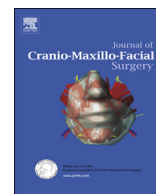




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Review

Three-dimensional evaluation of soft-tissue response to osseous movement after orthognathic surgery in patients with facial asymmetry: A systematic review

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ABSTRACT

To systematically assess the current literature on soft-tissue response associated with osseous movement following orthognathic surgery in patients with facial asymmetry.

Six electronic databases (PubMed, EMBASE (via Ovid), Medline (via Ovid), Cochrane Library, Scopus, and Web of Science) and gray literature were searched for studies evaluating hard- and soft-tissue responses three-dimensionally after orthognathic surgery, using MeSH terms and keywords. The methodological quality and level of evidence of the included studies were analyzed using *EPHPP* and *GRADE*, respectively.

The primary search yielded 125 articles, and 10 articles that satisfied the predefined inclusion criteria were finally included. All the included articles evaluated soft-tissue response, with six of them additionally investigating the magnitude of this response. Soft tissues move with hard tissues horizontally and anteroposteriorly; however, soft-tissue movement is less than hard tissue movement. In addition, soft tissue movement is more pronounced in the lower central facial region. Six articles were judged as having 'strong' methodological quality, while the evidence was found to be of 'low' quality for the soft-tissue response and the magnitude of this response.

Despite a low level of evidence, the review substantiates a favorable three-dimensional soft-tissue response following osseous surgery. The soft-tissue response is more pronounced horizontally, anteroposteriorly, and in the lower central facial region. Nevertheless, well-designed prospective studies with a higher level of evidence are needed.

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1. Introduction

Asymmetry of the face is a relatively common phenomenon in patients with dentofacial deformities, with a prevalence of 34–38.6% (Severt et al., 1997; Chew, 2006). Although facial asymmetry is often subclinical (Plooij et al., 2009), significant asymmetry can cause not only functional but also esthetic problems. Traditionally, two-dimensional (2D) methods, such as cephalograms (Grummons et al., 1987) and panoramic views (Van Elslande et al., 2008) have been used for evaluating facial asymmetry. However, owing to their inherent limitations, such as lack of

information about complex asymmetry, their usefulness has been limited (Gateno et al., 2011). Currently, non-invasive three-dimensional (3D) techniques, such as 3D CT (computed tomography), 3D CBCT (cone-beam computed tomography), laser surface scanning, and stereophotogrammetry, are more favored for analyzing facial asymmetry (Kau et al., 2007; Tzou et al., 2011; Christou et al., 2013) because they facilitate the 3D representation and measurement of complex facial morphology (You et al., 2010).

The primary goals of orthognathic surgery include the correction of discrepancies in the maxilla–mandibular relationship (Jeon et al., 2020) as well as improvement of facial esthetics (Gabardo et al., 2019), using osteotomies and optimized placement of bony segments in positions that facilitate optimal function (Panula et al., 2000). However, these objectives may not always be achievable since the esthetic outcomes depend on underlying skeletal

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movement. Therefore, a thorough understanding of the association between osseous movements and corresponding soft-tissue responses is imperative for predicting postoperative esthetic outcomes. Although soft tissues tend to move with hard tissue and adapt accordingly, the correlation between hard- and soft-tissue movements is not well defined (Almeida et al., 2011). This is overlooked in treatment planning (Jung et al., 2009; Almeida et al., 2011) for patients with facial asymmetry, thereby affecting the postsurgical outcomes. Previously published systematic reviews have investigated the relationship between soft- and hard-tissue changes following maxillary and mandibular repositioning surgeries in patients with skeletal malocclusion (Joss et al., 2010; San Miguel Moragas et al., 2014; Olate et al., 2016; Lisboa et al., 2018). However, no study has systematically reviewed the effect of hard-tissue movement on soft tissues after orthognathic surgery in patients with facial asymmetry. Therefore, this systematic review aimed to investigate the soft-tissue response to the underlying osseous movement following orthognathic surgery in patients with facial asymmetry.

2. Materials and methods

2.1. Protocol and registration

The methodology of the protocol was devised beforehand, and it adhered strictly to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Liberati et al., 2009). After a full consensus among the authors, the review protocol was registered in the PROSPERO database (registration number: CRD4202021190; https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD4202021190).

2.2. Eligibility criteria

The inclusion criteria for the studies were based on a focused question defined in the Population-Intervention-Control-Outcome (PICO) format, as follows: ‘What is the effect of hard-tissue changes on the soft tissues after orthognathic surgery in patients with facial asymmetry?’ Those studies that addressed this question were deemed eligible. The PICO elements are listed in Table 1. Studies with an appropriate analytical design that analyzed orthognathic surgery outcomes three-dimensionally in patients with facial asymmetry, and evaluated the correlation between hard- and soft-tissue changes after orthognathic surgery, were included in this review. The studies were excluded if they did not involve facial asymmetry subjects or focused on 2D analysis of orthognathic surgery outcomes. No articles were excluded based on publication status or publication year; however, review articles,

meta-analyses, letters to editors, commentaries, conference papers, animal studies, and studies on nonhuman models were excluded. Studies with unavailable full texts or those published in a language other than English were also excluded from the review.

2.3. Information sources and literature search

A comprehensive search was performed systematically and independently by two authors (DA and PS) until September 2020, using the following electronic databases: PubMed, EMBASE (via Ovid), Medline (via Ovid), Cochrane Library, Scopus, and Web of Science. For each database search, a combination of Medical Subject Headings (MeSH) terms was used for keywords (Table 1). In addition, syntax and vocabulary were adjusted across databases. No restrictions based on publication date or publication status were imposed on the literature search. Manual searching of key scientific journals and reference lists from potentially relevant reviews and retrieved articles was also performed. Furthermore, the OpenGrey database (<http://www.opengrey.eu/>) was searched for unpublished data.

