

Three-dimensional nasolabial changes after maxillary advancement osteotomy in class III individuals: a systematic review and meta-analysis

Mohammed Almuzian,¹ Josh Rowley,² Hisham Mohammed,³ Mark B. Wertheimer,⁴ Aman Ulhaq⁵ and Samer Mheissen*⁶

Abstract

Background Class III malocclusions with maxillary retrognathia are commonly treated with single jaw Le Fort I maxillary advancement. The three-dimensional (3D) effects of surgery on the nasolabial region varies among the clinical studies. Quantifying these changes is of great importance for surgical planning and obtaining valid consent.

Objectives To investigate the 3D relationship between soft tissue and skeletal changes secondary to Le Fort I maxillary advancement surgery in skeletal class III patients.

Search methods Comprehensive search of multiple electronic databases supplemented by a manual and grey literature search were undertaken from inception to 9 June 2020.

Selection criteria Studies that evaluated the 3D soft tissue changes of patients before and after maxillary advancement surgery alone.

Data collection and analysis Study selection, data extraction and risk of bias assessment were performed independently by two reviewers, with disputes resolved by a third reviewer. A quantitative synthesis of the data was pre-planned for pooling similar outcome measures.

Results Four studies were included in the final review and meta-analysis, with a total of 105 patients (mean age 16.7 + 33.9 years). The mean maxillary advancement of the included studies was 5.58 mm (95% CI 5.20–5.96). The sagittal effects of surgery on nose tip projection and prominence were insignificant ($P > 0.05$, two studies); however, subnasal projection (MD 1.7 mm, two studies) and upper lip projection (MD 2.90 mm, four studies) increased significantly in a forward direction after surgery ($P < 0.05$). Le Fort I osteotomy widens the upper philtrum width (MD 0.84 mm, two studies) ($P < 0.05$). Inconsistencies among the included studies were identified; therefore, the results should be interpreted with caution.

Conclusions There is weak evidence based on quantitative assessments that Le Fort I maxillary advancement significantly affects the nasolabial soft tissue envelope mainly in a sagittal dimension. These changes are concentrated around the central zone of the nasolabial region. Future prospective studies on maxillary advancement osteotomy with a standardised method of assessment, taking into consideration the confounding factors, are required.

Introduction

Le Fort I maxillary advancement surgery has been used widely to correct maxillary retrognathia in patients with a class III malocclusion and concave profile. The goal of such a procedure is to achieve a good occlusion and to improve facial harmony.¹ Although Le Fort I osteotomy affects the facial soft tissue at different degrees, the effect is mainly concentrated at the region

of the upper lips and the base of the nose. The approximate ratio of nasolabial soft to hard tissue changes secondary to maxillary advancement is not well defined; therefore, estimating these changes is of vital importance.²

Traditionally, two-dimensional (2D) lateral cephalometric radiographs are utilised for both pre-surgical planning and prediction as well as post-surgical evaluation of outcomes.³ However, the accuracy of algorithms intended to forecast 2D-profile soft tissue changes as a result of skeletal movements is limited, owing to overlapping radiographic structures that do not represent the three-dimensional (3D) object.² On the other hand, 3D virtual models and surgical planning are useful for accurate prediction and informed patient counselling.^{4,5} Several techniques to capture and analyse the 3D digital images of the soft and hard tissue are available, and these include surface and volumetric methods.

Computed tomography (CT),⁶ cone beam CT (CBCT) and magnetic resonance imaging (MRI) fall under the umbrella of volumetric methods. Poor surface texture and resolution can limit the accuracy and reproducibility of landmarks acquired from CT/CBCT renderings, allowing only rough evaluation. However, 3D surface imaging methods including stereophotogrammetry⁷ and laser surface scanning⁸ overcome these drawbacks, making them the superior methods of acquiring the 3D anatomy of the facial soft tissue.⁹ Recent studies validated the use of stereophotogrammetry for that purpose.^{4,5}

Quantifying 3D soft and hard tissue changes in response to jaw surgery can be achieved using linear, angular and volumetric surface measurements,^{10,11} using reliable software such as Dolphin, 3dMD Vultus and Maxilim.^{12,13,14,15,16} However, the measured and quantified 3D soft to hard tissue changes as a result of jaw surgery

¹DClinDent (Orthodontics), Research Fellow, University of Edinburgh, Edinburgh, UK; ²DClinDent (Orthodontics), Specialist Orthodontist in Private Practice, Edinburgh, UK; ³MSc (Orthodontics), Research Fellow, University of Edinburgh, Edinburgh, UK; ⁴MDent (Orthodontics), Specialist Orthodontist in Private Practice, Johannesburg, South Africa; ⁵MSc (Orthodontics), Consultant Orthodontist, University of Edinburgh, Edinburgh, UK; ⁶DDS, Syrian Board in Orthodontics, Former Instructor in Orthodontic Department, Syrian Ministry of Health Private Practice, Damascus, Syrian Arab Republic.
*Correspondence to: Samer Mheissen
Email address: mheissen@yahoo.com

Advanced Online Publication 12 July 2021
<https://doi.org/10.1038/s41432-021-0188-9>

SYSTEMATIC REVIEW

vary among the studies and mainly focus on combined jaw surgery.^{13,14,15,16} A recent narrative systematic review¹⁷ with no prior registration tried to explore the 3D soft tissue effects of maxillary structures; however, the study included different types of jaw surgery (bimaxillary, surgically assisted rapid maxillary expansion procedures and Le Fort I advancement/setback/impaction) which were used to treat different types of malocclusion, including class III malocclusion and facial asymmetry. Consequently, the author of that review could not present the combined pool estimate. Therefore, the literature lacks consensus regarding the quantity of 3D soft tissue changes secondary to isolated maxillary advancement surgery in class III malocclusion with maxillary retrognathia. The aim of this systematic review and meta-analysis was to investigate and quantify the 3D nasolabial soft tissue changes of isolated Le Fort I maxillary advancement surgery in skeletal class III individuals.

