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CLINICAL REVIEW

# Maxillomandibular advancement versus multilevel surgery for treatment of obstructive sleep apnea: A systematic review and meta-analysis[☆]

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## SUMMARY

Multilevel surgery (MLS) and maxillomandibular advancement surgery (MMA) are two established options in surgical management of obstructive sleep apnea (OSA), which target different levels of airway obstruction. The objective of this review was to comparatively evaluate the clinical efficacy and safety of MMA and MLS in the treatment of OSA. MEDLINE and Embase databases were searched for studies on MMA and/or MLS in OSA patients. Twenty MMA studies and 39 MLS studies were identified. OSA patients who underwent MMA showed significant improvements in AHI, LSAT, ODI, and ESS by −46.2/h, 13.5%, −30.3/h, and −8.5, respectively. The pooled rates of surgical success and cure for MMA were 85.0% and 46.3%, respectively. Patients who underwent MLS showed significant improvements in AHI, LSAT, ODI, and ESS by −24.7/h, 8.7%, −19.1/h, and −5.8, respectively. The pooled surgical success and cure rates for MLS were 65.1% and 28.1%, respectively. The rates of major complication of MMA and MLS were 3.2% and 1.1%, respectively, and the rate of minor complication of MMA was higher than that of MLS. We conclude that both MMA and MLS are effective treatment options for OSA. Compared to MLS, MMA may be more effective in improving OSA. However, the complication rate of MMA is higher.

## Introduction

Obstructive sleep apnea (OSA), a potentially life-threatening sleep-related breathing disorder, is characterized by repetitive partial or complete obstruction of the upper airway during sleep, causing hypoxemia and sleep fragmentation [1]. A recent systematic review reported that the overall prevalence of OSA ranges from 9% to 38% in the general adult population [2].

Continuous positive airway pressure (CPAP) is generally accepted as a first-line therapy for patients with moderate to severe OSA [3]. However, the clinical efficacy of CPAP can be hampered by its often low compliance rate, prompting a substantial proportion of OSA patients to seek therapeutic alternatives, such as a mandibular advancement device (MAD) and surgical treatment [4]. Surgical treatment is a viable alternative for patients who have specific surgically correctable anatomical abnormalities, which play an important role in upper airway obstruction [5].

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**Abbreviations**

| | |
|---|---|
| AHI | apnea-hypopnea index |
| BMI | body mass index |
| CI | confidence interval |
| CPAP | continuous positive airway pressure |
| ESS | Epworth sleepiness scale |
| DISE | drug-induced sleep endoscopy |
| LSAT | lowest saturation of oxygen |
| MAD | mandibular advancement device |
| MINORS | methodological index for non-randomized studies |
| MLS | multilevel surgery |
| MMA | maxillomandibular advancement |
| ODI | oxygen desaturation index |
| OSA | obstructive sleep apnea |
| PAV | pharyngeal airway volume |
| PRISMA | preferred reporting items for systematic reviews and meta-analyses |
| PSG | polysomnography |
| RCT | randomized controlled trial |
| RDI | respiratory disturbance index |
| SMD | standardized mean difference |
| WMD | weighted mean difference |

Moderate to severe OSA is usually characterized by multilevel obstructions [6], hence the surgical interventions aimed to correct only one region cannot eliminate all obstructions in the upper airway. In 1986, Riley et al. [7] have first proposed multilevel surgery (MLS) for OSA patients with multiple obstructions. Today, MLS for OSA is widely accepted as treatment modality in case of multilevel obstruction.

MLS however, is not suitable for all OSA patients. Another commonly employed surgical procedure that targets multiple levels is maxillomandibular advancement (MMA), which has been demonstrated to be the most effective surgical option for OSA [8]. The reported surgical success rate for MMA is 86.0% [9].

Currently, there is still no universally accepted guideline of surgical procedures for OSA given the variations in anatomy, disease severity, patient comorbidities, and patient preference. For OSA cases with diffusely complex or multiple sites of obstruction, the indications and staged protocols of surgical treatment remain unclear. When there is no generally accepted indicative results of clinical, laboratory, or endoscopic examination in patients with moderate to severe OSA (e.g., significant skeletal-dental deformity, complete concentric collapse at velum observed with drug-induced sleep endoscopy [DISE]), some surgeons are inclined to start with MLS and keep MMA as a reserve therapeutic option in case of surgical failure, while others prefer to start with MMA as the primary treatment option. Thus, further definition of the role of MMA and MLS in the treatment protocol for OSA is called for, which is vital for both patients and physicians in final decision-making regarding the choice of surgery type. To our knowledge, only one systematic review [10] published in 2010 has compared MMA and MLS for OSA treatment, but only regarding the aspect of clinical efficacy, which places emphasis on the need for an updated and thorough assessment and comparison of the two types of surgical interventions. Thus, the aim of this systematic review was to comprehensively evaluate and compare the treatment outcome of MMA and MLS for OSA treatment, through the assessment of apnea-hypopnea index (AHI) and Epworth sleepiness scale (ESS) as primary outcomes. The secondary objective was to investigate the differences in complication rates for both treatment options.

## Methods

In accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement, the protocol for the systematic review was registered (PROSPERO ID: CRD42020 152077; https://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42020152077).

### *Selection criteria*

The inclusion criteria were: 1) adult patients (>18 y old) with OSA diagnosed by means of polysomnography (PSG; AHI ≥5/hour); 2) patients that underwent MMA or one-phase MLS (at least one velopharyngeal and one hypopharyngeal surgery in single stage); 3) studies that reported pre- and postoperative PSG data; 4) studies with a follow-up ≥6 mo; 5) studies with the following designs: randomized controlled trials (RCTs), quasi-experimental studies, and cohort studies; and 6) English language.

Studies were excluded from the review if: 1) sample size <10 patients; 2) studies with patients who underwent other adjunctive procedures at the time of MMA (e.g., tonsillectomy, uvulopalatopharyngoplasty, partial glossectomy); and 3) preliminary studies in which the findings had been nested in other studies with larger sample size and/or longer follow-up.

### *Literature search*

With the assistance of an information specialist, a literature search was performed using the MEDLINE and Embase database on May 6, 2020. Search terms and full search strategies used for each database utilized are available as supplementary information (Supplementary Tables S1a and S1b).

### *Study selection*

Two reviewers (NZ and ZH) independently selected studies for further assessment by title and abstract review. All potentially eligible studies were retrieved in full texts for further evaluation. In case of disagreement, a third reviewer (JH) was consulted. The reference lists of the retrieved papers were manually checked by NZ and ZH.

### *Data extraction*

A specially designed data-extraction form was used to extract data from the included studies. Extracted information included:

- General information: article title, year of publication, and first author.
- Study characteristics: study design and length of follow-up.
- Participant characteristics: sample size, age, gender, and body mass index (BMI).
- Intervention and setting: specific surgical technique.
- Outcome data: results of pre- and postoperative PSG, including apnea-hypopnea index (AHI), respiratory disturbance index (RDI), lowest saturation of oxygen (LSAT), and oxygen desaturation index (ODI) ; pre- and postoperative Epworth sleepiness scale (ESS) score; surgical success rate and cure rate; postoperative complications; and duration of hospital stay.

Data were extracted by NZ and ZH independently. Discrepancies were resolved through discussion with JH. If RDI was reported in a study, it would be extracted as AHI, since these two respiratory parameters have been consolidated based on the 2013 American Academy of Sleep Medicine's manual for the scoring of sleep and associated events [11]. We defined “surgical success” as “at least 50% reduction in AHI following surgery accompanied by a postoperative AHI of <20” [12], and “surgical cure” as “a postoperative AHI <5” [13]. If there were multiple follow-up data in the results, the data with the longest follow-up time were selected.

### *Quality assessment*

Methodologic quality assessment of each study was performed by NZ and ZH independently, and any discrepancies were resolved through discussion with JH.

The risk of bias of included RCTs were assessed using the Cochrane Collaboration “Risk of bias” tool [14]. Six domains of bias, including selection, attribution, detection, performance, reporting, and other bias, were classified as “low risk”, “high risk” or “unclear risk”. The total quality of each study was considered as good (low risk of bias for at least 3 items), fair (low risk of bias for 2 items), or low (low risk for no items or 1 item) [15].

The quality assessment of non-randomized studies was based on the Methodological Index for Non-Randomized Studies (MINORS), which is a validated tool for the methodological assessment of non-randomized surgical studies [16]. The MINORS tool includes 12 items for comparative studies, the first eight being specifically for non-comparative studies. Each item was scored as 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate). The global ideal score was 24 for comparative studies and 16 for non-comparative studies. The categorization of comparative studies was as follows: 0−6 “very low quality”, 7−10 “low quality”, 11−15 “fair quality”, and ≥16 “high quality”. For non-comparative studies, the total score of 0−4 indicates very low quality, 5−7 indicates low quality, 8−12 indicates fair quality, and ≥13 indicates high quality [17].

The studies categorized as “high risk of bias” or “low/very low quality” were excluded from the meta-analysis.

### *Statistical analysis*

The weighted mean ( $\overline{x}^{*}$ ) and weighted standard deviation ( $\overline{SD}^{*}$ ) of parameters (age, BMI, AHI, LSAT, and ESS) were calculated using the following equations, respectively [18]:

$$\overline{x}^{*} = \frac{\sum_{i=1}^{N} w_i x_i}{\sum_{i=1}^{N} w_i}$$

$$\overline{SD}^{*} = \sqrt{\frac{\sum_{i=1}^{N} w_i \left(x_i - \overline{x}^{*}\right)^2}{\frac{(M-1)}{M}\sum_{i=1}^{N} w_i}}$$

$N$ is the number of observations; $M$ is the number of nonzero weights; $W_i$ are the weights; and $x_i$ are the observations.