2.4. Study selection

A reference manager software, Endnote™, version X9 (Clarivate Analytics, Philadelphia, USA), was used for the collation and management of potentially eligible records and bibliographic citations obtained from the literature search. After the removal of duplicates, the titles and abstracts of all the potential articles were screened independently by two authors (DA and PS) in an organized manner to ascertain their eligibility based on the predefined inclusion/exclusion criteria. At this stage, any disagreement over inclusion was resolved by mutual discussion. Next, the articles that fulfilled the inclusion criteria were retrieved, and their full texts were reviewed. Cohen's kappa statistic (κ) was calculated to deduce the level of inter-reviewer agreement. When disagreements over the final inclusion were inevitable, suitability was verified independently by the third author (GM), thus leading to a consensus.

2.5. Data extraction and outcomes of interest

Two reviewers (DA and PS) independently extracted the data and characteristics of the included studies using a predefined and standardized data format. The following data were extracted from the full-text articles:

1. Demographic data (age, sex, ethnicity, sample size, and type of skeletal discrepancy)

Table 1

Description of the PICO (P = population; I = intervention; C = comparator/control; O = outcomes) elements used in structuring the research question and the search strategy.

Criteria	Specification
Focus question	‘What is the effect of hard-tissue changes on the soft tissues after orthognathic surgery in patients with facial asymmetry?’
Population	Patients diagnosed with clinically apparent facial asymmetry and who underwent orthognathic surgery for asymmetry correction.
Intervention	Orthognathic surgery (single-jaw or two-jaw surgery) alone or with adjunctive surgeries, such as genioplasty, chin contouring, or mandibular body contouring.
Comparator/control	Standard orthognathic treatment or no-intervention control; presurgery or postsurgery; different imaging modalities, such as 3D facial laser scan or 3D CT images or 3D CBCT scans or 3DFM (three-dimensional facial morphometry).
Outcomes	a) Response of the soft tissues following hard-tissue surgery b) Magnitude of soft-tissue changes following hard-tissue surgery.
Search strategy	Search ((((((facial asymmetry) OR asymmetrical face) OR asymmetric face) OR facial asymmetry[MeSH Terms])) AND (((((orthognathic surgery) OR bimaxillary surgery) OR two-jaw surgery) OR maxillofacial surgery) OR maxillomandibular surgery) OR orthognathic surgery[MeSH Terms])) AND ((((((hard tissue) OR bone tissue) OR osseous tissue) OR hard tissue[MeSH Terms])) AND (((soft tissue) OR skin tissue) OR soft tissue[MeSH Terms])) AND ((((((3D) OR 3-D) OR 3-dimensional) OR three dimensional) OR three-dimensional) OR 3 d imaging, computer generated[MeSH Terms]) OR three dimensional imaging, computer generated[MeSH Terms]))

2. Characteristics of the study (study design, method of 3D analysis, comparison groups, asymmetry criteria, software used, landmark type, and landmark digitization)
3. Features of surgery (single jaw/two jaw surgery, surgery type, and follow-up period)
4. Features of the analysis (measurement type, measurements/landmarks compared, and residual asymmetry)

The primary outcomes of interest were: (a) the response of the soft tissues following hard-tissue surgery; and (b) the magnitude of soft-tissue changes following hard tissue surgery.

2.6. Quality analysis

The Effective Public Health Practice Project (EPHPP) (Thomas et al., 2004) was used to assess the methodological quality of each study. This instrument evaluates the risks and quality across six domains: selection bias, study design, confounders, blinding, data-collection methods, and withdrawals and dropouts. The EPHPP is recommended for assessing the quality of public health interventions and studies with varying experimental designs (Jackson et al., 2005). In addition, better interrater reliability has been reported with EPHPP than with the Cochrane Collaboration Risk of Bias Tool (Armijo-Olivo et al., 2012). Based on the information provided by each study, the six methodological components were classified as weak (w), moderate (+), or strong (++). An overall grading of 'weak' was assigned if there were two or more weak ratings; 'moderate' was assigned for one weak rating, and 'strong' was assigned if there were no weak ratings.

2.7. Level of evidence

The level of evidence on the response of the soft tissues following hard-tissue surgery and the magnitude of soft-tissue changes following hard-tissue surgery was determined using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach (Ryan, 2016). The certainty of the evidence was categorized as very low, low, moderate, or high. The ratings were downgraded if serious or very serious concerns were raised relating to the risk of bias, inconsistency, imprecision, indirectness, or publication bias.

3. Results

3.1. Study selection

A PRISMA flow diagram showing the various stages of the study selection process is presented in Fig. 1. The primary search retrieved 125 articles from five databases and other sources. After excluding 33 duplicates, the titles and abstracts of 92 were screened. Subsequently, 42 articles were found to be potentially eligible for full-text reading. Out of these potentially eligible articles, 32 were excluded because they assessed either soft tissues or hard tissues, assessed soft and hard tissues separately (not compared), included dental landmarks and not skeletal landmarks, performed the study on normal subjects (non-asymmetric patients), or orthognathic surgery was not performed. Finally, 10 articles were considered to be suitable for qualitative synthesis because they fulfilled the pre-defined inclusion criteria mentioned in our protocol. The Cohen's κ -value for the study selection was 0.88, suggesting excellent inter-reviewer agreement.

