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Mandibular distraction osteogenesis versus sagittal split ramus osteotomy in managing obstructive sleep apnea: A randomized clinical trial

Wai Kin Tsui [a], Yanqi Yang [b], Colman Mcgrath [c], Yiu Yan Leung [a, *]

[a] Oral and Maxillofacial Surgery, Faculty of Dentistry, The University of Hong Kong, Hong Kong
[b] Orthodontics, Faculty of Dentistry, The University of Hong Kong, Hong Kong
[c] Public Health, Faculty of Dentistry, The University of Hong Kong, Hong Kong

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ABSTRACT

Purpose: To compare mandibular distraction osteogenesis (MDO) to sagittal split ramus osteotomy (SSRO) to treat moderate-to-severe obstructive sleep apnea (OSA), and their surgical morbidities and skeletal stability.

Materials and methods: A randomized clinical trial was conducted on non-syndromic adult patients with apnea-hypopnea index (AHI) 15 or above to receive MDO or SSRO as part or whole skeletal advancement surgery. Post-operative 1 year OSA cure rate (AHI < 5/hour) and treatment success rate (50% reduction of AHI and AHI< 20/hour) were compared. Polysomnography were conducted pre-operatively and post-operatively up to 2 years. Surgical morbidities and skeletal stability were analyzed.

Results: Eighteen patients (9 in each group) were recruited. Patient recruitment was terminated after two major complications in the MDO group. The OSA cure rate and treatment success rate showed no statistical difference between MDO group or SSRO group at post-operative 1 year. Major complication rate was 44.4% in the MDO group and 0 in the SSRO group. No statistical difference was found in skeletal stability between the two groups.

Conclusion: Both MDO and SSRO were highly effective to treat moderate-to-severe OSA. MDO had a high major complication rate and was not superior than SSRO in airway function improvement and skeletal stability.

1. Introduction

Obstructive sleep apnea (OSA) is one of the most common sleep disorders characterized by repeated episodes of pharyngeal collapse associated with increased resistance of airflow during sleep, causing multiple arousals. The poor pattern of sleep causes the classic symptom of excessive daytime somnolence and it can lead to cardiovascular and cerebrovascular-related morbidities and mortalities (Somers et al., 2008). The prevalence of OSAS in Hong Kong is 4.1% (Ip et al., 2001), similar to other global prevalence estimates. However, if including estimated undiagnosed OSAS in the community, the prevalence may reach about 17% (Ip et al., 2001).

The current gold standard medical treatment for OSA is continuous positive airway pressure (CPAP). A Cochrane systematic review has found CPAP to be effective in reducing excessive daytime sleepiness and improving the quality of life in patients with moderate and severe OSA but the compliance as poor as less than 50% (Giles et al., 2006). Surgical treatment provides another means for treatment of OSA patients who are intolerant to CPAP and it might lead to a permanent cure. Uvulopalatopharyngoplasty and its variations were the commonly performed soft tissue surgeries for OSA but their reported success rates are lower at 40–60% (Sher et al., 1996; Kezirian and Goldberg, 2006; Lin et al., 2008). This may be due to the nature of OSA in which airway obstruction usually occurs at multiple levels rather than being localized at one single region (Rojewski et al., 1984; Iwanaga et al., 2003; Fairburn

* Corresponding author. Oral and Maxillofacial Surgery, 34 Hospital Road, Hong Kong. Fax: +852 28575570.
E-mail address: mikeyyleung@hku.hk (Y.Y. Leung).

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et al., 2007; Abdullah et al., 2011). Skeletal advancement has been shown to be safe and highly effective for treating OSAS patients, with promising results in terms of apnea-hypopnea index (AHI) reduction (Holty and Guilleminault, 2010). Skeletal advancement was traditionally performed with a Le-Fort I osteotomy followed by a sagittal split ramus osteotomy (SSRO), and mandibular distraction osteogenesis (MDO) provides another option for mandibular advancement. MDO has been shown to lengthen severely retrognathic mandibles successfully beyond the limits of conventional orthognathic surgery while reducing the potential for skeletal relapse and also neurosensory deficits (McCarthy et al., 1992; Klein and Howaldt, 1995; Walker, 2002; Vos et al., 2009). Studies on MDO in the treatment of OSA in adult patients are scanty and the evidence-based data for the comparison between MDO with the traditional SSRO is very weak. Most of the available reports on this aspect are restricted to case reports, retrospective or cross-sectional studies.

The aim of this randomized clinical trial was to compare the effectiveness of MDO and SSRO in the treatment of moderate-to-severe OSA. The specific aims of the study were to compare the OSA cure rate (AHI < 5/hour) and treatment success rate (50% reduction of AHI and AHI< 20/hour) of patients who received MDO or SSRO at 12 months after treatment, and to compare the longitudinal AHI changes and surgical morbidities of patients who received MDO or SSRO.