The inverse variance methods for meta-analysis was conducted to pool the results of AHI, LSAT, and ESS, respectively, and rendered a weighted mean difference (WMD) and its associated 95% confidence interval (CI). The magnitude of the effect was interpreted through the value of standardized mean difference (SMD); small = 0.2, medium = 0.5 and large = 0.8 [19]. The random effects model and fixed effects model were used depending on the presence of heterogeneity. Heterogeneity between studies was evaluated by Cochran $Q$ statistic, with a statistical heterogeneity cutoff of $P < 0.10$ [20], as well as $I^2$ statistic with cutoff of 25% (low), 50% (moderate), and 75% (high) [21]. Pooled surgical success and cure rates were generated in the meta-analysis by using the DerSimonian-Laird random effects pooling method.

Given the inconsistency of surgical interventions utilized in MLS, the subgroup analysis was done for the subsets of study groups according to the combination of different target levels of surgery (surgery addressing obstruction at the levels of soft palate and tongue base − subgroup 1; soft palate and hyoid − subgroup 2; and soft palate, tongue base, and hyoid − subgroup 3). Based on current literature, it is suggested that increasing preoperative severity of OSA is likely an important predictor of treatment failure [9,22], combined with the heterogeneity of patients' baseline AHI in the analyzed studies. Therefore, we calculated separate pooled estimates for studies with different range of mean baseline AHI (AHI <40/h; 40/h ≤ AHI ≤70/h; AHI >70/h). These cut-off values were determined based on the range of average baseline AHI of all included studies. A subgroup analysis was also conducted in the studies with long follow-up periods (≥2 y). The comparison of the estimates for each outcome between MMA and MLS was performed by using Z test, as proposed by Altman and Bland [23].

Risk of publication bias across studies was assessed by Begg's test and Egger's test, with $P$ value of <0.05 suggesting the presence of bias. Sensitivity analyses were conducted to assess the stability of the results. Statistical analyses were conducted using Review Manager version 5.3 (Cochrane Centre, Copenhagen, Denmark) and Stata version 16.0 (StataCorp LLC, College Station, USA).

## Results

The PRISMA flow diagram of study selection progress is described in Supplementary Fig. S1. The search in the electronic database resulted in 3383 publications after deduplication, from which 205 full articles were retrieved for further full-text evaluation.

**MMA group** Twenty studies were identified [24−43]. One of these was a RCT, one was a retrospective quasi-experimental study, nine were prospective cohort studies, and nine were retrospective cohort studies. Their characteristics are shown in Table 1. The mean follow-up period from surgery to postoperative PSG was 25.4 mo (range, 6.0 mo − 12.5 y).

**MLS group** Thirty-nine articles fulfilled the inclusion criteria, including one article added from hand searching of included articles' reference lists [22,44−81]. One was a randomized controlled trial, five were prospective quasi-experimental studies, six were retrospective quasi-experimental studies, eleven were prospective cohort studies, and 17 were retrospective cohort studies. Their characteristics are shown in Table 2. The mean follow-up period from surgery to postoperative PSG was 9.9 mo (range, 6.0 mo − 3.3 y).

### *Quality assessment of individual studies*

**MMA group** The only RCT [41] was considered of good quality (Supplementary Fig. S2). Of the non-randomized studies, two studies were classified as “high quality”, and the other 17 studies as “fair quality” (Supplementary Table S2a).

**MLS group** The only RCT [53] was considered of fair quality (Supplementary Fig. S2). Of the non-randomized studies, seven studies were classified as “high quality”, twenty-nine studies as “fair quality”, and two studies as “low quality” (Supplementary Table S2b).

### *Demographic data*

**MMA group** Twenty studies on MMA were reviewed. Excluding duplication of data yielded a total of 528 distinct patients, most of whom were overweight (weighted BMI: 28.6 ± 6.6 kg/m$^2$) males (78.9%) with a weighed mean age of 42.9 y (Table 3).

**Table 1**
Characteristics of studies on maxillomandibular advancement surgery.

| Study | Design | N | Age (years) (mean ± SD) | % Male | Degree of advancement (mm) (mean ± SD) | | Follow-up (mean ± SD) | BMI (mean ± SD) | | AHI (mean ± SD) | | LSAT (mean ± SD) | | ODI (mean ± SD) | | ESS (mean ± SD) | | % Success | % Cure | Day |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Max | Mand | | Pre-op | Post- op | Pre-op | Post- op | Pre-op | Post- op | Pre-op | Post-op | Pre-op | Post- op | | | |
| Bettega et al., 2000 [24] | Retrospective | 20 | 44.4 ± 10.6 | 90 | 11.8 ± 0.5 | 11.8 ± 0.5 | 6 m | 26.9 ± 4.3 | 25.4 ± 3.3 | 59.3 ± 29.0 | 11.1 ± 8.9 | 82 ± 11 | 90 ± 7 | | | | | 75[c] | | 7 |
| Bianchi et al., 2014 [25] | Retrospective | 10 | 45 ± 14 | 100 | 10 | 10 | 6 m | | | 56.8 ± 5.2 | 12.3 ± 5.5 | | | | | | | | | |
| Boyd et al., 2015 [26] | Prospective | 14 | | | 7.0 ± 2.3 | 9.2 ± 3.3 | 6.6 ± 2.8 y | | | 50.0 ± 20.0 | 8.0 ± 10.7 | | | | | | | | | 2.3 |
| Conradt et al., 1997 [27] | Retrospective | 15 | 44 ± 12 | 93.3 | | | >2 y | 28.3 ± 3.4 | | 51.4 ± 16.9 | 8.5 ± 9.4 | | | | | | | | | |
| Gerbino et al., 2014 [28] | Prospective | 10 | 44.9 | | 9.2 ± 1.2 | 10.4 ± 2.2 | 6 m | 31.6 ± 5.5 | 28 ± 1.4 | 69.8 ± 35.2 | 17.3 ± 16.7 | | | 59.5 ± 5.3 | 9.1 ± 8.0 | | | 80[d] | | |
| Goh et al., 2003 [29] | Prospective | 11 | 42.8 ± 8.2 | 100 | 10 | 10 | 7.7 m | 29.4 ± 4.6 | 27.2 ± 3.3 | 70.7 ± 15.9 | 11.4 ± 7.4 | 58.6 ± 12.3 | 83.9 ± 8.8 | | | | | 81.8 | | 4.2 |
| Goodday et al., 2016 [30] | Retrospective | 13 | 37.8 ± 8.57 | 84.6 | | | 9.6 m | 38.8 ± 10.9 | 37.3 ± 8.0 | 117.9 ± 9.2 | 16.1 ± 26.2 | | | | | 12.9 ± 5.5[b] | 5.0 ± 4.1[b] | 76.9 | 46.2 | |
| Hsieh et al., 2014 [31] | Prospective | 16 | 33 ± 7.9 | 75 | | | 12±8 m | 22.0 ± 3.3 | | 35.7 ± 18 | 4.8 ± 4.4 | | | | | | | 100 | | |
| Kastoer et al., 2020 [32] | Prospective | 14 | 51.1 ± 7.3 | 57.1 | | | 6 m | 25.7 ± 3.7 | | 40.2 ± 25.6 | 9.9 ± 7.2 | | | 13.5 ± 8.6 | 4.0 ± 3.5 | 13 ± 6 | 9 ± 7 | | | |
| Li et al., 1999 [35] | Retrospective | 175 | 43.5 ± 11.5 | 83 | | | 6 m | | | 72.3 ± 26.7[a] | 7.2 ± 7.5[a] | 63.2 ± 17.5 | 86.6 ± 3.4 | | | | | 95[e] | | 2.4 |
| Li et al., 2000 [34] | Retrospective | 40 | 45.6 ± 20.7 | 82.5 | 10.8 ± 2.7 | 10.8 ± 2.7 | 4.2 ± 2.7 y | 31.4 ± 6.7 | 32.2 ± 6.3 | 71.2 ± 27.0[a] | 7.6 ± 5.1[a] | 67.5 ± 14.8 | 86.3 ± 3.9 | | | | | 90[e] | | 2.4 |
| Li et al., 2001 [36] | Retrospective | 52 | 46.6 ± 6.7 | 82.7 | 10.5 ± 1.5 | | 6 m | 32.0 ± 6.0 | | 61.6 ± 23.9[a] | 9.2±8[a] | 75.9 ± 10.6 | 87.5 ± 4.7 | | | | | 90[f] | | |
| Li et al., 2002 [33] | Prospective | 12 | 47.3 ± 9.8 | 75 | 10.5 ± 1.2 | 10.5 ± 1.2 | 6 m | 33.5 ± 6.2 | 32.3 ± 4.1 | 75.3 ± 26.4[a] | 10.4 ± 10.8[a] | 74.2 ± 12 | 86.9 ± 6.7 | | | | | 83.3[f] | | |
| Liao et al., 2015 [37] | Prospective | 20 | 33.4 ± 6.5 | 85 | | | 14 ± 9.3 m | 22.4 ± 3.4 | | 41.6 ± 19.2 | 5.3 ± 4 | 80.2 ± 9.7 | 88.9 ± 5 | | | 11.9 ± 7.3 | 7 ± 3 | 100[c] | | |
| Liu et al., 2016 [38] | Retrospective | 20 | 44 ± 12 | 85 | 7 ± 1.4 | | 6 m | 27 ± 4.6 | 27.4 ± 4.6 | 53.6 ± 26.6 | 9.5 ± 7.4 | 80.9 ± 8.9 | 94.1 ± 3.5 | 38.7 ± 30.3 | 8.1 ± 9.2 | 17 ± 4.8 | 5.7 ± 2.7 | 90 | 50 | |
| Rubio-Bueno et al., 2017 [39] | Prospective | 34 | 40.8 ± 13.9 | 41.2 | 4.9 ± 3.2 | 10.4 ± 3.9 | 6 m | 27.6 ± 4.5 | 25.5 ± 4.3 | 38.3 ± 10.7 | 6.5 ± 4.3 | | | 34.7 ± 12.5 | 5.4 ± 4.1 | 17.4 ± 5.4 | 0.8 ± 1.4 | 100 | 52.9 | <2 |
| Veys et al., 2017 [40] | Prospective | 10 | 44.7 ± 9.5 | 80 | 4.8 ± 2.8 | 8.3 ± 2.3 | 6 m | | | 26.8 ± 12.7 | 12.3 ± 14.4 | | | | | 14.1 ± 5.9 | 5.7 ± 3.0 | 70 | 40 | |
| Vicini et al., 2010 [41] | RCT | 25 | 49.1 ± 9.1 | 92 | | 11 | 13 ± 2.5 m | 32.7 ± 5.8 | 31.4 ± 6.5 | 56.8 ± 16.5 | 8.1 ± 7 | | | | | 11.6 ± 2.8 | 7.7 ± 1.3 | 88 | 36 | <7 |
| Vigneron et al., 2017 [42] | Retrospective | 29 | 40.7 ± 12.6 | | 8.4 ± 4.1 | 11.7 ± 5.1 | 12.5 ± 3.5 y | 24.6 ± 4 | | 56.6 ± 24 | 25.5 ± 20.6 | | 83.1 ± 5.8 | | | | 7.5 ± 4.7 | 41.4 | | 5–8 |
| Wu et al., 2019 [43] | Retrospective | 28 | 37.2 ± 11.8 | 53.6 | 2.0 ± 3.1 | 8.8 ± 3.7 | >1 y | 24.2 ± 5.1 | | 59.3 ± 14.5 | 10.9 ± 3.3 | 73.4 ± 10.8 | 87.9 ± 3.7 | | | 12.8 ± 2.8 | 6.9 ± 2.5 | 85.7 | 46.4 | |