3.2. Study characteristics

The characteristics of the studies included in this review are presented in Tables 2 and 3. Out of the selected 10 studies, six were prospective in nature (Kobayashi et al., 1990; Ferrario et al., 1999; Jung et al., 2009; Hwang et al., 2012; Suzuki-Okamura et al., 2015; Kim et al., 2018), and included a total of 94 patients; four studies were retrospective (Landes et al., 2002; Lee et al., 2013; Jeon et al., 2017; Lo et al., 2018) and included 198 subjects. The age range for the included studies was 16–38 years. The ethnic background of the treated subjects in eight of the ten studies was Asian (Kobayashi et al., 1990; Jung et al., 2009; Hwang et al., 2012; Lee et al., 2013; Suzuki-Okamura et al., 2015; Jeon et al., 2017; Kim et al., 2018; Lo et al., 2018); the other two studies involved Italian (Ferrario et al., 1999) and Caucasian (Landes et al., 2002) subjects. The preoperative diagnosis in nine of the studies was Class III skeletal discrepancy with facial asymmetry (Kobayashi et al., 1990; Ferrario et al., 1999; Landes et al., 2002; Jung et al., 2009; Hwang et al., 2012; Lee et al., 2013; Suzuki-Okamura et al., 2015; Jeon et al., 2017; Lo et al., 2018); one study recruited patients with facial asymmetry (without Sturge-Webber Syndrome, SWS) but failed to report the type of skeletal discrepancy (Kim et al., 2018).

Regarding the surgical methods, bimaxillary orthognathic surgery using Le Fort I, combined with unilateral or bilateral sagittal split osteotomy (SSO) or sagittal split ramus osteotomy (SSRO), was performed in six studies (Ferrario et al., 1999; Landes et al., 2002; Hwang et al., 2012; Suzuki-Okamura et al., 2015; Kim et al., 2018; Lo et al., 2018). Adjunctive surgery, such as genioplasty, was also performed along with bimaxillary orthognathic surgery in three studies (Landes et al., 2002; Kim et al., 2018; Lo et al., 2018). Four studies described single-jaw surgery (Kobayashi et al., 1990; Jung et al., 2009; Lee et al., 2013; Jeon et al., 2017) using unilateral or bilateral SSO, SSRO, or bilateral mandibular body osteotomy (BMBO). The minimum follow-up duration was 1 month and the maximum was 45 months. A menton (Me) deviation of ≥ 4 mm was considered as the criterion for asymmetry in three studies (Jung et al., 2009; Suzuki-Okamura et al., 2015; Jeon et al., 2017), whereas one study considered a chin deviation of >6 mm as asymmetric (Lee et al., 2013). In addition, an occlusal cant of ≥ 3 mm (Hwang et al., 2012) and an absolute difference of ≥ 2 mm (Lo et al., 2018) in the distance between the first upper molars perpendicular to the FH (Frankfurt horizontal) plane on each side were regarded as asymmetric in the respective studies. Four studies failed to define the asymmetry criteria (Ferrario et al., 1999; Kobayashi et al., 1990; Landes et al., 2002; Kim et al., 2018), although one of these (Ferrario et al., 1999) did mention that the patients were moderately to severely asymmetric.

3.3. Study quality assessment

The evaluation of methodological quality and risk of bias is illustrated in Fig. 2. All the studies were highly representative of the target population and judged to be 'strong' for the domain of selection bias. In terms of the analytical design of the studies, seven studies (Kobayashi et al., 1990; Ferrario et al., 1999; Jung et al., 2009; Hwang et al., 2012; Suzuki-Okamura et al., 2015; Jeon et al., 2017; Kim et al., 2018) were judged as moderate, whereas three studies (Landes et al., 2002; Lee et al., 2013; Lo et al., 2018) received a weak grading. Of the seven studies with a 'moderate' grading, one was a retrospective case-control study (Jeon et al., 2017). For the confounder domain, only two studies controlled for at least 80% of the confounders (age, sex, surgeon, surgery type, inclusion criteria, and observer) and were rated as 'strong' (Lee et al., 2013; Jeon et al., 2017). Likewise, five studies that controlled for 60–79% of the confounders were rated as moderate