2. Methods

This randomized clinical trial was designed according to the CONSORT 2010 statement. Ethical approval was obtained from the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (HKU/HA HKW IRB) (IRB Reference Number: UW 11-122).

2.1. Study design

A parallel-grouped clinical trial with balanced randomization (1:1).

2.2. Participants

Adults of Chinese ethnicity with moderate-to-severe obstructive sleep apnea (AHI 15/hour or above) attending the Discipline of Oral and Maxillofacial Surgery, Faculty of Dentistry, The University of Hong Kong with planned mandibular advancement as part or whole of orthognathic surgery for the treatment of the OSA were recruited. Pre-surgical orthodontics were performed by a single orthodontist.

The inclusion criteria were:

1. Non-syndromic adult patients who were physically fit to undergo major surgery under general anaesthesia
2. The magnitude of mandibular advancement was within 15 mm as determined by surgical planning

The exclusion criteria were:

1. Patients with body mass index (BMI) > 30
2. Patients with immuno-compromised diseases, immunosuppressed states or with metabolic bone diseases or bone pathologies
3. Patients with facial asymmetry due to differential mandibular growth
4. Patients with pre-surgical temporomandibular joint pathology other than functional internal derangement
5. Patients with previous maxillofacial surgery in the last 6 months.

Patients requiring mandibular advancement of more than 15 mm were treated by MDO and were excluded from this study. Informed consent was obtained from all recruited patients.

2.3. Interventions

The two arms of intervention were mandibular ramus advancement by mandibular distraction osteogenesis (MDO) or sagittal split ramus osteotomy (SSRO).

2.3.1. Mandibular distraction osteogenesis (MDO)

The distraction procedure and protocol followed a standardized protocol for adult MDO (Ow and Cheung, 2010). Mucosal incision was made along the external oblique ridge to the first molar region. The mucoperiosteal flap was raised to expose the lateral surface of the posterior body of the mandible. A retractor was placed below the lower border of mandible at the first-second molar region. The vertical osteotomy was cut through the lower border cortex and then mono-cortically on the lateral cortex of the body of mandible. Osteotomy was performed on the superior-medial aspect joining the lateral vertical osteotomy with a piezoelectric saw (SYNTHES, Monument, USA). The intra-oral bone-borne single-vector mandibular distractor (CMF Distractor, SYNTHES, Monument, USA) was inserted and the footplates were adjusted to adapt to the lateral surface of the mandible across the osteotomy cut according to the correct vector. The distractor was removed and the mandible was split with a blunt-end osteotome and slightly mobilized. The distractor was repositioned and fixed with 4 titanium screws on each footplate on both the proximal and distal segments (Fig. 1). The same procedure was performed on the contralateral side. The distractors were activated slightly to confirm the distraction vector was correct. The distractor rods were placed to exit at the mucosal wound. The wound was then primarily closed.

After a latency period of 5–7 days, activation was commenced at 1 mm per day in three rhythms until a Class I incisors relationship was achieved as planned. Light intra-oral elastics were used to help guide the occlusion and prevent the development of anterior open bite during the distraction period and early consolidation period. The distractors were kept for 6 months during the consolidation period. Removal of distractors was performed under general

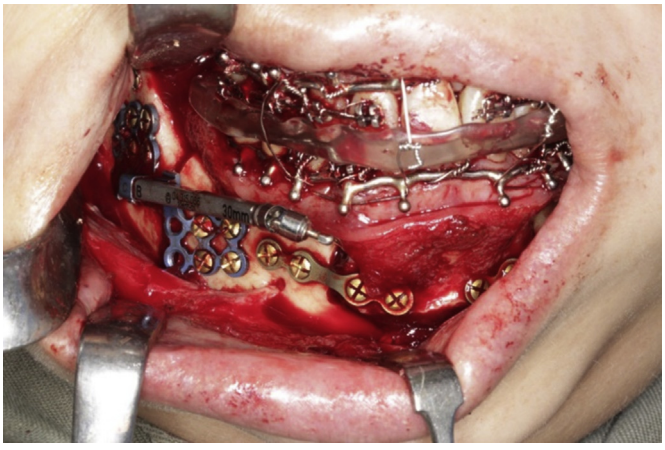

Fig. 1. A distractor was placed for mandibular distraction osteogenesis.

anaesthesia at post-operative 6 months, after radiographic confirmation of mineralization in the distraction regenerate.

2.3.2. Sagittal split ramus osteotomies (SSRO)

Conventional bilateral sagittal split osteotomies with modifications from Hunsuck and Dalpont were performed (Dal Pont, 1961; Hunsuck, 1968). The mucoperiosteal flap was raised to expose the lateral surface of the posterior body of the mandible. The vertical osteotomy was cut through the lower border cortex and then mono-cortically on the lateral cortex of the body of the mandible. The horizontal medial osteotomy was performed on the medial mandibular ramus above the lingula. The vertical and horizontal osteotomies were connected along the external oblique ridge. The mandible was split sagittally with two blunt-end osteotomes. The same procedure of osteotomies was performed on the contralateral side. The distal mandibular segment was advanced to the predefined dental occlusion and fixed with titanium miniplates and screws (Fig. 2). The wound was primarily closed.