AHI, apnea-hypopnea index (events/h); BMI, body mass index (kg/$m^2$); Day, days in hospital; ESS, Epworth sleepiness scale; LSAT, lowest oxygen saturation (%); m, months; Max, maxilla; Mand, mandible; N, number of patients; ODI, oxygen desaturation index; RCT, randomized controlled trial; y, years.

[a] Respiratory disturbance index (RDI) in this study was extracted as AHI.

[b] The number of patients was 9.

[c] This study defined surgical success as an AHI <15/h with ≥50% reduction in postoperative AHI.

[d] This study didn't define the criteria of surgical success.

[e] This study defined surgical success as a RDI <15/h with ≥50% reduction in postoperative RDI.

[f] This study defined surgical success as a postoperative RDI <20/h.

**Table 2**
Characteristics of studies on multilevel surgery.

| Study | Design | N | Age (years) (mean ± SD) | % Male | Follow-up (mean ± SD) | BMI (mean ± SD) | | AHI (mean ± SD) | | LSAT (mean ± SD) | | ODI (mean ± SD) | | ESS (mean ± SD) | | % Success | % Cure | Day (mean ± SD) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Pre-op | Post- op | Pre-op | Post- op | Pre-op | Post-op | Pre-op | Post-op | Pre-op | Post-op | | | |
| **Subgroup 1. Soft palate level & tongue base level** | | | | | | | | | | | | | | | | | | |
| Aynaci et al., 2018 [44] | Retrospective | 20 | 41.7 ± 8.4 | 85 | 6 m | | | 25.1 ± 6.0 | 13.40 ± 3.0 | 80.3 ± 6.0 | 91.9 ± 1.7 | | | 19.8 ± 2.5 | 11.1 ± 1.5 | | | 1.3 ± 0.4 |
| | | 20 | 45.0 ± 7.1 | 80 | 6 m | | | 36.4 ± 4.9 | 10.0 ± 1.9 | 78.8 ± 3.5 | 96.3 ± 1.2 | | | 20.1 ± 1.7 | 6.5 ± 1.3 | | | 2.6 ± 0.8 |
| Babademez et al., 2010 [45] | Retrospective | 16 | 41.3 ± 10.5 | 100 | 6 m | 29.6 ± 2.5 | 29.5 ± 2.6 | 20.1 ± 10.5 | 8.9 ± 6.5 | 84.6 ± 3.4 | 86.6 ± 2.0 | | | | | 62.5 | | |
| Bostanci et al., 2016 [47] | Retrospective | 82 | 50.5 ± 9.2 | 92.7 | 6 m | 30.6 ± 3.0 | | 47.3 ± 18.7 | 19.9 ± 17.4 | 75.7 ± 8.9 | 82.3 ± 7.4 | 44.8 ± 21.4 | 17.7 ± 15.9 | | | 74.4 | | |
| Cambi et al., 2019 [48] | Retrospective | 20 | 55.6 ± 9.1 | 85 | 6 m | 30.1 ± 2.3 | 28.9 ± 2.4 | 49.3 ± 18.5 | 19.4 ± 10.1 | 69.5 ± 9.9 | 80.0 ± 7.4 | | | 12.7 ± 4.3 | 7.7 ± 4.5 | 60 | | 5.2 ± 0.9 |
| Cammaroto et al., 2017 [49] | Retrospective | 10 | 58.4 ± 9.9 | | ≥6 m | 26.8 ± 3.7 | | 34.0 ± 14.0 | 22.9 ± 13.3 | | | | | 12.3 ± 4.2 | 8.5 ± 5.4 | 50 | | 6.7 ± 1.3 |
| | | 10 | 52.8 ± 11.4 | | ≥6 m | 27.0 ± 2.1 | | 35.6 ± 13.9 | 9.6 ± 9.3 | | | | | 13.0 ± 4.5 | 4.9 ± 3.9 | 90 | | 7.1 ± 1.5 |
| | | 10 | 48.2 ± 11.4 | | ≥6 m | 28.8 ± 2.6 | | 37.8 ± 21.6 | 13.5 ± 7.8 | | | | | 10.4 ± 2.5 | 3.9 ± 3.6 | 90 | | 7.1 ± 3.2 |
| Ceylan et al., 2009 [50] | Prospective | 26 | 46.3 ± 3.9 | 88.5 | 1 y | 28.6 ± 3.8 | | 29.6 ± 7.8 | 16.1 ± 3.9 | 86.8 ± 8.9 | 94.6 ± 4.9 | | | 10.8 ± 3.2 | 8.2 ± 2.7 | 53.8[c] | | |
| Chen et al., 2019 [51] | Prospective | 22 | 40.5 ± 6.8 | 90.9 | 6 m | 29.1 ± 3.5 | 28.9 ± 3.6 | 66.4 ± 17.0 | 35.1 ± 18.5 | 61.9 ± 12.5 | 67.8 ± 19.3 | | | | | 63.6[d] | | |
| Chen et al., 2014 [52] | Prospective | 24 | 42.3 ± 8.3 | 100 | 1 y | 27.5 ± 2.7 | | 46.1 ± 13.3 | 26.2 ± 18.9 | | | | | | | | | |
| | | 26 | 43 ± 9.4 | 100 | 1 y | 26.6 ± 2.4 | | 51.8 ± 14.7 | 25.2 ± 7.9 | | | | | | | | | |
| Chen et al., 2018 [53] − group 2 | RCT | 45 | | | 6 m | | | 49.7 ± 7.4 | 27.0 ± 4.0 | 60.3 ± 7.3 | 76.9 ± 4.0 | | | 13.0 ± 2.6 | 8.5 ± 2.0 | 64.4 | 11.1 | |
| Chiffer et al., 2015 [54] | Prospective | 18 | | 83.3 | 6–24 m | 34.2 ± 6.9 | 32.2 ± 7.2 | 53.9 ± 25.4 | 19.8 ± 22.1 | | | | | | | 61 | | |
| Emara et al., 2011 [57] | Prospective | 23 | | | 6 m | 27.5 ± 1.1 | | 40.7 ± 17.4 | 15.4 ± 10.7 | 78.9 ± 12.6 | 87.2 ± 11.1 | | | 14.2 ± 2.3 | 8.3 ± 3.9 | 86.9 | | |
| Eun et al., 2008 [58] | Prospective | 66 | 44.7 ± 10.6 | 87.9 | 6 m | 27.6 ± 3.4 | 27.4 ± 3.2 | 22.9 ± 14.7[a] | 13.9 ± 18.7[a] | 79.1 ± 5.7[a] | 79.4 ± 16.5[a] | | | 11.4 ± 5.0 | 7.5 ± 4.5 | 53.6 | 50 | 2 |
| Friedman et al., 2003 [59] | Retrospective | 143 | 47.0 ± 11.7 | 72.7 | ≥6 m | 31.5 ± 4.8 | | 43.9 ± 23.7 | 28.1 ± 20.6 | 81.4 ± 10.4 | 85.9 ± 9.8 | | | 15.2 ± 3.1 | 8.3 ± 3.9 | | | |
| Friedman et al., 2007 [60] | Retrospective | 122 | 42.2 ± 11.4 | 65.6 | 12.2 ± 4.2 m | 28.3 ± 5.0 | | 23.2 ± 7.6 | 14.5 ± 10.2 | 88.9 ± 4.8 | 90.4 ± 4.3 | | | 9.7 ± 3.9 | 6.9 ± 3.3 | 47.5 | | |
| Gunbey et al., 2015 [61] | Prospective | 42 | 47.1 ± 14.5 | 69 | 6 m | 32.6 ± 8.4 | 31.2 ± 9.1 | 35.8 ± 12.1 | 15.3 ± 9.8 | | | | | | | | | |
| Hendler et al., 2001 [62] | Retrospective | 33 | 47 ± 10.5 | 84.8 | 6 m | 32.6 ± 7.0 | | 60.2 ± 29.9[b] | 28.8 ± 27.4[b] | 72.4 ± 15.2 | 80.4 ± 12.3 | | | | | | | |
| Li et al., 2016 [63] | Retrospective | 30 | 41.5 ± 9.4 | 90 | 6–8 m | 26.4 ± 3.0 | 25.5 ± 3.0 | 48.4 ± 16.9 | 16.5 ± 11.2 | 76.4 ± 8.5 | 82.4 ± 5.4 | | | 10.9 ± 4.7 | 8.7 ± 3.9 | 73 | | |