Materials and methods

Protocol and registration

The authors followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines^{18,19} to develop the study protocol. The present systematic review was conducted according to the guidelines of the Cochrane handbook for systematic reviews of interventions (version 6)²⁰ and was reported according to the PRISMA statement.²¹ The study protocol was registered with PROSPERO (CRD42019132151).

Eligibility criteria

Table 1 describes the main research question, which was defined in PICO format. Case reports, case series, studies using 2D images, review articles, in vitro and animal studies, editorials and opinions were excluded. Moreover, studies that included syndromic patients, patients with cleft lip and/or cleft palate or surgery relating to pathology/trauma were excluded. Studies that included osteotomies other than isolated Le Fort I osteotomy – including bimaxillary orthognathic procedures, genioplasty procedures and multiple sectioning of the maxilla – were also excluded. Only studies with more than six months of follow-up after surgery, to allow for reduction in swelling, were included.

Table 1 PICOS format of the review question

PICOS	Description
Population	Adult patients with a class III (maxillary retrognathic) malocclusion who have undergone orthognathic surgery
Intervention	Le Fort I single piece maxillary advancement osteotomy that is clearly described with respect to hard tissue surgical movement reference
Comparators	Pre-surgical records
Outcome	Changes in facial soft tissues (mainly lip projection, nose projection) assessed using 3D digital image evaluation (CBCT, CT, stereophotogrammetry, laser facial scanning or MRI)
Type of studies	Prospective and retrospective cohort trials and randomised controlled trials

Table 2 The search strategy for MEDLINE on which other searches were based

Number	Search terms
1	Malocclusion, Angle Class III/
2	orthognathic surgical procedures/ or orthognathic surgery/
3	maxillary osteotomy/ or osteotomy, le fort/
4	((maxilla* or le fort 1 or le fort I) adj2 advancement).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
5	1 or 2 or 3 or 4
6	Imaging, Three-Dimensional/
7	(3-dimensional or three-dimensional or 3D).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
8	Photogrammetry/
9	anthropometry/ or cephalometry/
10	Cone-Beam Computed Tomography/
11	6 or 7 or 8 or 9 or 10
12	soft tissue*.mp.
13	facial profile.mp.
14	facial surface.mp.
15	12 or 13 or 14
16	5 and 11 and 15

The following Journals were searched manually:

British Dental Journal
Journal of Dental Research
Journal of Orthodontics
Journal of Clinical Orthodontics
American Journal of Orthodontics and Dentofacial Orthopedics
Journal of Orthodontics
Craniofacial Research
European Journal of Orthodontics

Information sources and search strategy

Six electronic databases (Medline and Embase via Ovid, Cochrane Library, Scopus, LILACs via Virtual Health Library and Web of Science) were searched for published, unpublished and ongoing studies up to 4

December 2020. Specific search strategies using keywords, truncations and Boolean operators were developed for each database (Table 2) with the guidance of an experienced librarian at the University of Edinburgh. The electronic search was supplemented by search

Table 3 Quality assessment of the studies included in the review (NA = not applicable, NR = not required)

Papers	DeSesa <i>et al.</i> , 2016 ²⁶	Metzler <i>et al.</i> , 2014 ²⁷	Nkenke <i>et al.</i> , 2008 ²⁸	Verdenik <i>et al.</i> , 2017 ²⁹
1. Was the study question or objective clearly stated?	Yes	Yes	Yes	Yes
2. Were eligibility/selection criteria for the study population pre-specified and clearly described?	Yes	Yes	Yes	Yes
3. Were the participants in the study representative of those who would be eligible for intervention in the general or clinical population?	Yes	Yes	Yes	Yes
4. Were all eligible participants that met the pre-specified entry criteria enrolled?	NR	NR	Yes	Yes
5. Was the sample size sufficiently large to provide confidence in the findings?	NR	NR	NR	NR
6. Was the intervention clearly described and delivered consistently across the study population?	Yes	Yes	Yes	Yes
7. Were the outcome measures pre-specified, clearly defined, valid, reliable and assessed consistently across all study participants?	Yes	Yes	Yes	Yes
8. Were the people assessing the outcomes blinded to the participants' interventions?	Yes	Yes	No	No
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	NA	NA	NR	NR
10. Did the statistical methods examine changes in the outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	Yes	Yes	Yes	Yes
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (that is, did they use an interrupted time-series design)?	NR	NR	No	Yes
12. If the intervention was conducted at a group level, did the statistical analysis take into account the use of individual-level data to determine effects at the group level?	NR	NR	NR	NR
Overall quality rating	Fair	Fair	Fair	Fair

of the reference lists in selected articles, as well as manual search in all available issues (Table 2) at the Library of the University of Edinburgh until 11 November 2020. There was no search restriction on date or language. The grey literature was also searched using OpenGrey (www.opengrey.eu). Authors

were contacted via e-mail when it was deemed necessary. Electronic searches were undertaken by two review authors (SM and MA) and a manual search was undertaken by one review author (MA). All the references retrieved through the search strategy were exported into and managed using EndNote

version X7.8 (Clarivate, Philadelphia, PA, USA). Microsoft Word and Excel (Microsoft Corporation, Redmond, WA, USA) were utilised for management of data extraction and completion of the report.

Study selection

Two independent reviewers (JR and AU) screened, in duplicate, titles and abstracts using the eligibility criteria. Full texts were also examined independently and in duplicate for eligibility. Any disagreements, if presented, were resolved by consensus and discussion with a third reviewer (MA). The degree of agreements in every step was tested using the Kappa test (Kappa 0.94), though a recent guideline discourages its use.²⁰

Data items and extraction

Data were extracted independently by two reviewers (JR and MA) using a pro forma. Data extraction involved items related to participant information, type of intervention, method of evaluation and the outcomes. Disagreements between the reviewers were resolved through discussion, and if needed, via consultation with a third reviewer (AU). It was pre-planned to contact corresponding authors if additional information was needed. The 3D effect of Le Fort I osteotomy on soft tissues was undertaken by comparing pre- and post-surgical data.