PRISMA 2009 Flow Diagram

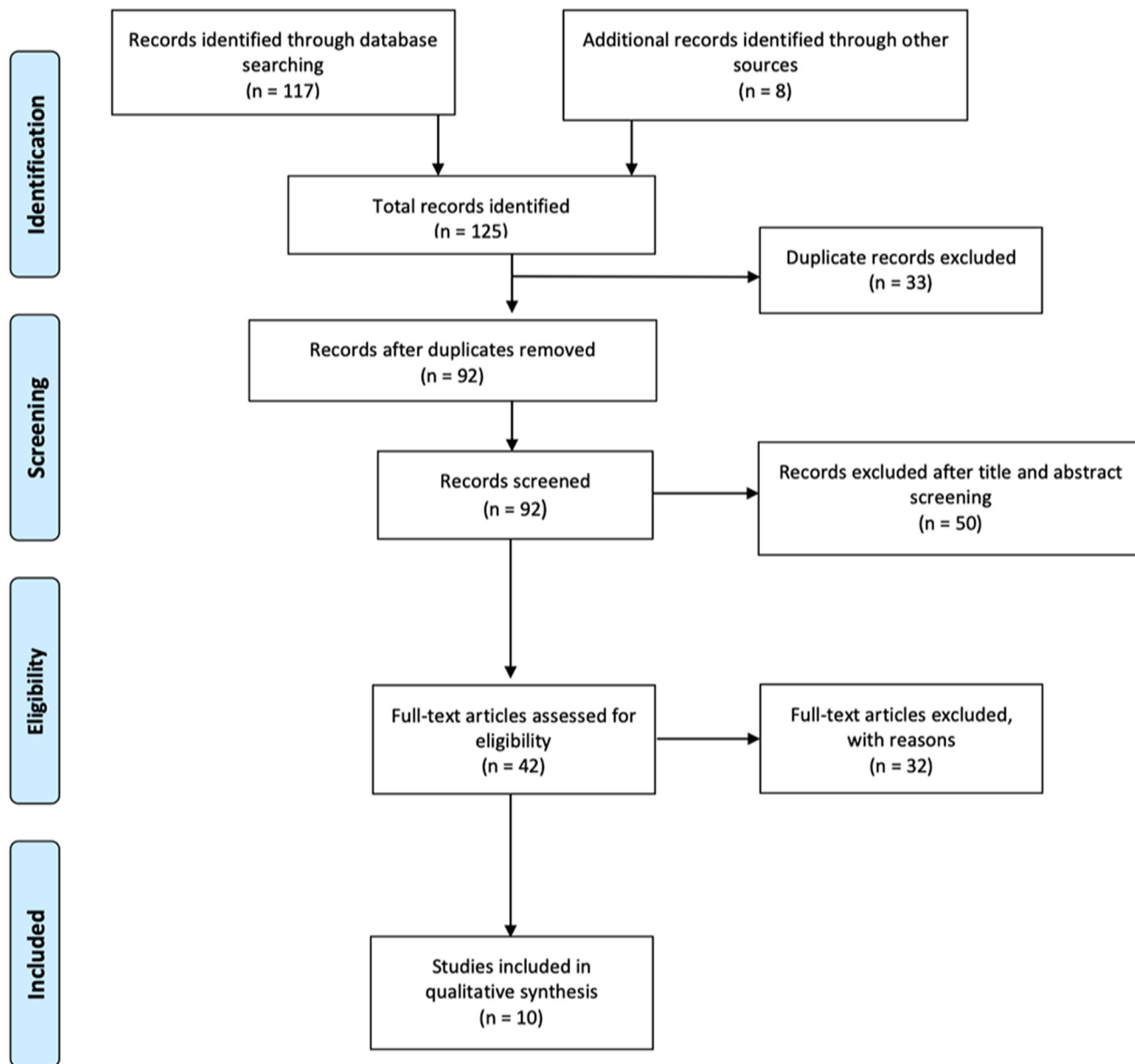


Fig. 1. PRISMA flow diagram illustrating the study selection process.

(Ferrario et al., 1999; Jung et al., 2009; Hwang et al., 2012; Suzuki-Okamura et al., 2015; Kim et al., 2018), and three studies that failed to control for confounders were rated as weak (Kobayashi et al., 1990; Landes et al., 2002; Lo et al., 2018). Regarding blinding, none of the studies explicitly reported blinding of patients, operators, or assessors. Therefore, blinding was rated as not applicable (X). Data collection methods were found to be valid and/or reliable; therefore, the studies were ranked as either ‘strong’ (Landes et al., 2002; Hwang et al., 2012; Lee et al., 2013; Suzuki-Okamura et al., 2015; Jeon et al., 2017) or ‘moderate’ (Kobayashi et al., 1990; Ferrario et al., 1999; Jung et al., 2009; Kim et al., 2018; Lo et al.,

2018). None of the studies reported any withdrawals or dropouts, and were thus ranked as ‘strong’ in this domain. Finally, each study was evaluated on overall quality according to its total score, based on its individual ratings for the respective domains. Of the ten studies reviewed, six were rated ‘strong’ for quality (Ferrario et al., 1999; Jung et al., 2009; Hwang et al., 2012; Suzuki-Okamura et al., 2015; Jeon et al., 2017; Kim et al., 2018), two were deemed ‘moderate’ in quality (Kobayashi et al., 1990; Lee et al., 2013) and two were rated as ‘weak’ (Landes et al., 2002; Lo et al., 2018).

Table 2
Demographic characteristics of the included studies.

Author (year) ^a	Study design	Sample size	Sex (M/F)	Mean age/age range (years)	Ethnicity	Skeletal discrepancy	Single jaw/two jaw surgery	Surgery type	Follow-up (months)	Asymmetry criteria
<i>Kobayashi (1990)</i>	Prospective	28	9/19	16–33 M: 24.10 F: 19.3	Asian	Class III	Single jaw	BSSO BMBO	6	n/r
<i>Ferrario (1999)^b</i>	Prospective	5	2/3	21–28	Italian	Class III	Bimax OS	Le Fort I SSO	12	Moderately to severely asymmetric
<i>Landes (2002)^b</i>	Retrospective	100		n/r	Caucasian		Bimax OS	Le Fort I BSSO Genioplasty	1	n/r
<i>Jung (2009)</i>	Prospective	17	8/9	AG: 23.8 ± 4.7 SG: 22.1 ± 3.4	Asian	Class III	Single jaw	BSSO	6	Me > 4 mm
<i>Hwang (2012)^b</i>	Prospective	25	12/13	22.3 ± 2.8/18–27 M: 23.3 ± 1.8 F: 21.3 ± 2.7	Asian	Class III	Bimax OS	Le Fort I SSRO	7.9 ± 1.1	Occlusal cant ≥ 3 mm
<i>Lee (2013)^b</i>	Retrospective	20	10/10	20.2/18–25	Asian	Class III	Single jaw	BSSRO	6	Chin >6 mm
<i>Suzuki-Okamura (2015)</i>	Prospective	9	5/4	24.8	Asian	Class III	Bimax OS	Le Fort I SSRO	4	Me > 4 mm
<i>Jeon (2017)^b</i>	Retrospective	50		21.9 ± 3.3/17–38	Asian	Class III	Single jaw	BSSO	6	Me ≥ 4 mm
<i>Kim (2018)^b</i>	Prospective	10	1/9	26.4/18–36	Asian	Facial asymmetry (without SWS)	Bimax OS	Le Fort I BSSRO Genioplasty	15–45	n/r
<i>Lo (2018)</i>	Retrospective	28	16/8	24.0 ± 4.8/18–35	Asian	Class III	Bimax OS	Le Fort I BSSO Genioplasty	9	Absolute distance difference between both the first upper molars perpendicular to the FH plane on each side ≥ 2 mm