| Li et al., 2016 [64] | Retrospective | 25 | 42 ± 9 | 80 | 6–8 m | 26.5 ± 3.0 | 25.6 ± 2.9 | 45.7 ± 21.7 | 12.8 ± 8.2 | 77.1 ± 10.5 | 83.3 ± 5.6 | | | 9.6 ± 4.9 | 7.5 ± 4.3 | 80 | | 5.6 ± 1.3 |
| Li et al., 2013 [65] | Retrospective | 45 | 40.3 ± 12.8 | 100 | 6 m | 27.7 ± 3.6 | 27.4 ± 3.4 | 39.4 ± 17.8 | 8.9 ± 5.9 | 66 ± 16 | 83 ± 5 | | | 12.9 ± 4.9 | 3.4 ± 2.9 | 51.1 | 37.8 | 7 |
| Lin et al., 2010 [66] | Retrospective | 43 | 39 | 95.3 | 6 m | 27.9 ± 3.9 | 28.0 ± 3.9 | 51.5 ± 25.4 | 23.4 ± 24.7 | 75.5 ± 10.4 | 82.1 ± 10.9 | | | 12.8 ± 5.1 | 10.0 ± 4.3 | 60.5 | | |
| Neruntarat et al., 2009 [22] | Prospective | 72 | 35.8 ± 10.9 | 95.8 | 14.2 ± 1.8 m | 28.8 ± 2.4 | 30.9 ± 2.8 | 35.6 ± 9.2 | 16.8 ± 3.2 | 85.6 ± 3.4 | 88.2 ± 2.4 | | | 14.2 ± 3.4 | 8.2 ± 2.5 | 55.6 | | 1 |
| Omur et al., 2005 [68] | Retrospective | 22 | 44.5 ± 8.0 | | 14.0 ± 6.7 m | 30.3 ± 3.8 | 29.2 ± 3.3 | 47.5 ± 15.7[b] | 17.3 ± 14.2[b] | | | | | 13.9 ± 2.2 | 5.4 ± 4.3 | 81.8[e] | | 3.8 ± 1.6 |
| Plzak et al., 2013 [69] | Retrospective | 79 | 50.5 ± 9.1 | 78.5 | 6 m | 28.1 ± 3.1 | 28.3 ± 3.5 | 28.7 ± 17.1 | 14.1 ± 18.2 | | | 15.1 ± 8.2 | 10.3 ± 7.9 | 10.6 ± 3.8 | 7.3 ± 3.2 | 51.7 | | 3 |
| Sezen et al., 2011 [70] | Prospective | 12 | 48.3 ± 8.8 | 83.3 | 1 y | 30.9 ± 2.8 | 30.6 ± 2.7 | 28.8 ± 10.7 | 15.3 ± 11.1 | | | | | 14.8 ± 2.5 | 7.6 ± 3.2 | 50[f] | | |
| Toh et al., 2014 [74] | Retrospective | 20 | 47.1 ± 11.4 | 80 | 8.2 ± 3.2 m | 26.9 ± 2.9 | 26.2 ± 3.0 | 41.3 ± 22.1 | 13.5 ± 17.1 | 72.9 ± 19.3 | 84.5 ± 7.1 | | | 13.0 ± 2.8 | 5.6 ± 4.4 | 55 | 35 | 4.1 ± 0.7 |
| Tsou et al., 2018 [75] | Retrospective | 36 | 40.2 ± 9.1 | 88.9 | 1 y | 26.9 ± 2.9 | 26.1 ± 2.9 | 25.1 ± 17.5 | 17.5 ± 18.9 | | | | | 11.9 ± 4.3 | 10.2 ± 4.3 | 66.7 | | |
| Turhan et al., 2015 [76] | Prospective | 90 | 48 | 91.1 | 6 m | 30.7 | | 51.8 ± 18.8 | 20.5 ± 17.7 | 75.6 ± 9.3 | 82.4 ± 6.6 | 48.0 ± 19.5 | 18.2 ± 15.5 | | | 74.4 | | |
| Vicente et al., 2006 [77] | Prospective | 54 | 47.3 ± 4.5 | 92.6 | 3 y | 29.6 ± 4.8 | 28.1 ± 4.8 | 52.8 ± 14.9 | 14.1 ± 23.5 | 76.2 ± 12.4 | 82.2 ± 11.2 | | | 12.2 ± 3.3 | 8.2 ± 6.1 | 78[g] | | |
| Vicini et al., 2014 [78] | Retrospective | 12 | 49.6 ± 11.3 | 100 | ≥6 m | 28.2 ± 2.7 | 27.0 ± 2.1 | 38.4 ± 19.7 | 19.8 ± 14.1 | | | | | 13.75 ± 4 | 7.6 ± 4.4 | 33.3 | | 8.3 ± 2.4 |
| | | 12 | 54.2 ± 10.8 | 75 | ≥6 m | 27.3 ± 2.0 | 26.1 ± 2.0 | 38.5 ± 14.3 | 9.9 ± 8.6 | | | | | 12 ± 4.9 | 4.4 ± 4.1 | 83.3 | | 7.3 ± 1.5 |
| Wang et al., 2013 [79] | Retrospective | 36 | 44 | 86.1 | 1 y | 29.2 ± 2.9 | 28.9 ± 2.8 | 59.8 ± 20.5 | 23.2 ± 18.4 | 70.5 ± 12.4 | 85.6 ± 10.0 | | | 12.2 ± 5.8 | 5.5 ± 3.6 | 66.7 | | |
| Yuksel et al., 2016 [81] | Prospective | 14 | 41.4 ± 8.9 | 92.9 | 2 y | 30.8 ± 3.7 | | 33.2 ± 18.9 | 18.0 ± 11.3 | | | 30.3 ± 16.9 | 15.5 ± 13.2 | 11.9 ± 7.0 | 5.0 ± 4.4 | 57.1 | | |
| **Subgroup 2. Soft palate level & hyoid level** | | | | | | | | | | | | | | | | | | |
| Benazzo et al., 2008 [46] | Retrospective | 109 | 51.3 ± 9.4 | 100 | 6 m | 28.2 ± 3.1 | 27.7 ± 2.9 | 37.0 ± 19.1 | 18.7 ± 16.0 | | | | | 10.5 ± 3.1 | 7.2 ± 2.3 | 61.5 | | |
| El-Anwar et al., 2018 [56] | Prospective | 20 | 47.1 ± 9.2 | | 6–14 m | 33.4 ± 2.5 | | 48.8 ± 31.6 | 24.5 ± 10.9 | 73.5 ± 14.8 | 84 ± 5.3 | | | 12.6 ± 5.6 | 4.1 ± 2.7 | | | |
| Tantawy et al., 2018 [73] | Prospective | 32 | 46 ± 4.7 | 43.8 | 6–14 m | 33.4 ± 2.01 | | 68.4 ± 25.3 | 25.6 ± 9.5 | 66.8 ± 11.3 | 83.2 ± 2.9 | | | 13.8 ± 5.4 | 5.2 ± 1.6 | | | |
| **Subgroup 3. Soft palate level & tongue base level & hyoid level** | | | | | | | | | | | | | | | | | | |
| Chen et al., 2018 [53] − group 1 | RCT | 45 | | | 6 m | | | 52.3 ± 6.3 | 14.9 ± 2.2 | 58.7 ± 8.3 | 86.0 ± 5.4 | | | 12.8 ± 2.2 | 6.0 ± 1.3 | 84.4 | 11.1 | |
| Cillo et al., 2013 [55] | Retrospective | 13 | 43.0 ± 2.4 | 100 | 18 ± 3.6 m | | | 28.3 ± 13.2 | 12.1 ± 8.2 | | | | | 15.2 ± 3.0 | 6.3 ± 3.9 | | | |
| Neruntarat et al., 2003 [67] | Retrospective | 46 | 40.1 ± 4.2 | 82.6 | 3.3 ± 0.5 y | 28.9 ± 2.1 | 31.1 ± 2.7 | 47.9 ± 8.4[b] | 18.6 ± 4.1[b] | 81.2 ± 2.9 | 87.2 ± 3.1 | | | 15.9 ± 2.7 | 7.3 ± 2.7 | 65.2[e] | | |
| Sorrenti et al., 2006 [71] | Retrospective | 10 | 51.7 ± 7 | 100 | 14.6 m | 31.0 ± 2.5 | 28.5 ± 2.4 | 54.7 ± 11.5 | 9.4 ± 5.4 | 77 ± 6.2 | 90.7 ± 3 | | | 14.3 | 5.3 | 100 | | 16 ± 2 |
| Sun et al., 2008 [72] | Prospective | 31 | 41 ± 9.8 | 100 | 6 m | 28.5 ± 3.2 | 28.4 ± 3.6 | 65.9 ± 23.8 | 28.6 ± 29.1 | 72.7 ± 11.9 | 75.0 ± 12.5 | | | 17.1 ± 4.1 | 8.9 ± 4.9 | 64.5[h] | | |
| Yi et al., 2011 [80] | Prospective | 26 | 47 | 84.6 | 6 m | 29.3 | 28.0 | 65.6 ± 17.6 | 30.1 ± 23.1 | 74 ± 28 | 82.8 | | | 13.5 ± 5.9 | 6.8 ± 5.2 | 46.2 | | |

AHI, apnea-hypopnea index (events/h); BMI, body mass index (kg/m$^2$); Day, days in hospital; ESS, Epworth sleepiness scale; LSAT, lowest oxygen saturation (%); m, months; N, number of patients; ODI, oxygen desaturation index; RCT, randomized controlled trial; y, years.