Risk of bias in the individual studies

SM and MA assessed the risk of bias for each study using the quality assessment of controlled intervention studies (<https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>). Disagreements between the reviewers were resolved through discussion, and if needed, via consultation with a third reviewer (AU). This checklist was developed for medical studies and was adapted for use in orthognathic surgery studies.²² The bias assessment tool for all included articles was analysed to give an overall quality rating found in Table 3. The quality of the included studies was rated as good quality (9–12 ‘yes’ answers), fair quality (5–8 ‘yes’ answers) or poor quality (1–4 ‘yes’ answers).

Summary measures and approach to data synthesis

Quantitative analysis of the assigned studies was pre-planned to be conducted by SM using

SYSTEMATIC REVIEW

Review Manager (RevMan, version 5.4.1, Copenhagen; The Nordic Cochrane Centre, The Cochrane Collaboration, 2020). It was pre-planned to undertake statistical synthesis, if possible, by inspecting the included studies with respect to the population groups, described variables, study design and outcome reporting. The statistical heterogeneity detection was pre-planned using Tau^2 and I^2 .²³ If there was a substantial statistical heterogeneity ($I^2 > 50\%$), the random-effect model would be adopted. Otherwise, the fixed-effect model would be used. The continuous data were expressed using the mean difference and 95% confidence interval (CI).²³ However, the narrative description of the findings was pre-planned to be used if significant clinical and methodological heterogeneity of the included studies was present.

Risk of bias across studies and additional analyses

For the quality of the evidence, the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach was used.²⁴ The authors decided in advance to use sensitivity and subgroup analyses, if possible. Also, the authors pre-planned to detect the potential publication bias in a meta-analysis using Egger's linear regression test,²⁵ and by visually inspecting a generated contour-enhanced funnel plot if the number of included trials that address the same intervention and outcome was sufficient (>10 trials).

Results

Selection of the studies

The selection of studies is summarised in the PRISMA flowchart (Fig. 1). The initial search resulted in 1,092 records. After removing the duplicates, 822 articles remained. Reviewing the 822 titles and abstracts led to excluding 783 articles. Thirty-nine articles were identified for full-text reading. Thirty-five articles were excluded because of various reasons (Figure 1 and online Supplementary Table 1). Finally, four studies were included in this systematic review^{26,27,28,29} and were pooled in meta-analysis.

Characteristics of the studies

Characteristics of the included studies are presented in Table 4. The included studies were two prospective studies^{28,29} and two retrospective studies,^{26,27} with a total of 105 patients (mean age 16.7 ± 33.9

Fig. 1 PRISMA flow diagram

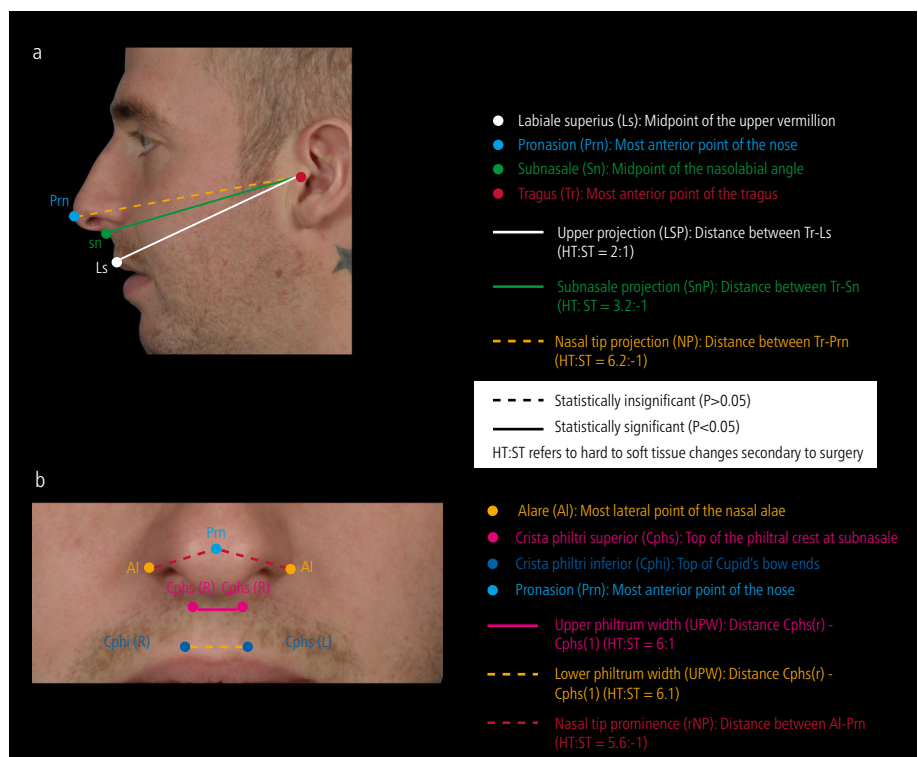
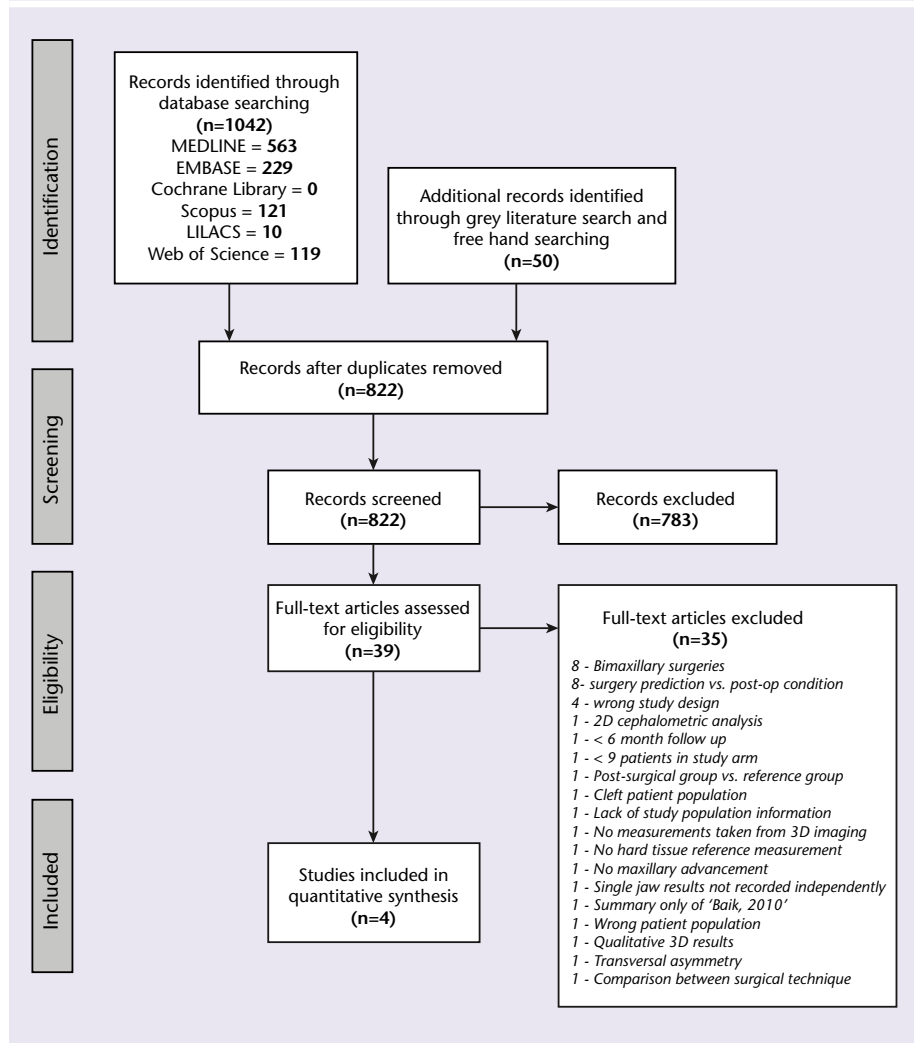


