2010[30].

MMA traditionally consists of a Le Fort I osteotomy of the maxilla and bilateral sagittal split osteotomy of the mandible. The mean advancement of 10–12 mm in OSA patients should be coupled with a balanced facial profile and functional occlusal stability. The studies reviewed employed the conventional MMA technique, incorporating certain modifications to achieve this aim. More specifically, the surgical methods included a Le Fort I osteotomy with segmentation or modified step design[11,14], counterclockwise rotation of the maxillomandibular complex, reverse T mandibular osteotomy (combination of genioglossal advancement and advancing genioplasty)[11], piriform rim recontouring, anterior nasal spine reduction, limited septoplasty[14], and augmentation with autogenous[12] or allogeneic grafts. Use of the segmental maxillomandibular rotational advancement technique (extrusion of the anterior segment, elongation of the posterior maxilla, and counterclockwise rotation of the maxillomandibular complex) was described for the Far East Asian population with a convex craniofacial profile and dentoskeletal class II malocclusion[17]. Rigid osteosynthesis and intermaxillary fixation for a minimum of 2 weeks were employed in all studies.

MMA expands the skeletal frame to which the pharyngeal structures and tongue are attached. This results in a reduction in airway collapsibility during negative-pressure inspiration and an increased upper airway space[9,30,31]. Holty and Guilleminault performed a meta-analysis of 22 studies reporting AHI outcomes and studying 627 adults who underwent MMA for the treatment of OSA[30]. The studies included were performed during the period January 1950 to May 2009. The mean AHI decreased from 63.9 events/h to 9.5 events/h ($P < 0.001$) following surgery. The pooled surgical success and cure rates were 86.0% and 43.2%, respectively. They identified younger age, lower preoperative weight, lower preoperative AHI, and greater degree of maxillary advancement to be predictive of increased surgical success. Most subjects reported satisfaction after MMA, with improvements in quality of life measures and most of their OSA symptomatology.

In 2015, Zaghi et al. performed a meta-analysis in which individual data of 518 patients were collected[29]. The mean (standard deviation) postoperative changes in the AHI and RDI after MMA were −47.8 (25.0) and −44.4 (33.0), respectively, with the negative result denoting a net decrease in the value. Rates of surgical success and cure were 85.5% ($n = 389$) and 38.5% ($n = 175$), respectively, among 455 patients with AHI data, and 64.7% ($n = 44$) and 19.1% ($n = 13$), respectively, among 68 patients with RDI data. They concluded that MMA is an effective treatment for OSA. Most patients with high residual AHI and RDI after other unsuccessful surgical procedures for OSA are likely to benefit from MMA.

With regard to complications, Schendel et al. reported two minor complications, one being infection leading to plate removal and the other being an unfavourable split, which was managed intraoperatively by complete osteotomy and advancement[12]. Vicini et al. reported that all patients suffered transient paresthesia in the infraorbital and mandibular areas[18]. Of the 25 patients studied, one had no paresthesia upon follow-up. Blumen et al. observed wound bleeding in two cases and phlebitis in one case[19]. Eight patients had late complications of fixation plate infection, of whom six underwent removal of the fixation plate. Ninety-four percent had immediate postoperative sensory disorders (anaesthesia or sensory loss) in the region of the mandibular nerve and inferior alveolar nerve. Eighteen months later, 48% no longer experienced sensory disorders, but 52% had persistent sensory disorders (although rarely anaesthesia), mainly affecting the lips and chin. Lin et al. reported transient hypaesthesia of the inferior alveolar nerve of the mandible on two of 24 sides[17]. In the study by Goh and Lim, postoperative wound pain in two of 11 patients led to removal of the titanium screw and plates at 7 and 9 months, respectively, and three of the 11 patients (27.3%) had persistent mandibular paresthesia at 9 months postoperative[22]. Li et al. found that eight of 52 patients experienced regurgitation of liquids when drinking hastily, which had resolved 1 year later[24]. In another study, postoperative complications were reported in six out of the 21 morbidly obese patients, which included one with transient velopharyngeal insufficiency that resolved within 6 months and four who encountered complications related to the stability of the fixation or suspension[28]. An infection was reported in the other patient, which required debridement and subsequent removal of the fixation. On analyzing all of the studies, the complication rates are unremarkable and acceptable. No morbidity was reported in any of the studies. The duration of follow-up mentioned in the studies ranged from a minimum of 2 months to a maximum of 66 months.