[a] The number of patients was 58.

[b] Respiratory disturbance index (RDI) in this study was extracted as AHI.

[c] This study defined surgical success as an AHI <20/h with ≥50% reduction in postoperative AHI and a postoperative ESS score <10.

[d] This study defined surgical success as ≥ 50% reduction in postoperative AHI.

[e] This study defined surgical success as a RDI <20/h with ≥50% reduction in postoperative RDI.

[f] This study defined surgical success as an AHI <15/h with ≥50% reduction in postoperative AHI.

[g] This study defined surgical success as an AHI <20/h with ≥50% reduction in postoperative AHI and a postoperative ESS score <11.

[h] This study defined surgical success as an AHI <20/h with significant clinical improvement reported by patients.

**Table 3**
Summary of weighted data for studies on maxillomandibular advancement surgery and multilevel surgery.

| Variable | | Pre-op | | Post-op | | Change | | | $P$[b] |
|---|---|---|---|---|---|---|---|---|---|
| | | N | Weighted mean ± SD | N | Weighted mean ± SD | WMD | 95% CI | $P$[a] | |
| Age (years) | MMA | 504 | 42.9 ± 11.3 | – | – | – | – | – | – |
| | MLS | 1313 | 45.5 ± 10.8 | – | – | – | – | – | |
| BMI (kg/m$^2$) | MMA | 359 | 28.6 ± 6.6 | 185 | 29.4 ± 6.2 | – | – | – | – |
| | MLS | 1420 | 29.1 ± 4.2 | 878 | 28.4 ± 4.1 | – | – | – | |
| AHI (/h) | MMA | 393 | 57.3 ± 26.6 | 393 | 10.4 ± 11.2 | −46.2 | [-52.4, −39.9] | <0.001 | <0.001 |
| | MLS | 1639 | 42.2 ± 21.0 | 1639 | 19.0 ± 16.4 | −24.7 | [-28.1, −21.4] | <0.001 | |
| LSAT (%) | MMA | 203 | 74.4 ± 12.9 | 203 | 88.1 ± 5.5 | 13.5 | [10.5, 16.5] | <0.001 | 0.014 |
| | MLS | 1164 | 76.7 ± 12.5 | 1164 | 84.2 ± 9.5 | 8.7 | [6.2, 11.1] | <0.001 | |
| ODI (/h) | MMA | 78 | 35.1 ± 22.8 | 78 | 6.3 ± 6.4 | −30.3 | [-46.3, −14.2] | <0.001 | 0.322 |
| | MLS | 265 | 36.3 ± 22.5 | 265 | 15.5 ± 14.1 | −19.1 | [-34.2, −4.0] | 0.010 | |
| ESS | MMA | 164 | 14.1 ± 5.4 | 164 | 4.8 ± 4.1 | −8.5 | [-12.2, −4.9] | <0.001 | 0.143 |
| | MLS | 1309 | 12.6 ± 4.4 | 1309 | 7.3 ± 3.9 | −5.8 | [-6.6, −5.0] | <0.001 | |
| Success rate (%) | MMA | 340 | – | – | – | 85.0 | [76.4, 91.9] | <0.001 | <0.001 |
| | MLS | 1339 | – | – | – | 65.1 | [60.6, 69.5] | <0.001 | |
| Cure rate (%) | MMA | 130 | – | – | – | 46.3 | [38.0, 54.7] | <0.001 | 0.135 |
| | MLS | 221 | – | – | – | 28.1 | [13.2, 46.1] | <0.001 | |

AHI, apnea-hypopnea index; BMI, body mass index; CI, confidence interval; ESS, Epwoth sleepiness scale; LSAT, lowest oxygen saturation; MLS, multilevel surgery; MMA, maxillomandibular advancement; N, number of patients; ODI, oxygen desaturation index; SD, standard deviation; WMD, weighted mean difference.

[a] Z test for overall effect size.

[b] Z-test for comparison the difference between two estimates.

**MLS group** As shown in Table 3, the identified studies produced a pooled data set of 1712 OSA patients who underwent MLS. The majority of the patients were obese (weighted BMI: 29.1 ± 4.2 kg/m$^2$) males (85.0%) with a weighted mean age of 45.5 y.

### *Respiratory parameters*

**MMA group** One study [35] was excluded from the meta-analysis, because the data of a small subset of the patients with longer follow-up time were reported in another study [34]. As shown in Table 3, nineteen studies, describing 393 patients with weighted preoperative AHI of 57.3 ± 26.6/h, reported a statistically significant improvement in AHI of −46.2/h (95% CI, −52.4 to −39.9, $P < 0.001$), LSAT of 13.5% (95% CI, 10.5 to 16.5, $P < 0.001$), and ODI of −30.3/h (95% CI, −46.3 to −14.2, $P < 0.001$) (Supplementary Fig. S3). The SMDs of AHI, LSAT, and ODI were −2.90 (95% CI, −3.40 to −2.40) (large effect), 1.49 (95% CI, 1.21 to 1.76) (large effect), and −2.61 (95% CI, −4.23 to −1.00) (large effect), respectively.

**MLS group** Two studies [44,62] were excluded from the meta-analysis because of the low methodological quality. As shown in Table 3, thirty-seven studies, totaling 1639 patients with weighted preoperative AHI of 42.2 ± 21.0/h, reported a statistically significant improvement in AHI of −24.7/h (95% CI, −28.1 to −21.4, $P < 0.001$), LSAT of 8.7% (95% CI, 6.2 to 11.1, $P < 0.001$), and ODI of −19.1/h (95% CI, −34.2 to −4.0, $P = 0.010$) (Supplementary Fig. S4). The SMDs of AHI, LSAT, and ODI were −1.79 (95% CI, −2.06 to −1.52) (large effect), 1.06 (95% CI, 0.79 to 1.34) (large effect), and −1.18 (95% CI, −1.74 to −0.62) (large effect), respectively. The results of weighted data for three subgroups according to the different target levels of obstructive sites addressed by surgery were summarized in Table 4 (Supplementary Fig. S5).

The improvements of AHI and LSAT after MMA were significantly higher than after MLS, with $P$ value of <0.001 and 0.014, respectively. No significant difference in the improvement of ODI between MMA and MLS was found.

### *Subjective outcomes*

**MMA group** Seven studies, totaling 164 patients with weighted preoperative ESS of 14.1 ± 5.4, reported a significant decrease of 8.5 (95% CI, −12.2 to −4.9, $P < 0.001$) (Table 3; Supplementary Fig. S3). The ESS SMD was −2.15 (95% CI, −3.06 to −1.24) (large effect).

**MLS group** Twenty-nine studies, totaling 1309 patients with weighted preoperative ESS of 12.6 ± 4.4, reported a significant reduction of −5.8 (95% CI, −6.6 to −5.0, $P < 0.001$) (Table 3; Supplementary Fig. S4). The ESS SMD was −1.51 (95% CI, −1.78 to −1.25) (large effect). The results of subgroup analysis based on surgical technique were shown in Table 4 (Supplementary Fig. S5).

No significant difference in the improvement of ESS between MMA and MLS was found.

### *Surgical success and cure*

**MMA group** The pooled rate of surgical success reported in 15 studies (n = 340) was 85.0% (95% CI, 76.4%–91.9%), and the pooled rate of surgical cure reported in six studies (n = 130) was 46.3% (95% CI, 38.0%–54.7%).

**MLS group** The overall pooled rate of surgical success reported in 31 studies (35 MLS groups, n = 1339) was 65.1% (95% CI, 60.6%–69.5%), and the overall pooled rate of surgical cure was 28.1% (95% CI, 13.2%–46.1%) in five studies (5 MLS groups, n = 221). The pooled surgical success and cure rates for each subgroup with regard to surgical technique were listed in Table 4.

The overall pooled surgical success rate of MMA was significantly higher than that of MLS ($P < 0.001$), and no significant difference was found in the pooled surgical cure rate between these two therapies.

### *Severity of OSA: impact on results*

All MMA study groups were divided into the following three cohorts with respect to the mean baseline AHI: less than 40/h, from 40/h to 70/h, and greater than 70/h. For MLS groups, they were only divided into two cohorts according to the mean baseline AHI, due to the absence of included MLS studies with mean baseline AHI >70/h.