Fig. 2 Nose changes secondary to Le Fort I maxillary advancement

Table 4 Characteristics of potential articles related to aim of the report and participants (M = male, F = female, F = female, ND = not described)

Author, year (country)	Study design	Number	Gender (M/F)	Age (years)	Surgical intervention and malocclusion	Average maxillary advancement	Outcomes	Follow-up
DeSesa <i>et al.</i> , 2016 ²⁶ (United States)	Retrospective	23	1:1	23.5	Le Fort I maxillary advancement for treatment of class III malocclusion with maxillary retrognathia	5.8 ± 1.8 mm	3D photogrammetry Nose: Nasofrontal angle, nasolabial angle Nasal tip projection, nasal tip prominence, alar base width Alar width Sill width right Sill width left Nostril height right, nostril height left, nostril width right, nostril width left Soft triangle angle right, soft triangle angle left, lateral alar angle right, lateral alar angle left, columella width, columella height, columella projection Lip: Subnasale projection, lower philtrum width, upper philtrum width, philtrum height Lip width Labiale superius projection	8.7 months
Metzler <i>et al.</i> , 2014 ²⁷ (United States)	Retrospective	44	1:1.43	16.7		5.5 ± 1.9 mm	3D photogrammetry Nasofrontal angle Nasal tip projection Columella projection and height Nasal tip prominence Alar base and alar width Nostril height Lip projection Upper and lower philtrum width	7.8 months
Nkenke <i>et al.</i> , 2008 ²⁸ (Germany)	Prospective	20	1:1	33.9		5.3 ± 2.1 mm	Optical 3D surface scan The maximal parasagittal advancement The facial convexity (N'SnPg') The malar-midfacial region The accommodation vectors The labrale superius to the incision superius	6 months
Verdenik <i>et al.</i> , 2017 ²⁹ (Slovenia)	Prospective	18	ND	24		5.7 ± 1.7 mm	Optical 3D scan	6 months

SYSTEMATIC REVIEW

years). All patients underwent maxillary advancement osteotomy in isolation and were followed up for at least six months after the surgery. The overall mean of the amount of maxillary advancement in the included studies was 5.58 mm (95% CI 5.20–5.96). Two studies were undertaken in the US^{26,27} and the others in Germany²⁸ and Slovenia.²⁹

Different methods were used to assess the nasolabial soft tissue changes, with some studies^{26,27} using direct linear and angular anthropometric parameters measured separately on pre- and post-surgery 3D renderings. Two studies evaluated the soft tissue changes in the whole face,^{28,29} while two of the included studies^{26,27} evaluated changes in the nasal and upper lip regions of the face. Included studies used either 3D photogrammetry^{26,27} or optical 3D surface scan^{28,29} to acquire soft tissue scans. MRI or CT were not used in any of the included studies.

Risk of bias within studies

Risk of bias assessment for the included studies is summarised in Table 3. All studies received a fair score, indicating a high risk of bias owing to the lack of sample size calculation, lack of blinding of researchers and no mention of intention-to-treat or per-protocol analysis in the prospective trials.

Results of individual studies and data synthesis – soft tissue changes

Nasolabial soft tissue changes were pooled into two main categories based on the outcomes and the measurements: nose and lip changes. All of these occurred as a result of 5.58 mm (95% CI 5.20–5.96) of maxillary advancement as reported by the included studies. Figure 2 explains the nasolabial soft tissue measurements and their landmarks, which were used in the included studies.