2.3.3. Adjunctive surgeries

Adjunctive surgeries including LeFort 1 osteotomy and mandibular anterior subapical osteotomy were performed when considered necessary as determined by clinical condition and pre-operative drug-induced sleep endoscopy (DISE) findings. LeFort 1 osteotomy was used for maxillary advancement when DISE showed obstruction at the nasopharynx and uvula region. Mandibular anterior subapical osteotomy was used to create an increased overjet for mandibular advancement when the anterior dentoalveolus was protrusive.

Patients receiving either arm of interventions were prescribed a standard course of antibiotics and analgesics. A standard post-operative management protocol was applied to all patients in the study.

2.4. Outcome measures

The primary outcomes of the study were the post-treatment 1 year OSA cure rate and OSA treatment success rate (as defined by the American Academy of Sleep Medicine (AASM) guideline) (Kushida et al., 2005). OSA cure was defined as AHI <5/hour and treatment success was defined as more than 50% reduction of AHI and AHI <20/hour. The secondary outcomes include the longitudinal AHI and LSAT changes, the treatment morbidities and the skeletal relapse after MDO or SSRO as part or whole of the OSA treatment within post-treatment 24 months.

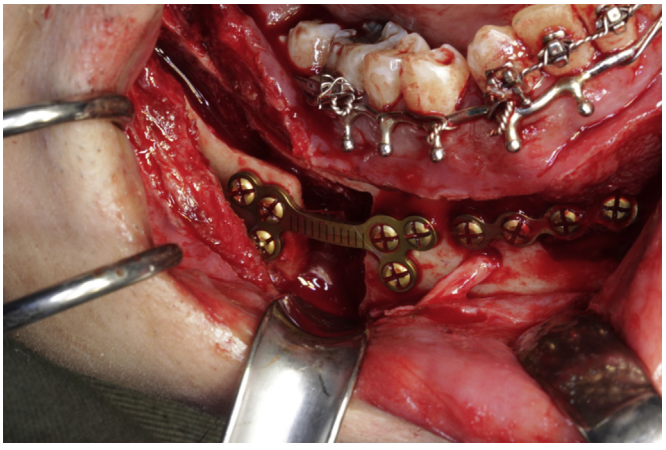

Fig. 2. Osteotomy and internal fixation for sagittal split ramus osteotomy.

2.5. Data collection

2.5.1. Polysomnography (PSG)

All patients were confirmed to have moderate-to-severe obstructive sleep apnea by respiratory physicians based on attended polysomnography before they were recruited to the study. In-hospital un-attended polysomnography was carried out pre-operatively to provide the baseline measurement. Follow-up polysomnography was repeated at intervals of post-operative 1 month (T1), 3 months (T2), 6 months (T3), 1 year (T4) and 2 years (T5).

Overnight polysomnography was performed with a 16-channel PSG machine (Somte PSG, Compumedics Limited, Texas, USA). The PSG recordings were automatically scored by the associated computer software (ProFusion PSG, Compumedics Limited, Texas, USA) according to the latest standard criteria defined by the American Academy of Sleep Medicine (AASM) guidelines (Kushida et al., 2005), and then verified with hand scoring by an in-house trained AASM-certified sleep technician. Pre-operative and post-operative AHI, mean oxygen saturation (MSAT, %) and lowest oxygen saturation (LSAT, %) were obtained from the PSG for analysis.

2.5.2. Surgical morbidities

Surgical morbidities were assessed by clinical and radiographic examinations at follow-up appointments. Major complications were defined to be non-union of mandible, or another other severe complications. Minor surgical morbidities including post-operative infection, occlusion discrepancies (anterior open bite or posterior open bite), distraction device failure, subjective neurosensory disturbance in visualized analog scale [0 (normal) to 10 (most severe)] of inferior alveolar nerve and asymmetry were recorded.

2.5.3. Skeletal stability

The evaluation of the skeletal stability was based on superimposition of standardized lateral cephalometric radiographs taken using the same machine (Gendex Orthoralix 9200, Hatfield, PA, USA) with a standard setting: 70 kV, 6 mA and 0.8 s exposure time. Lateral cephalographs were taken before surgery (T0) and repeated after surgery at intervals of post-operative 1 month (T1), 3 months (T2), 6 months (T3), 1 year (T4) and 2 year (T5). All tracings were superimposed using stable cranial base structures: sella (S) and nasion (N), employing a method of anatomical best fit and were traced manually on acetate paper (Orthotrace, RMO Inc., Denver, USA) by one single investigator. An x-y co-ordinate system was constructed with the sella as the origin. A line was drawn connecting the sella and the nasion (SN line). The horizontal x-axis (Snx) was drawn made at 7° to the SN line. The vertical y-axis (Sny) was drawn passing through sella perpendicular to the x-axis. The relative linear changes between the serial radiographs of the same patient were compared to calculate skeletal relapse. An electronic caliper (Digit Cal, Tesa, Switzerland) was used for all linear measurements. Mandibular skeletal stability was measured as horizontal change of B-point (B) relative to Sny in mm.