### *Baseline AHI less than 40/h*

**MMA group** In Table 5, three studies, totaling 60 patients with weighted preoperative AHI of 35.7 ± 13.7/h, reported a significant improvement in AHI of −27.1/h ($P < 0.001$), and ESS of −12.7

**Table 4**

Summary of weighed data for studies on multilevel surgery – three subgroups according to the different target levels of obstructive sites addressed by surgery.

| Variable | Pre-op | | Post-op | | Change | | |
|---|---|---|---|---|---|---|---|
| | N | Weighted mean ± SD | N | Weighted mean ± SD | WMD | 95% CI | $P$[a] |
| **Subgroup 1. Soft palate level & tongue base level** | | | | | | | |
| Age (years) | 1052 | 45.2 ± 11.2 | – | – | – | – | – |
| BMI (kg/m$^2$) | 1172 | 29.0 ± 4.3 | 682 | 28.4 ± 4.4 | – | – | – |
| AHI (/h) | 1307 | 40.4 ± 20.3 | 1307 | 18.7 ± 16.6 | −22.7 | [-25.7, −19.7] | <0.001 |
| LSAT (%) | 980 | 77.9 ± 12.1 | 980 | 84.2 ± 9.8 | 7.2 | [5.0, 9.3] | <0.001 |
| ODI (/h) | 265 | 36.3 ± 22.5 | 265 | 15.5 ± 14.1 | −19.1 | [-34.2, −4.0] | 0.010 |
| ESS | 987 | 12.4 ± 4.3 | 987 | 7.5 ± 4.1 | −5.2 | [-6.1, −4.4] | <0.001 |
| Success rate (%) | 1072 | – | – | – | 64.2 | [59.3, 68.9] | <0.001 |
| Cure rate (%) | 176 | – | – | – | 33.0 | [16.1, 52.5] | <0.001 |
| **Subgroup 2. Soft palate level & hyoid level** | | | | | | | |
| Age (years) | 161 | 49.7 ± 8.9 | – | – | – | – | – |
| BMI (kg/m$^2$) | 161 | 29.9 ± 3.7 | 109 | 27.7 ± 2.9 | – | – | – |
| AHI (/h) | 161 | 44.7 ± 25.4 | 161 | 20.8 ± 14.6 | −28.4 | [-45.2, −11.5] | 0.001 |
| LSAT (%) | 52 | 69.4 ± 13.0 | 52 | 83.5 ± 3.9 | 14.1 | [8.5, 19.8] | <0.001 |
| ESS | 161 | 11.4 ± 4.2 | 161 | 6.4 ± 2.5 | −6.7 | [-10.8, −2.5] | 0.002 |
| Success rate (%) | 109 | – | – | – | 61.5 | – | – |
| Cure rate (%) | – | – | – | – | – | – | – |
| **Subgroup 3. Soft palate level & tongue base level & hyoid level** | | | | | | | |
| Age (years) | 100 | 41.9 ± 7.3 | – | – | – | – | – |
| BMI (kg/m$^2$) | 87 | 29.0 ± 2.7 | 87 | 29.8 ± 3.3 | – | – | – |
| AHI (/h) | 171 | 54.0 ± 17.4 | 171 | 20.1 ± 17.0 | −33.4 | [-39.7, −27.1] | <0.001 |
| LSAT (%) | 132 | 71.2 ± 12.4 | 132 | 84.2 ± 8.8 | 12.4 | [0.6, 24.3] | 0.040 |
| ESS | 161 | 14.8 ± 3.9 | 161 | 7.1 ± 3.7 | −7.8 | [-8.9, −6.7] | <0.001 |
| Success rate (%) | 158 | – | – | – | 72.4 | [55.3, 86.7] | <0.001 |
| Cure rate (%) | 45 | – | – | – | 11.1 | – | – |

AHI, apnea-hypopnea index; BMI, body mass index; CI, confidence interval; ESS, Epworth sleepiness scale; LSAT, lowest oxygen saturation; N, number of patients; ODI, oxygen desaturation index; SD, standard deviation; WMD, weighted mean difference.

[a] Z test for overall effect size.

($P = 0.002$) (Supplementary Fig. S3). No study described LSAT. Only one study with 34 patients reported data concerning the preoperative and postoperative ODI (34.7 ± 12.5/h and 5.4 ± 4.1 ($P < 0.001$), respectively). The pooled rates of success and cure were 94.0% (95% CI, 74.3%–99.9%) and 50.0% (95% CI, 35.7%–64.2%), respectively.

**MLS group** In Table 5, fifteen studies, comprising 706 patients with weighted preoperative AHI of 30.7 ± 15.6/h, showed a significant improvement in AHI of −16.7/h ($P < 0.001$), LSAT of 4.4% ($P < 0.001$), and ESS of −5.4 ($P < 0.001$) (Supplementary Fig. S4). No significant improvement of ODI was found. The pooled rates of success and cure were 57.1% (95% CI, 51.7%–62.5%) and 44.7% (95% CI, 33.2%–56.4%), respectively.

Compared to the MLS, the AHI reductions after MMA was significantly higher, with $P$ values of 0.030. The pooled surgical success rate of MMA was significantly higher than MLS ($P < 0.001$), while there is no difference in the surgical cure rates between these two types of therapies.

### *Baseline AHI from 40/h to 70/h*

**MMA group** In Table 5, twelve studies, comprising 257 patients with weighted preoperative AHI of 55.7 ± 23.0/h, reported a significant improvement in AHI of −44.1/h ($P < 0.001$), LSAT of 11.6% ($P < 0.001$), ODI of −30.4/h ($P = 0.030$), and ESS of −7.0 ($P < 0.001$) (Supplementary Fig. S3). The pooled rates of success and cure were 82.3% (95%CI, 69.1%–92.5%) and 44.0% (95%CI, 33.1%–55.3%), respectively.

**MLS group** In Table 5, twenty-two studies, comprising 933 patients with weighted preoperative AHI of 51.0 ± 20.3/h, showed a significant improvement in AHI of −30.7/h ($P < 0.001$), LSAT of 9.9% ($P < 0.001$), ODI of −28.6 ($P < 0.001$), and ESS of −6.1 ($P < 0.001$) (Supplementary Fig. S4). The pooled rates of success and cure were 70.5% (95% CI, 65.4%–75.3%) and 17.4% (95% CI, 7.1%–31.0%), respectively.

The reduction in AHI after MMA was significantly higher than that after MLS ($P < 0.001$), and no difference was found in the improvement of LSAT, ODI, and ESS postoperatively between these two therapies. The pooled surgical cure rate of MMA was significantly higher than that of MLS ($P = 0.020$), while there was no difference in the surgical success rates between these two therapies.

### *Baseline AHI greater than 70/h*

**MMA group** As shown in Table 5, four studies, totaling 76 patients with weighted preoperative AHI of 79.8 ± 28.9/h, reported a significant improvement in AHI of −71.8/h ($P < 0.001$), LSAT of 18.7% ($P < 0.001$), and ESS of −7.9 ($P < 0.001$) (Supplementary Fig. S3). No study described ODI. The pooled rate of success was 84.2% (95%CI, 75.5%–91.3%). One study reported a surgical cure rate of 46.2%.

### *Long-term follow-up outcomes*

**MMA group** Four studies [26,27,34,42] reported long-term follow-up (≥2 y) in 98 OSA patients treated by MMA. At a mean follow-up of 8.9 y, a reduction of AHI was shown from 60.8 ± 25.2 to 13.1 ± 15.1/h. The meta-analysis showed a statistically significant improvement of −45.2/h (95% CI, −59.6 to −30.9, $P < 0.001$). Only one study with 40 patients presented long-term follow-up LSAT, reporting preoperative LSAT of 67.5 ± 14.8% and postoperative LSAT of 86.3 ± 3.9%. Surgical success rates were available for only two studies (90% and 41.4%, respectively).

**MLS group** Three studies [67,77,81] with 114 patients presented long-term follow-up (≥2 y) data. In two of these studies, totaling 68

**Table 5**
Summary of weighted data for studies on maxillomandibular advancement surgery and multilevel surgery in OSA patients with baseline AHI less than 40, from 40 to 70, and greater than 70.