Nose changes

Two studies^{26,27} reported on the changes in the nasal tip projection. Maxillary advancement resulted in 0.89 mm (95% CI, -2.44–4.22, $P = 0.60$, $I^2 = 0$) increase in nasal tip projection, which was statistically non-significant (Fig. 3a).

In terms of the changes in the nasal tip prominence, the pooled estimate of two of the included studies,²⁷ showed that it decreased post-surgically by 0.77 mm

Fig. 3 Forest plot showing upper lip changes secondary to Le Fort I maxillary advancement. a) Upper lip projection. b) Upper lip philtrum width. c) Lower lip philtrum width

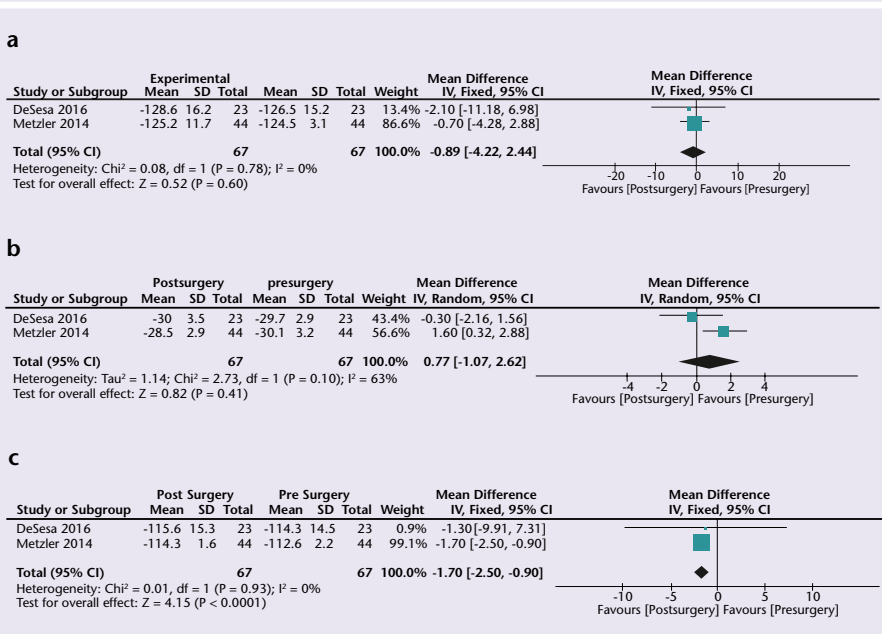
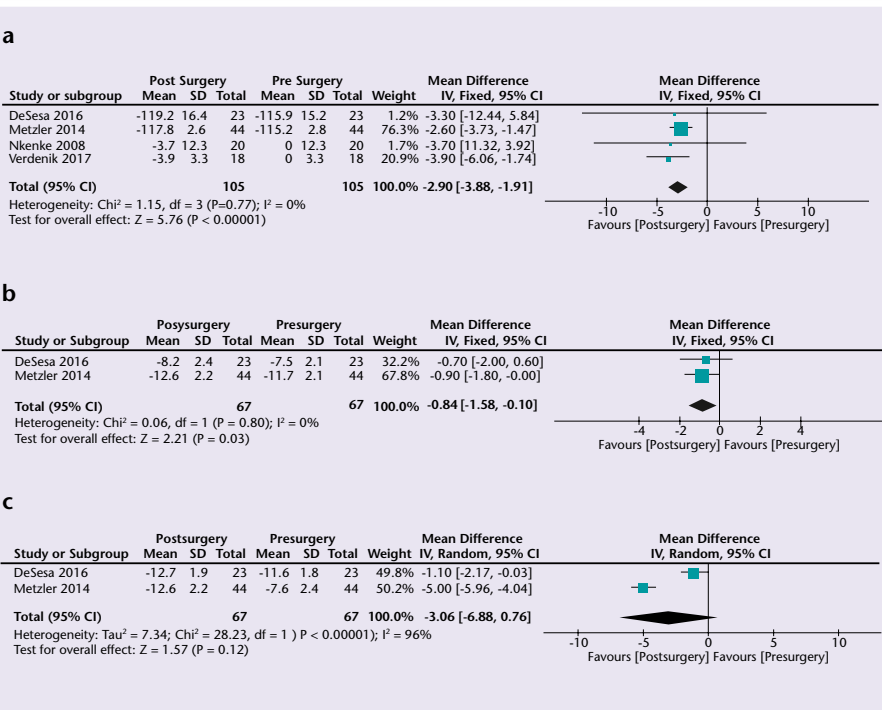


Fig. 4 Forest plot showing nose changes secondary to Le Fort I maxillary advancement. a) Nasal tip projection. b) Nasal tip prominence. c) Subnasal projection



(95% CI, -2.62–1.07, $P = 0.41$, $I^2 = 63\%$) and this was not statistically significant (Fig. 3b). On the other hand, the pooled outcomes of two of the included studies^{26,27} showed that osteotomy resulted in forward advancement of the subnasal region, which was statistically significant (mean difference [MD]; 1.7 mm, 95% CI, 0.9–2.5, $P = 0.0001$, $I^2 = 0\%$) (Fig. 3c).