2.6. Sample Size Calculation

There were no similar studies on the OSA cure rate and OSA treatment success rate of MDO in non-syndromic adult patients. We therefore used surgical relapse of the two techniques to calculate the sample size. Based on the study conducted by our center (Ow and Cheung, 2010), assuming a 0.5 mm (S.D. 0.75 mm) difference on the mean horizontal relapse between the two surgical

techniques, with a type 1 error rate of 5% and an 80% power, 36 subjects were required in each group.

2.7. Randomization

An eligible patient was randomized by a simple randomization procedure into one of the two study groups. A randomization table was generated from a computer program. The allocation sequence was kept concealed in sequentially numbered, opaque and sealed envelopes. The surgeon in-charge opened the sealed envelope containing the allocation sequence after the study consent was obtained from the participant.

2.8. Statistical Analysis

The data were analyzed with the Statistical Package for Social Sciences (SPSS version 24.0, SPSS Inc, Chicago, IL, USA). Statistical analyses were performed to compare the MDO group and SSRO group. OSA cure rate and treatment success rate at post-treatment 12 months, and the incidence of surgical morbidities were analyzed with chi-square tests. The mean AHI and LSAT between the MDO and SSRO groups at all-time points were compared with independent t tests. The 5% probability level was taken as the cut-off for statistical significance.

3. Results

Eighteen patients (6 females, 12 males) were recruited into this study. Nine patients were randomized to the MDO group and to the SSRO group. The mean ages of the MDO group and SSRO group were 40.7 years (S.D. 14.3 years) and 44.7 years (S.D. 7.1 years), respectively. The mean AHI were 41.5/hour (S.D. 13.3/hour) and 53.2/hour (S.D. 11.9/hour) for MDO group and SSRO group, respectively. There were no statistical differences in their demographic profile (gender or mean age), BMI or the severity of OSA (mean AHI, mean LSat, OSA severity) between the two groups.

There was no statistical difference in the mean mandibular advancement for the MDO group and SSRO group (11.5 mm (S.D.1.9 mm) versus 13.0 mm (S.D. 1.5 mm) $p = 0.082$). There was no statistical difference in the adjunctive surgeries the two groups received. The osteotomy time was longer for the SSRO group when compared to the MDO group ($p = 0.008$), but the fixation time was longer in the MDO group ($p = 0.001$). Table 1 summarized the comparisons of the demography, baseline OSA severity and surgical treatment of the two groups.

Early termination of new recruitments was decided when two cases of major complications happened in the MDO group (see ***Surgical morbidities*** below). It was also noted that the patients in the MDO group required a prolonged stay in the intensive care unit at the immediate post-operative period due to the swollen airway. It was decided by the surgeon-in-charge (Leung YY) to terminate patient recruitment for the study and perform analysis at this point. Therefore, the study fell short of the targeted sample size with only 18 patients recruited.

3.1. Airway functional improvement

Eight out of nine patients (88.9%) in the MDO group had an AHI of less than 20/hour (range 0.8–4.7/hour) and more than a 50% reduction of AHI level at T0; and were considered as a success. All 8

Table 1
Comparison of demography, baseline OSA severity and surgical treatment between the two groups.

	MDO Group (n = 9)		SSRO Group (n = 9)		p value
Gender					0.62
Female	44.4%	(4/9)	22.2%	(2/9)	
Male	55.6%	(5/9)	77.8%	(7/9)	
Mean age (years) (S.D)	40.7	(14.3)	44.7	(7.1)	0.463
Mean BMI (kg/m^2)	22.7	(4.1)	25.5	(3.1)	0.111
Mean AHI (/hour)	41.5	(13.3)	53.2	(11.9)	0.067
Mean LSat (%)	72.8	(12.6)	70.7	(11.4)	0.714
OSA Severity					0.134
Severe	77.8%	(7/9)	100%	(9/9)	
Moderate	22.2%	(2/9)	0		
Mean mandibular advancement (mm) (S.D.)	11.5	(1.9)	13.0	(1.5)	0.082
Mean osteotomy time (min) (S.D.)	34.1	(3.6)	39.2	(3.6)	0.008
Mean fixation time (min) (S.D.)	39.4	(3.7)	14.78	(1.5)	0.001
Adjunctive surgery					
LeFort 1					0.257
Yes	88.9%	(8/9)	66.7%	(6/9)	
No	11.1%	(1/9)	33.3%	(3/9)	
Mandibular anterior subapical osteotomy					1
Yes	88.9%	(8/9)	88.9%	(8/9)	
No	11.1%	(1/9)	11.1%	(1/9)	
Genioplasty					1
Yes	100%	(9/9)	100%	(9/9)	
No	0		0		