| Variable | | Pre-op | | Post-op | | Change | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | N | Weighted mean ± SD | N | Weighted mean ± SD | WMD | 95% CI | $P^{a}$ | $P^{b}$ |
| **Baseline AHI less than 40** | | | | | | | | | |
| Age (years) | MMA | 60 | 39.4 ± 12.4 | – | – | – | – | – | – |
| | MLS | 706 | 45.2 ± 11.7 | – | – | – | – | – | |
| BMI (kg/m$^2$) | MMA | 50 | 25.8 ± 4.9 | 34 | 25.5 ± 4.3 | – | – | – | – |
| | MLS | 693 | 28.5 ± 4.2 | 501 | 28.4 ± 4.2 | – | – | – | |
| AHI (/h) | MMA | 60 | 35.7 ± 13.7 | 60 | 7.0 ± 7.3 | −27.1 | [−36.0, −18.2] | <0.001 | 0.030 |
| | MLS | 706 | 30.7 ± 15.6 | 706 | 15.1 ± 13.3 | −16.7 | [−19.9, −13.4] | <0.001 | |
| LSAT (%) | MMA | – | – | – | – | – | – | – | – |
| | MLS | 347 | 83.0 ± 10.5 | 347 | 87.0 ± 9.3 | 4.4 | [1.9, 6.8] | <0.001 | |
| ODI (/h) | MMA | 34 | 34.7 ± 12.5 | 34 | 5.4 ± 4.1 | −29.3 | [−33.7, −24.9] | <0.001 | – |
| | MLS | 93 | 17.4 ± 11.3 | 93 | 11.1 ± 9.0 | −8.2 | [−17.6, 1.1] | 0.080 | |
| ESS | MMA | 44 | 16.7 ± 5.6 | 44 | 1.9 ± 2.8 | −12.7 | [−20.8, −4.7] | 0.002 | 0.076 |
| | MLS | 648 | 11.5 ± 4.7 | 648 | 7.1 ± 3.6 | −5.4 | [−6.6, −4.2] | <0.001 | |
| Success rate (%) | MMA | 60 | – | – | – | 94.0 | [74.3, 99.9] | <0.001 | <0.001 |
| | MLS | 651 | – | – | – | 57.1 | [51.7, 62.5] | <0.001 | |
| Cure rate (%) | MMA | 44 | – | – | – | 50.0 | [35.7, 64.2] | <0.001 | 0.579 |
| | MLS | 111 | – | – | – | 44.7 | [33.2, 56.4] | <0.001 | |
| **Baseline AHI from 40 to 70** | | | | | | | | | |
| Age (years) | MMA | 233 | 43.5 ± 11.0 | – | – | – | – | – | – |
| | MLS | 607 | 45.8 ± 9.7 | – | – | – | – | – | |
| BMI (kg/m$^2$) | MMA | 233 | 27.9 ± 6.0 | 75 | 28.3 ± 5.3 | – | – | – | – |
| | MLS | 727 | 29.7 ± 4.1 | 377 | 28.4 ± 4.1 | – | – | – | |
| AHI (/h) | MMA | 257 | 55.7 ± 23.0 | 257 | 11.4 ± 11.4 | −44.1 | [−47.8, −40.4] | <0.001 | <0.001 |
| | MLS | 933 | 51.0 ± 20.3 | 933 | 22.0 ± 17.9 | −30.7 | [−34.0, −27.5] | <0.001 | |
| LSAT (%) | MMA | 140 | 77.6 ± 10.7 | 140 | 89.1 ± 5.2 | 11.6 | [ 9.4, 13.8] | <0.001 | 0.387 |
| | MLS | 817 | 74.1 ± 12.3 | 817 | 82.9 ± 9.4 | 9.9 | [6.9, 13.0] | <0.001 | |
| ODI (/h) | MMA | 44 | 35.4 ± 28.5 | 44 | 7.0 ± 7.7 | −30.4 | [−57.6, −3.1] | 0.030 | 0.900 |
| | MLS | 172 | 46.5 ± 20.4 | 172 | 18.0 ± 15.6 | −28.6 | [−32.4, −24.8] | <0.001 | |
| ESS | MMA | 107 | 13.2 ± 5.1 | 107 | 6.0 ± 4.0 | −7.0 | [−10.7, −3.4] | <0.001 | 0.633 |
| | MLS | 661 | 13.6 ± 4.2 | 661 | 7.5 ± 4.1 | −6.1 | [−7.1, −5.2] | <0.001 | |
| Success rate (%) | MMA | 204 | – | – | – | 82.3 | [69.1, 92.5] | <0.001 | 0.061 |
| | MLS | 688 | – | – | – | 70.5 | [65.4, 75.3] | <0.001 | |
| Cure rate (%) | MMA | 73 | – | – | – | 44.0 | [33.1, 55.3] | <0.001 | 0.020 |
| | MLS | 110 | – | – | – | 17.4 | [7.1, 31.0] | <0.001 | |
| **Baseline AHI greater than 70** | | | | | | | | | |
| Age (years) | MMA | 76 | 44.1 ± 16.4 | – | – | – | – | – | |
| BMI (kg/m$^2$) | MMA | 76 | 32.7 ± 7.7 | 76 | 32.4 ± 6.6 | – | – | – | |
| AHI (/h) | MMA | 76 | 79.8 ± 28.9 | 76 | 10.0 ± 12.6 | −71.8 | [−88.4, −55.2] | <0.001 | |
| LSAT (%) | MMA | 63 | 67.2 ± 14.5 | 63 | 86.0 ± 5.6 | 18.7 | [12.7, 24.6] | <0.001 | |
| ESS | MMA | 13 | 12.9 ± 5.5 | 13 | 5.0 ± 4.1 | −7.9 | [−11.6, −4.2] | <0.001 | |
| Success rate (%) | MMA | 76 | – | – | – | 84.2 | [75.5, 91.3] | <0.001 | |
| Cure rate (%) | MMA | 13 | – | – | – | 46.2 | – | – | |

AHI, apnea-hypopnea index; BMI, body mass index; CI, confidence interval; ESS, Epworth sleepiness scale; LSAT, lowest oxygen saturation; MLS, multilevel surgery; MMA, maxillomandibular advancement; N, number of patients; ODI, oxygen desaturation index; SD, standard deviation; WMD, weighted mean difference.

[a] Z test for overall effect size.

[b] Z-test for comparison the difference between two estimates.

patients who had undergone uvulopalatopharyngoplasty (UPPP) and tongue base suspension with a mean follow-up of 2.8 y, AHI and ESS score decreased from 48.8 ± 17.8/h to 14.9 ± 21.5/h, 12.1 ± 4.3 to 7.5 ± 5.9, respectively. The WMD between pre- and post-surgery were −27.4/h (95% CI, −50.4 to −4.4, $P = 0.020$) and −4.5 (95% CI, −6.2 to −2.8, $P < 0.001$), respectively. One of the two studies with 54 patients presented long-term follow-up LSAT increasing from 76.2 ± 12.4% preoperatively to 82.2 ± 11.2% postoperatively ($P = 0.009$). Another study with 14 patients reported long-term follow-up ODI from 30.3 ± 16.9/h preoperatively to 15.5 ± 13.2/h postoperatively ($P < 0.001$). Surgical success rates were 78% and 57.1%, respectively. In the third study consisting of 46 patients who had undergone uvulopalatal flap, genioglossus advancement, and hyoid suspension with a mean follow-up of 3.3 y, AHI and ESS score decreased from 47.9 ± 8.4/h to 18.6 ± 4.1/h, 15.9 ± 2.7 to 7.3 ± 2.7, respectively; the LSAT increased from 81.2 ± 2.9% to 87.2 ± 3.1%. The surgical success rate was 65.2%.

### *Surgical morbidity and mortality*

**MMA group** The average length of hospitalization for OSA patients who underwent MMA was 3.5 d (range 2 d–8 d). Among studies reporting participants' complications (n = 346) [24,26,29,35,39–43], no death was encountered. The rate of major complication was 3.2%, including ten re-operations for removal of osteosynthesis screws and plates (n = 8) [26,29,42] and maxillary non-union (n = 2) [24,42], and one sudden dyspnea [41]. The most frequent minor complication was facial paresthesia caused by the impairment of inferior alveolar nerve and/or maxillary nerve. In total, 76.9% of patients (n = 266) had transient facial paresthesia in mandibular and/or infraorbital areas, and 18.5% of patients (n = 64) reported persistent symptoms (mean follow-up of 6.0 y).

Excluding facial paresthesia, the rate of other minor complications was 10.1%, consisting of developed malocclusion (n = 13), temporomandibular disorders (n = 11), local infection (n = 5), minor postoperative wound pain (n = 2), unfavorable split (n = 1), loss of an interdental gingiva (n = 1), a perforation of the palate (n = 1), and transient unilateral angulus oris deviation (n = 1). Besides, only 9 of 206 patients perceived worsening of their facial appearance after MMA [24,26,28,37,39–43].

**MLS group** After surgery, patients required 4.1 d (range 1.25 ± 0.44 d to 16 ± 2 d) of hospitalization. No death was reported in 1386 patients [22,44–46,48–51,53,56–60,62–71,73–75,77–81]. The rate of major complications was 1.1%, including nine postoperative bleedings necessitating surgical exploration or surgical treatment [51,53,64,74], five pillar extrusion requiring removal and replacement [60] and one pneumonia [78].

The minor complications included postoperative pain (n = 160), tongue discomfort (n = 74), velopharyngeal insufficiency (n = 70), dysphagia (n = 65), dysarthria (n = 25), odynophagia (n = 22), ulceration (n = 21), taste change (n = 14), and others (n = 112), which yield the minor complication rate of 40.6%. The majority of these complications were self-limited or could be cured by conservative treatment, with the exception of nine persistent complications: taste disturbance (n = 1) [64], dysphonia and dysphagia (n = 1) [53], oropharyngeal globus sensation (n = 2) [48], and dysphagia (n = 5) [51].

### *Publication bias and sensitivity analysis*

Both Begg's test and Egger's test suggested no significant publication bias for the included MMA and MLS studies (Supplementary Figs. S6 and S7). The sensitivity analysis indicated high stability and robustness of the results (Supplementary Figs. S8 and S9).

## Discussion

### *Respiratory parameters, and surgical success and cure*

Although there are no comparative trials between MMA and MLS, greater improvement of OSA was found in MMA studies by pooling results from both surgical options, in terms of surgical success rate and improvement in the respiratory parameters. The observed superiority of MMA over MLS in treating OSA is explained by enlargement of the entire retropalatal and retrolingual airway by expanding the skeletal framework, while MLS cannot. Currently, there are a few studies [25,31,40] reporting the significant increases in pharyngeal airway volume (PAV) in OSA patients treated with MMA, by 60.5%, 35.7% and 35.4%, respectively. However, to our knowledge, only Chiffer et al. [54] quantitatively measured the volumetric changes in upper airway before and after MLS for treating OSA. They found a significant increase in PAV by 19.4%. Therefore, we inferred that the extent of the enlargement of the pharyngeal space could be associated with the therapeutic efficacy of upper airway surgery. Further investigation is essential to fully understand the treatment mechanisms of MMA and MLS, which may partly clarify the reason of differences in surgical outcome between them.