Six studies discussed the changes in facial profile pre and post MMA[13,17,23,25,26,28]. A maxillomandibular deficiency was demonstrated in all studies except one[26], and the post MMA results showed maxillomandibular protrusion in all studies. However, postoperative facial aesthetics depend on the patient's perception. Young patients and those with a thinner soft tissue profile may have unfavourable changes[25]. Six studies reported patient satisfaction, providing feedback data for a total of 146 patients[11,13,17,19,25,26]. Fifty-six patients (38.35%) were very satisfied with the outcome, 39 (26.71%) were satisfied, and another 39 (26.71%) reported indifference regarding their pre- and postsurgical appearance. Twelve patients (8.21%) were disappointed, of whom six were unsatisfied with the results of the MMA surgery. The need for orthodontics was mentioned in a few studies, although few studies provided details about presurgical orthodontics. The combination of surgical–orthodontic treatment in OSA patients allows the correction of malocclusion in larger advancements. Presurgical orthodontic treatment was performed in the studies by Schendel et al.[12] and

Cohen-Levy et al.[13], whereas a surgery-first modified MMA was done in the study by Liao et al.[11]. Maintaining maxillomandibular fixation (MMF) for 2–6 weeks post MMA was performed in four studies[15,19,21,22], whereas no MMF was done in two studies[16,20]. Thus the studies emphasize the need for patient-specific treatment planning in regards to the age, aesthetic, and functional components, along with the relief of OSA symptoms.

Among the studies included, those by Butterfield et al., Schendel et al., Abramson et al., Lin et al., and Fairburn et al. demonstrated significant three-dimensional upper airway changes post MMA[10,12,16,17,20]. Ten studies documented the amount of advancement done in MMA, the mean being 9.68 mm for the maxilla and 10.39 mm for the mandible.

Even though tremendous changes in the outcome of sleep parameters were shown from pre MMA to post MMA, one major concern in this meta-analysis is that most of the studies had performed intrapharyngeal surgery prior to MMA and only a few studies reported MMA as an isolated primary procedure. In view of the improved sleep parameters, quality of life, surgical success, and fewer complications, there is a need for more studies so that MMA can be advocated as a primary isolated procedure for OSA.

This meta-analysis focused on studies performed after 2000, aiming to analyze the recent evidence and trends in MMA. Only one randomized controlled trial on MMA was identified and included in the review. There is a need for more randomized controlled trials, as well as studies of MMA or modified MMA according to ethnicity in order to evaluate the amount of advancement and the cosmetic results. A limitation of this study is that only articles in the English language were included and all were published after 2000, which may have resulted in selection bias. Another limitation is that the individual patient data were not available for all of the studies, therefore generalization is not possible to an extent.

This meta-analysis included studies in which modified MMA techniques were used[11,17,22]. Further modification of the surgical technique will make MMA a more acceptable treatment modality. In addition, well-validated standardized outcomes should be assessed in further studies so that comparisons can be made with other similar trials. Studies with larger sample sizes and in varied demographic populations would go a long way in establishing results, with sample sizes calculated beforehand to ensure studies of adequate statistical power.

In conclusion, the preoperative severity of OSA based on AHI and RDI was found to significantly influence the outcome of MMA intervention. MMA is a successful treatment choice for OSA, improving the AHI and reducing other symptoms, and thus improving quality of life. Randomized controlled trials and long-term follow-up periods are required, along with the consideration of modified MMA techniques.

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Competing interests

There is no conflict of interest for the authors or institution.

Ethical approval

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Patient consent

Not required.

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