AHI, apnea-hypopnea index; BMI, body mass index; LSat, lowest oxygen saturation; MDO, mandibular distraction osteogenesis; OSA, obstructive sleep apnea; SSRO, sagittal split ramus osteotomy.

patients achieved AHI <5/hour and were regarded as cured. One patient had AHI of 23.5/hour at T4 and the treatment was considered unsuccessful. In the SSRO group, 8 of 9 patients (88.9%) had an AHI of <20/hour (range 0.5–12.7/hour) and more than a 50% reduction of AHI level at T0 and were considered successful. One patient had AHI of 62.8/hour and the treatment was considered unsuccessful. Six out of 9 patients (66.7%) achieved AHI <5/hour (range 0.5–4.1/hour) and were regarded as cured. There was no statistical difference between the two groups in terms of success rate at post-operative 1 year ($p = 1.00$). There was also no statistical difference between the two groups in cure rate at post-operative 1 year ($p = 0.527$). The overall success rate and cure rate at T4 were 88.9% and 77.8% respectively.

The post-operative 2-year longitudinal mean AHI changes (after excluding the unsuccessful case in each group) are presented in Fig. 3. The mean AHI (S.D.) of MDO group at T1, T2, T3, T4 and T5 were 2.8/hr (3.7/hr), 1.9/hr (1.5/hr), 3.3/hr (2.9/hr), 2.8/hr, (1.9/hr) and 2.4/hr (3.1/hr), respectively. The mean AHI (S.D.) of SSRO group at T1, T2, T3, T4 and T5 were 4.9/hr (6.8/hr), 6.9/hr (5.5/hr), 6.6/hr (7.0/hr), 3.8/hr, (4.2/hr) and 4.4/hr (3.9/hr), respectively. The mean AHI of MDO group was significantly less only at T2 when compared to the SSRO group ($p = 0.025$). There was no statistical difference of the mean AHI between the two groups at all other time-points.

The post-operative 2-year longitudinal mean LSAT changes (after excluding the unsuccessful case in each group) are presented in Fig. 4. The mean LSAT of MDO group peaked at T2 at 89.5% and gradually dropped to 75.4% at T5. The mean LSAT of SSRO group raised to 85.8% at T1 but dropped at T2 to 76.6%, which gradually improved to 85.8% at T5. There were no significant differences of mean LSAT between the two groups at all-time points.

3.2. Surgical morbidities

The surgical morbidities were recorded in Table 2. There were 4 cases (44.4%) of major complications in the MDO group. One patient developed hospital-acquired pneumonia on the second post-operative day in the ICU. Extubation was delayed to the post-operative 5th day until the pneumonia was controlled with a vigorous antibiotics regime and chest physiotherapy. The patient recovered subsequently. There were 2 cases presented with non-union of mandible and one case of non-union of maxilla. All three cases required re-operation for re-fixation and additional curettage/bone grafting. All three cases healed uneventfully after the re-operation. In contrast, there were no major complications in the SSRO group.

Minor complications were presented in both the MDO group and the SSRO group. There were 66.7% post-operative infections in the MDO group around the distractors, and 22.2% wound infections in the SSRO group. Occlusion discrepancies (anterior or posterior open bite) were more common in the MDO group when compared to the SSRO group (44.4% vs 11.1%). Both groups had a similar prevalence of inferior alveolar nerve deficit and facial asymmetry. There were no statistical differences in all comparisons of complication incidence.

3.3. Skeletal relapse

Longitudinal skeletal relapse within two post-operative years of the two groups is presented in Table 3. Skeletal relapse (i.e. posterior movement) was noted in the MDO group at post-operative 3 months (T2) onwards to 2 years (T5), with a mean total relapse of 0.32 mm (S.D. 0.20 mm) in 2 years. Skeletal relapse was noted in the SSRO group at post-operative 1 month (T2) onwards to 2 years (T5), with a mean total relapse of 1.0 mm (S.D. 0.23 mm) in 2 years. There were no statistical differences between the two groups in skeletal relapse at all time intervals and in terms of the total amount of relapse.

4. Discussion

This study was terminated early by the corresponding author after 2 cases (22.2%) of MDO cases presented with non-union of the distracted mandible. There was a further one case of maxillary non-union due to the long duration of elastics application in an MDO case. All three cases required re-operation for additional bone grafting and re-fixation. It was also noted that the MDO cases in general required a longer stay in the intensive care unit. The recruited cases that were operated on were followed-up according to the study protocol.