Lip changes

The pooled estimate of all included studies showed that maxillary advancement significantly increased upper lip projection (MD; 2.90 mm, 95% CI, 1.91–3.88, $P < 0.00001$, $I^2 = 0\%$; 105 participants) (Fig. 4a). Additionally, the data of two of the included studies^{26,27} showed that Le Fort I advancement osteotomy significantly widens the upper lip

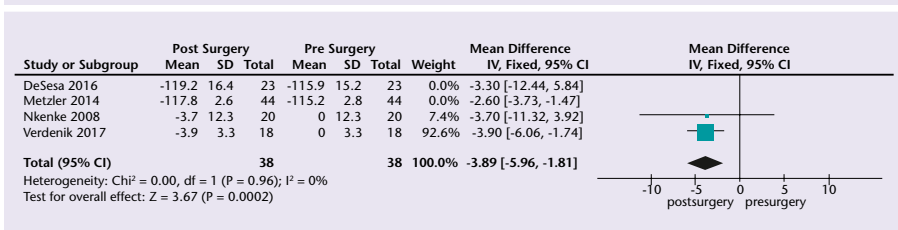
Table 5 Summary of findings clarifying the nasolabial change secondary to Le Fort I advancement and the certainty of the evidence

Pre-surgical compared to post-surgical for class III malocclusion*					
Patient or population			Class III malocclusion		
Intervention			Pre-surgical		
Comparison			Post-surgical		
Outcomes	Number of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Pre-surgical values	Changes
Upper lip changes follow-up: at least six months	(Four studies)	Very low**	-	The mean upper lip projection was 115.55 mm	MD 2.9 mm (CI 1.91–3.88)
	(Two studies)	Very low**	-	Upper lip philtrum width 10.4 mm	MD 0.84 mm (CI 0.10–1.58)
	(Two studies)	Very low**	-	Lower lip philtrum width 12.65 mm	MD 3.06 mm (CI 0.67–6.55)
Nose changes follow-up: at least six months	(Two studies)	Very low**	-	The mean nasal tip projection was 126.5 mm	MD 0.89 mm (CI 2.44–4.22)
	(Two studies)	Very low**	-	The mean nasal tip prominence was 29.25 mm	MD -0.77 mm (CI -2.62 –-1.07)
	(Two studies)	Very low**	-	The mean subnasal projection was 115.6 mm	MD 1.7 mm (CI 0.9–2.5)

Key:
 * = the risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% confidence interval).
 CI = 95% confidence interval; MD = mean difference of changes (post-surgical measurement-pre-surgical measurement); + = indicates forward movement; - = indicates backward movement
 ** = all studies received low scores indicating a high risk of bias

GRADE working group grades of evidence
 High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
 Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
 Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
 Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

Fig. 5 Sensitivity analysis of the upper lip projection outcome



philtrum (MD 0.84 mm, 95% CI, 0.10–1.58, P = 0.03, I² = 0%; 67 participants) (Fig. 4b). However, the effect of surgery on lower lip

philtrum width varied and it was statistically non-significant (MD; 3.06 mm, 95% CI, -0.67–6.55, P = 0.12, I² = 96%) (Fig. 4c).

Risk of bias across studies and additional analyses

The GRADE approach was used to assess the quality of the evidence for two outcomes. The quality of the evidence was very low due to the high risk of bias and the inherent limitations in the design of the included studies (Table 5). Sensitivity analysis, after excluding retrospective studies,^{26,27} showed a higher pooled estimate effect for the upper lip projection compared to the overall estimate effect (MD 3.89 mm, 95% CI, 1.81–5.96, P = 0.0002, I² = 0) (Fig. 5). This indicates adequate robustness of this outcome based on the remaining two prospective studies.^{28,29} The number of the included studies was not sufficient to perform publication bias.

Discussion

Single Le Fort I advancement surgery is likely to change the midfacial region, particularly the nasolabial region. Despite accurate hard tissue surgical planning, predicting the 3D nasolabial soft tissue changes can be difficult. The aim of this systematic review was to evaluate the current evidence regarding 3D nasolabial soft tissue changes that accompany Le Fort I maxillary advancement osteotomy in isolation from any other surgical procedures in class III malocclusion with maxillary retrognathia. This is of particular importance to orthodontists and maxillofacial surgeons.

Four studies met the inclusion criteria and their data were meta-analysed when possible. The mean maxillary advancement of the included studies was 5.58 mm. Meta-analysis demonstrated that advancing the maxilla has significant effects on the upper lip region, but mildly affected the nose region, while the effect on the lower lip region was negligible. Figure 2 represents a diagrammatic explanation of the soft tissue changes. Unsurprisingly, upper lip projection significantly increased post-surgically; hard tissue (maxilla) to soft tissue (HT:ST) changes in this region were approximately 2:1. Moreover, this review showed that the upper philtrum had mildly widened subsequent to maxillary advancement (HT:ST = 6:1). The changes in the upper lip projection and philtrum width could be due to the forward pressure of the dento-alveolar region on lip muscles secondary to maxillary advancement. These findings are similar to the findings of previous studies.^{30,31} Moreover, isolated Le Fort I osteotomy

SYSTEMATIC REVIEW

advancement significantly increased the subnasal projection (HT:ST = 3.2:1). These findings are close to the 2D outcomes of a previous qualitative systematic review.³ On the other hand, change in the lower philtrum width of the upper lip varies widely and was statistically non-significant; this is probably because the anatomy of this region is mainly dependent on free muscle with a high degree of adaptability.

It is generally agreed that Le Fort I osteotomy advancement affects the nasal region and widens the alar base width.^{31,32,33} One possible explanation is that the surgery involves elevation of the periosteum, muscles and ligaments that stabilise the alar region with the anterior surface of the maxilla.³⁰ However, our review showed that the effects of the surgery on flattening nasal prominence and nasal projection were mild and insignificant – HT:ST were 5.6:1 and 6.2:1, respectively. One of the possible explanations is the use of the nasal cinch suture and/or V-Y lip closure surgery in the included studies, which may have eased the effect of Le Fort I osteotomy advancement on nasal prominence and projection.^{3,26} Another explanation could be that the widening of the alar base as a result of maxillary advancement led the nasal tip to be restrained in the nasal complex.^{27,34} Furthermore, it is important to consider that the vertical changes and anticlockwise rotation of the occlusal plane as a consequence of jaw surgery may have a confounding influence on nasal prominence and projection.³⁵ It is crucial to consider clinical heterogeneity as a causative factor for these findings. Although two included studies^{26,27} were performed at the same institution with an interval of two years, the authors reported different results regarding the 3D changes of the nose. This may be due to differences in the demographics of the patients. Metzler *et al.*²⁷ recruited mainly young women (mean age was 16.7), while DeSesa *et al.*²⁶ collected their data from older participants with an equal gender distribution. A recent retrospective study,³⁶ using 2D cephalometric measurements of patients who underwent maxillary advancement, reported a significant decrease in nasal prominence and a non-significant increase in nasal projection that agreed to some extent with the 3D findings of our meta-analysis.