Abbreviations: bimax OS, bimaxillary orthognathic surgery; SSO, sagittal split osteotomy; BSSO, bilateral sagittal split osteotomy; BSSRO, bilateral sagittal split ramus osteotomy; BMBO, bilateral mandibular body osteotomy; n/r, not reported; AG, asymmetry group; SG, symmetry group; Me, menton; SWS, Sturge-Webber syndrome.

^a All the studies described the response of soft tissues following hard-tissue surgery.

^b Studies that evaluated the magnitude of soft-tissue response.

Table 3

Methodological characteristics of included studies.

Author (year) ^a	3D technique	3D reconstruction	Landmark digitization	Comparison	Measurements investigated	Comparison	Outcome	Residual asymmetry	Remarks/conclusion
<i>Kobayashi (1990)</i>	3D wire frame model	3D wire frame model displayed on CRT	Semi-automatic digitization	Pre vs post	Directional indices	Correlation between hard- and soft-tissue asymmetry	Hard tissue postsurgery ↓ Soft tissue postsurgery ↓	$r = 0.77$	Significant correlation was found between hard- and soft-tissue directional indices of asymmetry
<i>Ferrario (1999)^b</i>	3DFM	ELITE, BTS	Automatic digitization using ELITE software	Pre vs post	Angular	Hard-tissue vs soft-tissue parameters	A-N-B↑, sl-n-sn↑ N-A-Pg↑, n-sn-pg↑ (UI-UIA)–(LI-LIA)↑, (sn-ls)–(li-pg)↓ (S–N)–(Go–Me) ≠ (tm-n)–(go-pg) n-sn-pg↑ by 10° Soft-tissue response Horizontal dimension	Mandibular advancement > setback; 114% Setback genio plasty; 101% Maxillary advancement < setback; 84% Maxillary elongation > impaction; 94%	Hard-tissue and soft-tissue components interact with each other in a complex fashion, and surgery causes modifications in their reciprocal arrangement
<i>Landes (2002)^b</i>	3D anthro pometry using wire frame	Computer algorithm	Manual digitization using calipers	Pre vs post	Linear	Soft-tissue ratios in relation to surgical bone repositioning	Vertical dimension	Soft-tissue ratios following bone advancements in general were greater than after setbacks	
<i>Jung (2009)</i>	3D-CT	Rapidform 2006	Rapidform 2006	Symmetry vs asymmetry	Linear	Correlation between the mandibular hard- and soft-tissue landmarks		$R^2 = 0.42–0.70$, $p < 0.05$	Mandibular hard-tissue landmarks were significantly correlated with changes in corresponding soft-tissue landmarks in the horizontal and AP aspects
				Pre vs post	Angular	Horizontal aspect	Pog vs Pog' L2-dev vs LLP-dev Id vs LL LIC vs LL-stomion B vs B'		
						A–P aspect	LIC vs LL-stomion	$R^2 = 0.51–0.86$, $p < 0.05$	
						Me–Me'	Me vs Me L2-ctl vs LLP-ctl L2-dev vs LLP-dev Id vs LL B vs B' Pog vs Pog' AP ratio 0.56 Horizontal ratio 0.45 Vertical ratio 0.27		
<i>Hwang (2012)^b</i>	CBCT	OnDemand 3D	n/r	Pre vs post	Linear	LIC vs LL-stomion Difference between long side and short side	>2.5 mm average in the soft-tissue response		Soft tissue was changed in all areas after leveling LeFort I osteotomy and mandib