Despite the smaller recruited sample, this study had several valuable findings. The key findings of the study were: 1) There were no statistical differences between SSRO and MDO in the OSA cure

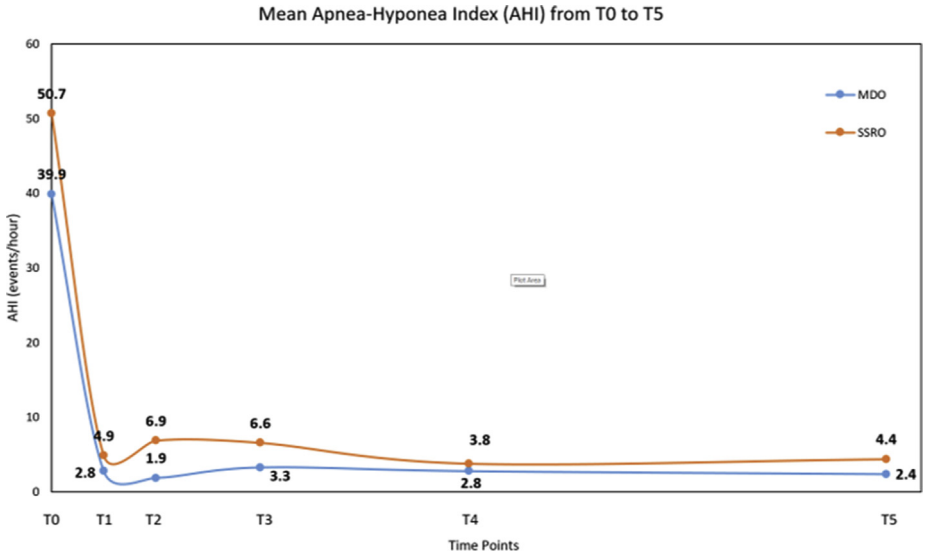

Fig. 3. The longitudinal mean AHI changes of the two groups within two post-operative years (one unsuccessful case from each group excluded).

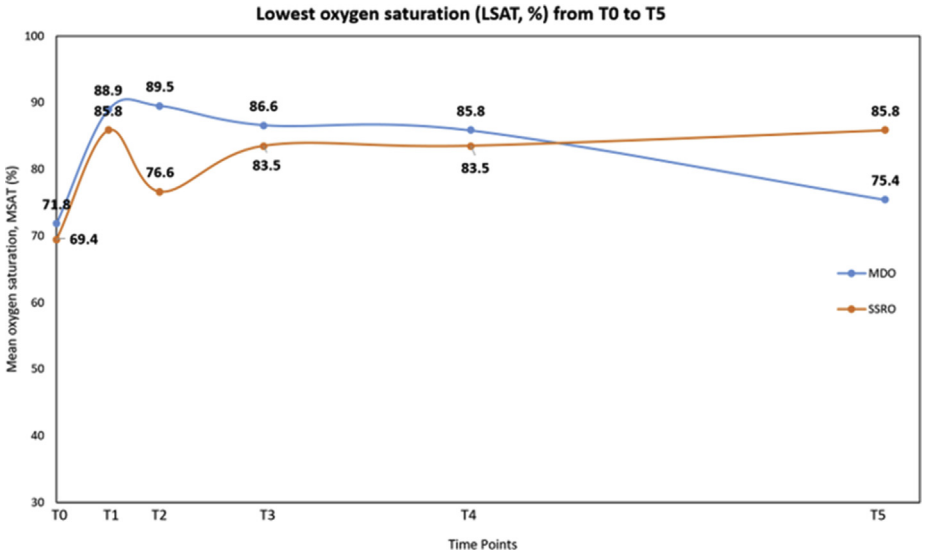

Fig. 4. The longitudinal mean LSAT changes of the two groups within two post-operative years (one unsuccessful case from each group excluded).

Table 2
Comparison of surgical morbidities between the two groups.

	MDO Group (n = 9)		SSRO Group (n = 9)		p value
Major complications					
Pneumonia	11.1%	(1/9)	0		0.303
Non-union	33.3%	(3/9)	0		0.058
Minor complications					
Post-operative infection	66.7%	(6/9)	22.2%	(2/9)	0.058
Occlusion discrepancies					0.114
Anterior open bite	11.1%	(1/9)	0	0	
Posterior open bite	33.3%	(3/9)	11.1%	(1/9)	
Distraction device failure	0		N/A		
Subjective neurosensory deficit					0.719
None (VAS = 0)	11.1%	(1/9)	11.1%	(1/9)	
Mild (VAS 1–3)	11.1%	(1/9)	33.3%	(3/9)	
Moderate (VAS 4–6)	33.3%	(3/9)	22.2%	(2/9)	
Severe (VAS 7–10)	44.4%	(4/9)	33.3%	(3/9)	
Facial asymmetry	11.1%	(1/9)	11.1%	(1/9)	1

MDO, mandibular distraction osteogenesis; SSRO, sagittal split ramus osteotomy.

rate and success rate, and both mandibular advancement techniques achieved excellent results in both criteria in the first two post-operative years; 2) The overall success rate and cure rate of OSA of this study were 88.9% and 77.8% respectively; 3) There were more major complications (4 out of 9 cases) in the MDO group compared to the SSRO group (0 case), and there were similar incidences of minor complications; 4) There were no statistical differences in the skeletal relapse between the two groups.