The discrepancy of surgical results between MMA and MLS varies with the different preoperative OSA severity. For example, there are benefits of MMA over MLS for the success rate in patients with baseline AHI <40, and for the cure rate in patients with baseline AHI from 40 to 70. The current evidence suggests that the pathophysiological causes of OSA are multifactorial and likely varies considerably between individuals, which puts an emphasis on personalized management for OSA based on its underlying causes [5]. Given the variable efficacy of these two types of surgeries, especially of MLS, careful selection of patients is needed. Therefore, one important objective in future research should be the identification of the factors that determine the success or failure in OSA patients treated by MMA or MLS. For the non-responders to upper airway surgery, non-anatomical traits may play a prominent role as well in the etiology of OSA.

In MLS, precise identification of sites of airway collapse is imperative for favorable surgical outcome [82,83], rather than only the severity of OSA. Among all the identified MLS studies, nasopharyngoscopy with Muller maneuver or DISE were performed preoperatively, except in four studies [55,59,60,78]. The significant improvement in OSA was noted in the three MLS subgroups with regard to surgical technique and the largest improvement in AHI was seen in subgroup 3. In one study [53], it was also demonstrated that compared with combined UPPP and tongue base radiofrequency ablation, combined hyoid suspension, UPPP, and tongue base radiofrequency ablation obtained better treatment outcome. However, due to the limited studies on subgroups 2 and 3, it is not possible to match each subgroup for baseline characteristics, which lead to the difficultly in comparing the clinical outcome between them in our study. Of interest is that in OSA surgery, palatal resection techniques such as UPPP are presently regarded as obsolete and are being replaced by modern reconstructive techniques, such as expansion sphincter pharyngoplasty, because of better clinical outcome and less side effects [84]. These better results are reported in both single level surgery and MLS [49,78]. In addition, upper airway stimulation [85], an emerging treatment option for moderate to severe OSA, has been found to be an effective therapy able to achieve success rate of 75% in patients with OSA [86]. Interest in this emerging treatment modality has been increasing during the past decade. In the premise of precisely identifying anatomical abnormalities of the upper airway, the development of surgical techniques may further optimize the surgical outcome for well-selected patients with OSA. The comparison of clinical efficacy and safety between contemporary approaches and older ones for OSA is called for in future studies.

### *Subjective outcomes*

Of note, not only the improvement in AHI but also the patients' subjective feeling should be taken into consideration when evaluating the efficacy of surgical interventions for OSA. Regrettably, ESS score was the only overlapping subjective index which was frequently reported in both MMA and MLS studies, leading to the impossibility of comprehensive comparison of other subjective outcomes (e.g., quality of life outcomes). There are studies that have assessed the improvement brought by MMA and MLS in patient's subjective feelings, such as snoring [40,58,59,87], and bodily pain [87,88]. Both surgery modalities can significantly improve patient's subjective feeling. However, the comparison of improvement in quality of life between them should be addressed in future studies.

### *Long-term follow-up outcomes*

The follow-up period of the included MMA studies ranges from 6 mo to 12.5 y, and that of the included MLS studies ranges from 6 mo to 3.3 y. Most of the retrieved studies reported short-term surgical outcomes at 6 mo after surgery. In our study, a significant decrease in AHI of 45.23/h was shown, at a mean follow-up of 8.9 y after MMA. In a meta-analysis by Camacho et al. [89], it was demonstrated that OSA patients who were treated with MMA maintained improvements in AHI, sleepiness, and LSAT in the long term (4 y to <8 y). However, the mean AHI increased to moderate OSA (mean AHI = 23.1/h) in the very long term (≥8 y). The longest follow-up result in MMA was reported by Pottel et al. [87], the long-term (range 14–20 y) success rate of nine patients performed MMA was 44.44%, and the short-term (within 2 y) success rate was 66.67%. Vigneron et al. [42] reported that the long-term (mean 12.5 y) success rate of MMA was 100% in young patients (age <45) with BMI <25 kg/m$^2$, AHI <45/h, SNB <75°, narrow retrolingual space (<8 mm), and preoperative orthodontics. Marked weight gain and significant skeletal relapse can counterbalance the positive effect of MMA in the long-term, while there is no consensus on the effect of aging in long-term outcome of MMA [34,87]. Compared with the studies on MMA, currently, there are less studies on MLS evaluating the long-term surgical outcome. Hou et al. [90] performed combined midline glossectomy and UPPP in 34 patients and reported short-term (6 mo) and long-term (5 y) outcome. At 6 mo, the surgical success and cure rate were 79.41% and 17.65%, respectively; at 5 y, the surgical success and cure rate were 20.59% and 50%, respectively. The longest follow-up result of MLS was reported by Andsberg et al. [91]. In this study, 16 patients had undergone UPPP combined with midline glossectomy and followed up 1 y and 8.4 y after surgery. The success rates were 59% and 56%, respectively; and the cure rates were 32% and 25%, respectively. The weight of these patients did not change during the follow-up period, which may explain the long-term stable outcome. Neruntarat et al. [67] also found that patients with significant weight gain were at risk of recurrence of OSA. Based on the current literature, we concluded that the benefits of MMA and MLS persist for most patients with moderate-to-severe OSA over a long-term follow-up time. Marked weight gain after surgery and significant skeletal relapse after MMA may negatively influence the stability of clinical outcome. Thus, a recommendation regarding weight control and regular follow-up postoperatively are crucial for OSA patients. Moreover, due to the limited availability of data, the long-term outcome and the factors related to relapse require further investigation.

### *Surgical morbidity and mortality*

Despite the apparent benefits, concerns about the safety and complications of surgical therapy for OSA still exist. In our study, both MMA and MLS were noted to be generally safe surgical therapies for OSA. Riley et al. [92] concluded that OSA patients with apnea index higher than 70/h and LSAT less than 80% were at high risk of postoperative complication. Sensory disturbance in the territory of the inferior alveolar nerve was the most common complication of MMA, and the main predisposing factors were the degree of mandibular advancement, the patient's advanced age, and addition of a genioplasty [93]. One study [24] demonstrated that the complication rate of MMA increased with increasing age, in particular after 45 y old. In a study of 487 consecutive OSA patients treated by MLS, Pang et al. [94] concluded that the overall complication rate was 7.1%, which is lower than our result. Besides, they pointed out that patients with severe OSA (AHI >60/h and LSAT <80%) might be at high risk of postoperative oxygen desaturation. Although the major postoperative complication rate was low, patients who underwent MMA or MLS for treating OSA were recommended to be closely monitored after surgery [95,96]. According to the available evidence, generally, more attention should be paid to the patients with highly severe OSA, who could be vulnerable to the postoperative complication, no matter after MMA or MLS.

### *Limitations*

The results presented here should be considered in the context of several limitations. Firstly, the majority of the included studies are non-randomized studies, thus the level of evidence is limited inherently by the study design. Moreover, the overall quality of evidence was fair, with moderate risk of bias in the majority of studies included in the analysis, as evidenced by the Cochrane Collaboration “Risk of bias” tool and MINORS tool. However, unlike other medical areas, the randomized evaluations of surgical interventions are difficult to conduct. Secondly, there was high heterogeneity in most of the parameters pooled by meta-analysis, which may be attributed to a variety of potential confounding factors, i.e., patient characteristics, surgical techniques, follow-up time, and techniques of PSG scoring. Thirdly, only articles in English were included in our study, which may result in the language bias [20]. Fourthly, since the comparison between MMA and MLS was clarified by separately pooling results from studies on these two types of surgery, it was not possible to quantify the differences in surgical outcomes between MMA and MLS for treatment of OSA. By the means of quasi-experimental studies or comparative cohort studies, the lack of comparative studies between MMA and MLS for treating OSA should be addressed in the future.

## Conclusion

This systematic review and meta-analysis demonstrate that both MMA and MLS are effective treatment options for OSA with an acceptable rate of morbidity. Regardless of disease severity, MMA may offer greater improvements in AHI compared to MLS. However, the complication rate of MMA is higher than that of MLS. This conclusion is based on separate analysis of MMA and MLS studies.

**Practice points**

1. Both MMA and MLS are effective treatment options for OSA with an acceptable rate of morbidity.
2. Regardless of disease severity, MMA may be a more effective treatment compared to MLS in improving OSA.
3. The discrepancy of surgical outcome between MMA and MLS varies with the different preoperative OSA severity levels. There are benefits of MMA over multilevel surgery for the success rate in patients with baseline AHI <40, and for the cure rate in patients with baseline AHI from 40 to 70.
4. The rates of major complication and minor complication of MMA are both higher than those of MLS.
5. Not only the improvement in PSG result, but also the patients' subjective symptoms and long-term morbidity and mortality should be taken into consideration when evaluating the efficacy of surgical interventions for OSA.
6. Evidence-based decision making in patients with OSA can be achieved only when having information regarding clinical outcomes, side effects, complications, treatment cost, and predictors of non-response for all of the treatment options.

**Research agenda**

1. Future research should entail comparative studies between MMA and MLS with large samples and long-term follow-up, in which thorough assessment of objective respiratory parameters, subjective outcomes, quality of life, morbidity and mortality, and surgical cost is performed.
2. Large-scale studies are needed to identify predictive factors for surgical success and reasons for failure after MMA or MLS for patients with OSA, in terms of individual, clinical, and surgical characteristics.
3. Upper airway stimulation, a novel treatment modality for moderate-severe OSA, has been found to be highly effective for OSA patients with multilevel airway collapse. The comparison among MMA, MLS, and upper airway stimulation is called for in future studies.
4. Future studies on the pathogenesis of OSA are essential to facilitate personalized medicine approach for OSA.

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## Conflicts of interest

The authors declare that they have no conflict of interest.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.smrv.2021.101471.

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