Author (Year) ^b	Modality	Software	Digitization	Comparison	Analysis	Findings	Soft-tissue changes	Correlation	Soft-tissue changes	Soft-tissue changes
Lee (2013) ^b	CBCT	OnDemand 3D	Automatic digitization	Pre vs post	Linear Radial	Correlation between hard- and soft-tissue changes	Hard-tissue contour > soft-tissue contour Id = 5.0–9.9 mm; Id' = 3.2–6.7 mm B = 6.7–9.2 mm; B' = 5.0–7.3 mm Pog = 8.3–9.6 mm; Pog' = 7.3–8.6 mm Soft-tissue contour positively correlated with the skeletal changes; $p < 0.05$ Soft-tissue thickness changes negatively correlated with hard-tissue changes; $p < 0.05$		Pog = 1.0 –1.6 mm; Pog' = 0.7–0.8 mm	bular setback SSRO Soft tissue responds favorably after skeletal surgery
Suzuki-Okamura (2015)	CT	3-D-Rugle	Manual digitization	Pre vs post	Angular	Correlation between hard and soft tissues	Upper jaw cant–nose cant; $p < 0.01$ Upper jaw cant–lip cant; $p < 0.01$ Lower jaw cant–Me'; $p < 0.01$ Me–Me'; $p < 0.01$			Roll rotation of the mandible had a positive correlation with Me'
Jeon (2017) ^b	CBCT	Simplant O&O	Cephalometric analysis tool	Case vs control	Linear	Correlation of degree of Me deviation and maxillary occlusal canting with peri-nasal soft-tissue asymmetry	subnasale, $r = 0.696$; $p < 0.01$ upper lip midline, $r = 0.847$; $p < 0.01$ lip cant, $r = 0.922$; $p < 0.01$ 6.4 ± 2.8 mm Me correction results in ...	subnasale, 0.6 mm; $p < 0.01$ upper cupid bow, 1.6 mm; $p < 0.01$ lower cupid bow, 1.5 mm; $p < 0.01$ lip line cant, 2.2 mm, 2.4°; $p < 0.01$	3 mm at Me 2.6 at chin'	The degree of Me deviation was highly correlated with degree of midline asymmetry in perioral soft-tissue landmarks Mandible deviation was associated with both lip cant and asymmetry of the perioral soft tissue
Kim (2018) ^b	3D stereo photogram metric camera	Vectra	Automatic digitization using Vectra software	Pre vs post	Linear	Soft-to-hard tissue ratio	[LC-OC]–[LO-OL] in non-SWS = 88.05% ± 10.44%; $p = 0.008$ [LC-Go']–[LO-AG] in non-SWS = 78.90% ± 47.56%; $p = 0.032$			Soft-to-hard tissue ratios after orthognathic surgery were significantly lower in SWS patients than in non-SWS patients Soft-tissue changes followed hard-tissue movements Mean ratios for the average soft-to-hard tissue movements in the facial regions varied Skin outline changes in critical regions could be reliably predicted from the underlying bone movements
Lo (2018)	CBCT	SimPlant Pro	Semi-automatic digitization	Pre vs post	Volumetric	Correlation between hard and soft tissues	Upper lip, $r \geq 0.8$; $R^2 = 0.786–0.857$ Upper vermilion, $r \geq 0.8$; $R^2 = 0.786–0.857$ Chin, $r \geq 0.8$; $R^2 = 0.786–0.857$			

Abbreviations: 3DFM, three-dimensional facial morphometry; 3D-CT, three-dimensional computed tomography; CBCT, cone beam computed tomography; SSRO, sagittal split ramus osteotomy; n/r, not reported; (') refers to soft-tissue landmark.

^a All the studies described response of soft tissues following hard-tissue surgery.

^b Studies that evaluated the magnitude of soft tissue response.

Table 4 shows the evidence profile for the soft-tissue response and the magnitude of soft-tissue response studied in this review. The evidence was of 'low' quality for both outcomes.

3.4. Response of the soft tissues following hard-tissue surgery

Four studies in this review evaluated soft tissue-to-hard tissue response using only linear measurements (Landes et al., 2002; Hwang et al., 2012; Jeon et al., 2017; Kim et al., 2018). Three studies used linear as well as angular measurements (Jung et al., 2009; Lee et al., 2013; Suzuki-Okamura et al., 2015). Three studies assessed angular (Ferrario et al., 1999), volumetric (Lo et al., 2018), or directional indices (Kobayashi et al., 1990) (including volumetric and area measurements), respectively. The soft tissues were found to follow their corresponding hard tissue movements (correlation coefficient, $r = 0.3$ to 0.922 ; $p < 0.01$) in all the studies but for two (Ferrario et al., 1999; Jung et al., 2009). The soft-tissue Me (menton) was not associated with the change in hard-tissue Me (0.56 for the AP ratio, 0.45 for the horizontal ratio, 0.27 for the vertical ratio), while the direction of LL–stomion (soft-tissue) movement was opposite from that of LIC (hard-tissue) movement (Jung et al., 2009). In addition, soft-tissue angular measurements (sn-ls)–(lip) decreased, with a corresponding increase in hard-tissue measurements (UI–UIA)–(LI–LIA) after surgery (Ferrario et al., 1999).

The results also showed that soft tissues responded more favorably to skeletal surgery in patients with facial asymmetry than in those with SWS (Kim et al., 2018). Interestingly, a greater response to advancement surgeries was observed compared with set-back surgeries (Landes et al., 2002). The soft-tissue movements were correlated with the hard-tissue movements not only in the horizontal and anteroposterior orientations (Jung et al., 2009), but also for mandibular roll rotations (Suzuki-Okamura et al., 2015). In addition, the soft tissues in the central facial regions showed a greater response to the underlying osseous movements than the soft tissues in the lateral regions (Lo et al., 2018).

3.5. Magnitude of soft-tissue changes following hard-tissue surgery

Regarding the magnitude of soft-tissue changes, one study reported that a transverse Me correction of 6.4 ± 2.8 mm can improve the subnasal, upper, and lower cupid bow deviations by 0.6 mm, 1.6 mm, and 1.5 mm (all $p < 0.01$), respectively, as well as the lip line cant by 2.2 mm or 2.4° ($p < 0.01$) (Jeon et al., 2017). Another study compared the differences between the long and short sides of the asymmetric face, and concluded that there was a statistically significant average difference of >2.5 mm in the soft-tissue response (Hwang et al., 2012). Two studies expressed the soft-to-hard tissue changes as percentages (Landes et al., 2002; Kim et al., 2018). Statistically significant changes of $88.05 \pm 10.44\%$ ($p = 0.008$) and $78.90 \pm 47.56\%$ ($p = 0.032$) were noticed in the oral commissure and soft-tissue gonion (Go) regions, respectively (Kim et al., 2018). Horizontally, soft-tissue responses of 114% after mandibular advancement, 101% after setback genioplasty, and 84% after maxillary advancement were reported. In addition, a vertical soft-tissue response of 94% following maxillary elongation was reported (Landes et al., 2002), while an anteroposterior change of approximately 10° in the n-sn-pg angle was demonstrated after orthognathic surgery (Ferrario et al., 1999). One study measured soft-tissue response in terms of the change in the soft-tissue contour; significant changes ($p < 0.05$) of 3.2–6.7 mm at the infra-dentale (Id), 5.0–7.3 mm at the B point (B), and 7.3–8.6 mm at the pogonion (Pog) were recorded, as compared with their corresponding hard-tissue contours, which decreased by 5.0–9.9 mm at the Id, 6.7–9.2 mm at the B, and 8.3–9.6 mm at the Pog following skeletal surgery (Lee et al., 2013).