MDO is used widely to treat OSA in paediatric syndromic cases like Pierre Robin Sequence and Treacher Collins Syndrome when conventional orthognathic surgery is not feasible.[21] The role of distraction osteogenesis is limited to specific conditions in adult OSA patients that are considered too challenging or unpredictable for routine orthognathic procedures like bilateral temporomandibular ankylosis that causes OSA (Leung and Lai, 2018). The use of MDO in adult non-syndromic OSA patients has not been studied sufficiently. Its effectiveness, safety and stability are not known especially when compared to the 'gold standard' SSRO for mandibular advancement. This study is the first randomized controlled clinical trial to compare MDO and SSRO for the treatment of moderate-to-severe OSA. The authors hoped to compare MDO to the traditional SSRO with an evidence-based approach on which technique is superior and more suitable for treating adult OSA patients. Our center has a long history of performing distraction osteogenesis in facial bone and also published numerous clinical and pre-clinical studies of the technique (Ow and Cheung, 2010; Leung and Lai, 2018; Cheung et al., 2003; Zheng et al., 2006; Ma et al., 2010; Hariri et al., 2016). Most of the distraction cases in our center are younger adults with severe mandibular hypoplasia or secondary cleft lip and palate deformities. The technique and protocol of distraction osteogenesis is therefore

Table 3
Longitudinal skeletal relapse of the two groups within two post-operative years.

	Time Interval								Total	
	T0	T1-T2		T2-T3		T3-T4		T4-T5		
Mean relapse, mm (S.D.)										
MDO Group	61.9 (6.3)	0.11	(0.46)	−0.49	(0.22)	−0.41	(0.18)	−0.02	(0.23)	−0.32	(0.20)
SSRO Group	61.7 (9.4)	−0.40	(0.36)	−0.62	(0.23)	−0.30	(0.18)	−0.22	(0.16)	−1.0	(0.23)
p value	0.942	0.760		0.755		0.765		0.618		0.970	

+, anterior movement; -, posterior relapse.
MDO, mandibular distraction osteogenesis; SSRO, sagittal split ramus osteotomy; T0, pre-operative; T1, post-operative 1 month; T2, 3 months; T3, 6 months; T4, 1 year; T5, 2 years.

mature, but the patient group that is indicated for the technique is yet to be tested.

The decision to opt for surgical treatment for OSA should be well justified. Waite and Li both pointed out that adolescents with signs of complete ossification of the cranial sutures, adults who had failed other therapeutic interventions including oral appliances or CPAP, and patients who had maxillomandibular deficiency or hypoplasia were suitable candidates to undergo skeletal correction (Waite and Shettar, 1995; Li, 2003). Holty and Guilleminault also showed that MMA could be successfully done in obese patients or with severe OSA (Holty and Guilleminault, 2010). Most of the patients (77.78%) in this study were overweight (BMI $\geq$ 23), with a mean age of 42.7 years and a mean AHI of 47.4/hour, which were comparable to the sample reported by Holty. All the patients in this randomized controlled trial fulfilled the above pre-requisites: adults, failed CPAP trial and all had mandibular hypoplasia.

Polysomnography has been the gold standard in the diagnosis of OSA and in the assessment of success or failure in patients receiving treatment. PSG can objectively show the frequency and severity of the apneic events, and provides other valuable information on a patient's sleep stages, sleep architecture, oxygen saturation and other important vital signs during the sleep process. Clinical studies on surgical treatment on OSA usually performed the post-operative PSG at 6 months so as to wait for the surgical swelling to fully subside and for the parapharyngeal soft tissue adaptation to complete before the assessment (Fairburn et al., 2007; Lye et al., 2008). In this study, PSG were also carried out at the 1st and 3rd months after surgery as well to investigate the progressive changes of the airway function during the early and intermediate post-operative periods. Holty and Guilleminault concluded the high effectiveness of MMA, and reported the pooled success and cure rates of 86.0% and 43.2%, respectively (Holty and Guilleminault, 2010). Case reports on using MDO in treating adult OSA cases were mostly because of the consequence of bilateral TMJ ankylosis (Lye et al., 2008; Feiyun et al., 2010). Our randomized controlled trial demonstrated that both SSRO and MDO as part or whole of the skeletal advancement surgery were highly successful in treating adult moderate-to-severe OSA patients, and there was no statistical difference between the two methods in terms of airway function improvement. This study showed that airway function of both groups was stable in long-term. For the majority of cases that had OSA successfully treated, the AHI was maintained at a very low level in both MDO and SSRO groups. It was also noted that after these patients recovered from the surgery with their OSA treated, they were more active and started to engage in exercise. This might contribute to further improvement in their OSA.