It is important to note that the best fit reference-based registration method used

for superimpositions and 3D measurement of data of the included studies in this review has not been considered as an accurate method of combining 3D images, and may have accounted for some error in measuring the changes.³⁷ Anthropometric landmark identification is a further source of bias when not repeated by different researchers over separate time periods to identify errors, particularly in the peri-labial region.³⁸

GRADE assessment showed that the evidence is of a very low certainty due to the high risk of bias and the inherent limitations in the design of the included studies. Therefore, the results should be interpreted with caution.

Strength and limitations

The registration of the a priori protocol, the non-restricted search, the strict inclusion criteria, and using validated risk of bias and GRADE approaches to assess the quality of the evidence are the strengths of the current systematic review. Moreover, confounding factors such as body mass index, facial expression during image capture, lip tonicity, fullness of soft tissue drape and presence of orthodontic appliances could influence soft tissue response;³⁹ hence, this review included studies with a minimum of six months' follow-up to minimise the confounders.

Although four studies that portrayed a fair quality of evidence were included, these studies demonstrated differences in patients' gender and age. The authors also acknowledge that the methods of image acquisition used in the included studies of this review were heterogeneous. These indicate some degree of heterogeneity among the included studies.

Recommendations

The authors disclose that there are inconsistencies in terms of study settings, study sample populations, the adopted surgical procedures and amount of surgical movement, as well as ethnicity, gender and soft tissue characteristics.

With the current advancement in technology and the growing number of orthognathic planning software, these findings would be beneficial for surgical prediction. Hence, the review highlights a need for better primary research directed towards more accurate methods of 3D facial surface acquisition, accounting for the whole

face in response to orthognathic surgical movements.

Conclusion

Low-level evidence concludes that the sagittal effect of isolated Le Fort I osteotomy on the nasolabial region is concentrated around the junction of the nose and upper lip, and the tip of the upper lip, but gradually diminishes in other regions. Post-surgical transverse nasolabial changes are negligible. Significant inconsistencies among the included studies were identified. Based on the quality of the available evidence presented in this study, long-term randomised controlled trials with standardised methods of 3D assessment are recommended to reach conclusive findings.

Conflict of interest

The authors declare that there is no conflict of interest.

Acknowledgements

The data underlying this article are available in the article and in its online supplementary material. No funding was received for this paper.

Author contributions

MA, HM, AU and JR designed the study and guided the protocol development. MA, HM and AU supervised this work. MA and SM performed the updated search of literature. JR and AU undertook study selection while MA was involved as a third reviewer in this process. JR and MA performed the data extraction while AU was involved as a third reviewer in this process. SM and MA judged the methodological quality while MW was involved as a third reviewer in this process. SM, AU, MA and MW analysed the data and worked on data interpretation. All authors carried out manuscript writing, refining the manuscript, and read and approved the final manuscript.

References

1. Proffit W R. *Contemporary orthodontics*. 5th ed. St Louis: Mosby, 2013.
2. Khamashta-Ledezma L, Naini F B. Systematic review of changes in maxillary incisor exposure and upper lip position with Le Fort I type osteotomies with or without cinch sutures and/or VY closures. *Int J Oral Maxillofac Surg* 2014; **43**: 46–61.
3. San Miguel Moragas J, Van Cauteren W, Mommaerts M Y. A systematic review on soft-to-hard tissue ratios in orthognathic surgery part I: maxillary repositioning osteotomy. *J Craniomaxillofac Surg* 2014; **42**: 1341–1351.
4. Ubaya T, Sherriff A, Ayoub A, Khambay B. Soft tissue morphology of the naso-maxillary complex following surgical correction of maxillary hypoplasia. *Int J Oral Maxillofac Surg* 2012; **41**: 727–732.
5. Wong K W F, Keeling A, Achal K, Khambay B. Using three-dimensional average facial meshes to