4. Discussion

Orthognathic surgery is aimed at occlusal rehabilitation using osteotomies and the placement of osteotomized segments in a position that facilitates optimal function and facial esthetics. Despite this, surgical esthetic outcomes remain a major concern for patients, especially those with facial asymmetry. Although stable surgical outcomes for hard tissues can be successfully predicted after orthognathic surgery, soft-tissue response remains relatively unpredictable.

Our systematic review investigated the soft-tissue response and the magnitude of soft-tissue changes following orthognathic surgery in patients with facial asymmetry. Reliable predictions of soft-tissue response are paramount for improving treatment planning and patient–doctor communication. Previously published systematic reviews that investigated and predicted soft-tissue changes following mandibular setback surgery either included studies that utilized 2D techniques or involved non-asymmetric subjects. No systematic review evaluating soft-tissue changes and their magnitudes in patients with facial asymmetry, using only 3D techniques, was found. Since the facial soft tissues can change in all three dimensions following surgery, the assessments of their changes should ideally be performed using 3D analysis (McCance et al., 1992).

In our review, articles utilizing 3D techniques for the assessment of soft-tissue response in asymmetric patients were analyzed. Four of the included articles used CBCT, two studies used CT, and each of the other four studies used one of 3DFM (three-dimensional facial morphometry), a 3D stereophotogrammetric camera, 3D wire-frame models displayed on a CRT (cathode-ray tube), and 3D anthropometry using a wireframe. Various image processing software solutions were used in the included studies (Table 3). Soft-tissue and hard-tissue landmarks were manually or automatically digitized on 3D images/models (Table 3). The methods used for the evaluation of soft-tissue changes varied among the included studies. Five studies compared the preoperative and postoperative data (Kobayashi et al., 1990; Hwang et al., 2012; Suzuki-Okamura et al., 2015; Jeon et al., 2017; Kim et al., 2018) while the other five articles reported the superimposition of preoperative images over postoperative images (Ferrario et al., 1999; Landes et al., 2002; Jung et al., 2009; Lee et al., 2013; Lo et al., 2018).

4.1. Response of soft tissues following hard-tissue surgery

The studies included in this review used several methods for the identification of soft-tissue changes. Most of the included studies confirmed that soft tissues respond favorably to their corresponding hard-tissue movements following orthognathic surgery. Patients with asymmetric mandibles often present with deviations of the lip cant and perioral soft tissue in the same direction, suggesting the association between mandibular deviation with lip cant and perioral soft tissue changes. Because the orbicularis oris muscle encircles the mouth like a rubber band, its adaptive changes caused by transverse mandibular movements may influence the subnasal and perioral soft tissues because of their proximity to the course of the orbicularis oris (Yamashita et al., 2009; Matin et al., 2014). For the same reason, a subnasal asymmetry can be corrected by isolated mandibular orthognathic surgery alone without the need for maxillary osteotomy (Jeon et al., 2017), thus indicating a significantly positive soft-tissue response following orthognathic surgery. Another region-based study revealed that soft tissues in the central region of the face, such as the upper lip, upper vermilion, and chin, follow underlying hard-tissue movements more closely than soft tissues in the lateral and horizontal regions owing to limited

Author (year)	Selection bias	Design	Confounders	Blinding	Data collection methods	Withdrawals and dropouts	Total score
	Kobayashi (1990)	++	+	w	x	+	++
Ferrario (1999)	++	+	+	x	+	++	++
Landes (2002)	++	w	w	x	++	++	w
Jung (2009)	++	+	+	x	+	++	++
Hwang (2012)	++	+	+	x	++	++	++
Lee (2013)	++	w	++	x	++	++	+
Suzuki-Okamura (2015)	++	+	+	x	++	++	++
Jeon (2017)	++	+	++	x	++	++	++
Kim (2018)	++	+	+	x	+	++	++
Lo (2018)	++	w	w	x	+	++	w

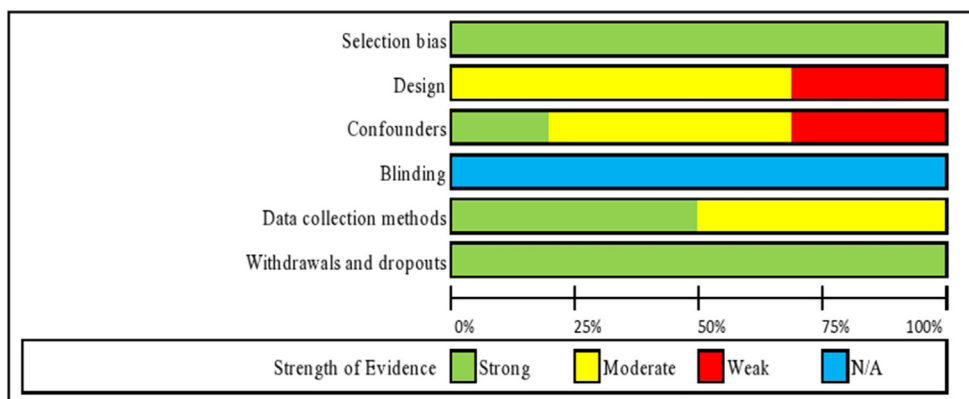


Fig. 2. The Effective Public Health Practice Project (EPHP) checklist criteria for the quality assessment of each study.

flexibility, less thickness, and firm adherence to the underlying bone (Lo et al., 2018).