Despite the effectiveness of treating OSA by MDO, the drawback of the technique was the high incidence of surgical complications. The older age group of patients with OSA is a risk factor for non-union of bone. The reduced healing capacity and blood supply in older patients might have contributed to the higher chance of non-union. The distraction protocol was similar to several standardized protocols of different centers for adult patients, which were likely to be developed and tested for use in young adults for orthognathic surgery (Wang et al., 2003; Feiyun et al., 2010; Ow and Cheung, 2010; Li et al., 2012). There was no specific distraction protocol for older patients like those in this study. The re-operation to graft the bone with autogenous bone graft and re-fixation posed additional suffering to the patients. The extended stay in intensive care unit in most of the MDO group patients was likely to be attributable to the swollen airway post-operatively, and precipitated by their OSA condition, which justified a delayed extubation for airway protection. In contrast, most of the patients in the SSRO group had immediate enlargement of the airway post-operatively, and their OSA symptoms were greatly improved even from the first post-operative day onwards. Li et al. did not report any major complications in their smaller case series, but their group noted minor complications including wound infection and neurosensory disturbance (Li et al., 2002). In our study, post-operative infection and a deranged occlusion were more prevalent in the MDO group than the SSRO group. Both groups had significant neurosensory deficit, which usually would not bother the patients. With the high incidence of major complications, it appears MDO is inferior to SSRO as whole or part of skeletal advancement for the treatment of OSA in terms of surgical morbidities.

As part of the secondary outcomes, this study also investigated the longitudinal relapse of both techniques. It was found that there were no statistical differences at any time-points on skeletal relapse between the two groups, which concurred an earlier study of our center comparing the two techniques for orthognathic patients (Ow and Cheung, 2010). The skeletal stability of MDO and SSRO was reflected by the stable post-operative airway function, as in theory any relapse of the mandibular advancement would reduce the airway and thus cause a relapse in the OSA indices. This provides evidence that both techniques have skeletal stability; at least in the first two post-operative years.

This study was limited by the relatively small same size due to the earlier termination of patient recruitment. The sample was only 25% of the planned sample size. Yet this randomized clinical trial provided useful information on the longitudinal changes of OSA parameters of the MDO and SSRO in an evidence-based manner, as well as the comparisons of other parameters including surgical morbidities and skeletal stability. To the authors' knowledge, this is the first attempt in the literature to compare MDO and SSRO by a randomized clinical trial. The reasons are probably: 1) MDO is a relatively newer technique and skeletal advancement is only becoming more popular in recent years; 2) It is challenging to recruit patients with moderate-to-severe OSA and in this age range to go through skeletal advancement surgery; 3) Randomized clinical trials with long term follow-up are difficult to conduct in surgical interventions. The initial sample size calculation was based on skeletal stability of MDO and SSRO because there were no available data for the primary outcome (i.e. OSA cure rate) of MDO in non-syndromic adult patients. From the results of this randomized clinical trial, it appeared the initial sample size calculation was over-estimated. However, as there are no similar studies in the literature, the statistical validity of this study is difficult to be verified. Therefore we recommend readers to interpret the results of this study carefully, and to choose the most suitable treatment modality in a case-by-case manner. Nonetheless, the authors believe the early termination of the patient recruitment was a correct decision as the incidence of major complications outweigh the potential benefits of MDO over SSRO.

In conclusion, this randomized clinical trial comparing MDO and SSRO as part or whole of skeletal advancement surgery as a treatment of moderate-to-severe OSA has found both techniques were highly effective in treating OSA in terms of high OSA cure rate and treatment success rate, with no statistical difference between the two techniques. Both techniques were stable within two post-operative years in terms of airway function and skeletal stability. However, MDO has a high incidence of major complications, in particular non-union of osteotomized mandible, when compared to SSRO. The study was terminated early as a consequence of the high major complication incidence. From the limited sample size of the study, given that MDO was not superior to SSRO in key outcomes but had higher complication rates, we believe MDO should not be recommended as a routine treatment modality for non-syndromic adult patients with moderate-to-severe obstructive sleep apnea.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcms.2019.01.046.

List of abbreviations

AASM	American Academy of Sleep Medicine
AHI	apnea-hypopnea index
BMI	body mass index
CPAP	continuous positive airway pressure
DISE	drug-induced sleep endoscopy
LSat	lowest oxygen saturation
MDO	mandibular distraction osteogenesis
MMA	maxillomandibular advancement
OSA	obstructive sleep apnea
PSG	polysomnography
SSRO	sagittal split ramus osteotomy

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