- determine nasolabial soft tissue deformity in adult UCLP patients. *Surgeon* 2019; **17**: 19–27.
6. Sarver D M, Johnston M W, Matukas V J. Video imaging for planning and counseling in orthognathic surgery. *J Oral Maxillofac Surg* 1988; **46**: 939–945.
 7. Van Loon B, Van Heerbeek N, Bierenbroodspot F et al. Three-dimensional changes in nose and upper lip volume after orthognathic surgery. *Int J Oral Maxillofac Surg* 2015; **44**: 83–89.
 8. Djordjevic J, Toma A M, Zhurov A I, Richmond S. Three-dimensional quantification of facial symmetry in adolescents using laser surface scanning. *Eur J Orthod* 2014; **36**: 125–132.
 9. Lagravère M O, Low C, Flores-Mir C et al. Intraexaminer and interexaminer reliabilities of landmark identification on digitized lateral cephalograms and formatted 3-dimensional cone-beam computerized tomography images. *Am J Orthod Dentofacial Orthop* 2010; **137**: 598–604.
 10. Almkhtar A, Ju X, Khambay B, McDonald J, Ayoub A. Comparison of the accuracy of voxel based registration and surface based registration for 3D assessment of surgical change following orthognathic surgery. *PLoS One* 2014; DOI: 10.1371/journal.pone.0093402.
 11. Nada R M, Maal T J, Breuning K H, Berge S J, Mostafa Y A, Kuijpers-Jagtman A M. Accuracy and reproducibility of voxel based superimposition of cone beam computed tomography models on the anterior cranial base and the zygomatic arches. *PLoS One* 2011; DOI: 10.1371/journal.pone.0016520.
 12. Olate S, Zaror C, Mommaerts M Y. A systematic review of soft-to-hard tissue ratios in orthognathic surgery. Part IV: 3D analysis – Is there evidence? *J Craniomaxillofac Surg* 2017; **45**: 1278–1286.
 13. Shafi M, Ayoub A, Ju X, Khambay B. The accuracy of three-dimensional prediction planning for the surgical correction of facial deformities using Maxilim. *Int J Oral Maxillofac Surg* 2013; **42**: 801–806.
 14. Ullah R. *The validity of 3dMD Vultus in predicting soft tissue morphology following orthognathic surgery*. Birmingham: University of Birmingham, 2014. Thesis.
 15. Resnick C, Dang R, Glick S, Padwa B. Accuracy of three-dimensional soft tissue prediction for Le Fort I osteotomy using Dolphin 3D software: a pilot study. *Int J Oral Maxillofac Surg* 2017; **46**: 289–295.
 16. Knoop P G M, Borghi A, Breakey R W F et al. Three-dimensional soft tissue prediction in orthognathic surgery: a clinical comparison of Dolphin, ProPlan CMF, and probabilistic finite element modelling. *Int J Oral Maxillofac Surg* 2019; **48**: 511–518.
 17. Paredes de Sousa Gil A, Guijarro-Martínez R, Haas Jr O L, Hernández-Alfaro F. Three-dimensional analysis of nasolabial soft tissue changes after Le Fort I osteotomy: a systematic review of the literature. *Int J Oral Maxillofac Surg* 2019; **48**: 1185–1200.
 18. Shamseer L, Moher D, Clarke M et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015; DOI: 10.1136/bmj.g7647.
 19. Bernardo W M. PRISMA statement and PROSPERO. *Int Braz J Urol* 2017; **43**: 383–384.
 20. Cumpston M, Li T, Page M J et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database Syst Rev* 2019; DOI: 10.1002/14651858.ED000142.
 21. Moher D, Shamseer L, Clarke M et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015; **4**: 1.
 22. Lisboa C O, Martins M M, Ruellas A C O, Ferreira D M T P, Maia L C, Mattos C T. Soft tissue assessment before and after mandibular advancement or setback surgery using three-dimensional images: systematic review and meta-analysis. *Int J Oral Maxillofac Surg* 2018; **47**: 1389–1397.
 23. Schmidt L, Shokraneh F, Steinhausen K, Adams C E. Introducing RAPTOR: RevMan Parsing Tool for Reviewers. *Syst Rev* 2019; **8**: 151.
 24. Guyatt G H, Oxman A D, Schunemann H J, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. *J Clin Epidemiol* 2011; **64**: 380–382.
 25. Egger M, Smith G D, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; DOI: 10.1136/bmj.315.7109.629.
 26. DeSesa C R, Metzler P, Sawh-Martinez R, Steinbacher D M. Three-dimensional Nasolabial Morphologic Alterations Following Le Fort I. *Plast Reconstr Surg Glob Open* 2016; DOI: 10.1097/GOX.0000000000000685.
 27. Metzler P, Geiger E J, Chang C C, Sirisoontorn I, Steinbacher D M. Assessment of three-dimensional nasolabial response to Le Fort I advancement. *J Plast Reconstr Aesthet Surg* 2014; **67**: 756–763.
 28. Nkenke E, Vairaktaris E, Kramer M et al. Three-dimensional analysis of changes of the malar-midfacial region after LeFort I osteotomy and maxillary advancement. *Oral Maxillofac Surg* 2008; **12**: 5–12.
 29. Verdenik M, Ihan Hren N. Three-dimensional facial changes correlated with sagittal jaw movements in patients with class III skeletal deformities. *Br J Oral Maxillofac Surg* 2017; **55**: 517–523.
 30. Schendel S A, Williamson L W. Muscle reorientation following superior repositioning of the maxilla. *J Oral Maxillofac Surg* 1983; **41**: 235–240.
 31. Yamada T, Mishima K, Moritani N et al. Nasolabial morphologic changes after a Le Fort I osteotomy: a three-dimensional anthropometric study. *J Craniofac Surg* 2010; **21**: 1089–1095.
 32. Khamashta-Ledezma L, Naini F B, Manisali M. Review of nasal changes with maxillary orthognathic surgery. *J Istanbul Univ Fac Dent* 2017; DOI: 10.17096/jiufd.09789.
 33. Mitchell C, Oeltjen J, Panthaki Z, Thaller S R. Nasolabial aesthetics. *J Craniofac Surg* 2007; **18**: 756–765.
 34. Sheen J H. Secondary rhinoplasty. *Plast Reconstr Surg* 1975; **56**: 137–145.
 35. Silva A, Magri L V, Osborne P R, Trivelatto A E, Sverzut C E, Silva M. Three-Dimensional Nasal Alterations in Le Fort I Advancement: Linear Measurements, Angles, Nasal Indices, and Volume Differences. *J Craniofac Surg* 2019; **30**: 1125–1130.
 36. Akan B, Gökçe G, Karadede Ünal B, Sezen Erhamza T. Assessment of soft tissue changes after LeFort I advancement. *Eur Arch Otorhinolaryngol* 2021; **278**: 813–839.
 37. Maal T J J, van Loon B, Plooi J M et al. Registration of 3-Dimensional Facial Photographs for Clinical Use. *J Oral Maxillofac Surg* 2010; **68**: 2391–2401.
 38. Aynechi N, Larson B E, Leon-Salazar V, Beiraghi S. Accuracy and precision of a 3D anthropometric facial analysis with and without landmark labelling before image acquisition. *Angle Orthod* 2011; **81**: 245.
 39. van der Vlis M, Dentino K M, Vervloet B, Padwa B L. Postoperative swelling after orthognathic surgery: a prospective volumetric analysis. *J Oral Maxillofac Surg* 2014; **72**: 2241–2247.