Osseous movement caused by orthognathic surgery primarily influences the adjacent soft tissues (Landes et al., 2002), and the commercial planning software disposes of integrated ratios for approximate soft-tissue prediction. Therefore, Landes et al. (2002) emphasized the measurement of the soft-tissue response anthropometrically, without the use of any sophisticated technical approaches. The authors reported an average magnitude of soft-tissue response of 100–125%, which was consistent with those reported by previous studies (Ewing et al., 1992; McCance et al., 1997). Conversely, Ferrario et al. reported a complex association between soft tissues and hard tissues, and suggested that soft tissues may

not always respond to osseous movement (Ferrario et al., 1999), which was consistent with the findings of Jung et al. (2009). Likewise, a negative correlation was observed between soft-tissue thickness and hard-tissue contour following mandibular setback surgery in the study by Lee et al. (2013). Their findings suggested that soft-tissue thickness on the deviated side was less than that on the contralateral side, and that this soft-tissue thickness difference compensated for the soft-tissue contour asymmetry, resulting in an improvement in the thickness of the chin and mandibular soft tissue outline following mandibular setback surgery.

Table 4
Evidence profile for the outcomes studied.

Certainty assessment							Impact	Certainty	Importance
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
10	Observational studies	Not serious	Serious ^a	Not serious	Serious ^b	Strong association All plausible residual confounding would reduce the demonstrated effect	Following orthognathic surgery, soft tissues not only respond favorably to hard-tissue movement but also follow the hard-tissue movement	⊕⊕○○ LOW	CRITICAL
Magnitude of soft tissue changes following hard tissue surgery (follow up: 1 months; assessed with hard tissue changes)									
6	Observational studies	Not serious	Serious ^c	Not serious	Serious ^d	Strong association All plausible residual confounding would reduce the demonstrated effect	1. The magnitude of soft-tissue movement following orthognathic surgery is less compared with hard-tissue movement 2. Soft-tissue movement is greater in the lower facial central region compared with the lateral regions	⊕⊕○○ LOW	CRITICAL

Explanations.

^a Methodological heterogeneity may exist due to differences in the timing of follow-up, timing of postoperative imaging, landmark selection, ethnicity, or 3D imaging techniques.

^b Only one study mentioned the sample size calculation to detect the precise estimate of the effect.

^c Methodological heterogeneity may exist due to differences in the timing of follow-up, timing of postoperative imaging, landmark selection, or 3D imaging techniques.

^d None of the studies mentioned the sample size calculation to detect the precise estimate of the effect.

4.2. Magnitude of soft-tissue changes following hard-tissue surgery

In patients with facial asymmetry, hard-tissue asymmetry is hidden by soft tissues (Lee et al., 2013), thus masking the degree of asymmetry and compromising the precise assessment of true skeletal asymmetry. Therefore, preoperative facial soft-tissue analysis and the assessment of the magnitude of predicted soft-tissue response is necessary to meet the patients’ postoperative esthetic satisfaction. Only a handful of studies have evaluated the magnitude of soft-tissue response after orthognathic surgery in patients with facial asymmetry. Nevertheless, the relative magnitude of hard-tissue correction required for the desired soft-tissue movement, in terms of best esthetic outcome, has not been clearly defined in any of the included studies. In this regard, Jeon et al. reported that a 6.4 mm correction of hard-tissue menton may facilitate a soft-tissue movement of 0.6–2.2 mm in the central region of the lower face (Jeon et al., 2017). To some extent, this relative magnitude may serve as a guide for facial asymmetry correction.

Lee et al. observed that the magnitude of change was comparatively low in soft tissues, although the patterns of soft- and hard-tissue changes were similar (Lee et al., 2013). The magnitudes of hard-tissue changes ranged from 5 to 9.9 mm at the infradentale, point B, and pogonion; those of soft-tissue changes were 3.2–8.6 mm for the same landmarks. A similar response was observed in a study by Lo et al., in which soft-tissue movements after orthognathic surgery had lower magnitudes than hard-tissue movements. However, the authors also suggested that the magnitude of soft-tissue movement may vary according to the region (Lo et al., 2018). Soft tissues in the central and lower facial regions showed more movement than those in the lateral and upper facial regions. According to previous findings, soft-to-hard tissue ratios ranging from 60 to 100% are generally accepted by surgeons (San Miguel Moragas et al., 2014, 2015; Kim et al., 2018). The studies included in our review showed a soft-to-hard tissue ratio of 78.9–114% (Kim et al., 2018; Landes et al., 2002), which was consistent with findings in previous studies.

Although most of the hard-tissue and soft-tissue asymmetry can be corrected by orthognathic surgery, some degree of residual asymmetry may persist after surgery, and may require secondary

correction. In our review, only two of the included studies addressed residual asymmetry (Lee et al., 2013; Jeon et al., 2017). Jeon et al. reported a residual asymmetry of 3 mm at the hard-tissue menton and 2.6 mm at the center of the soft-tissue chin (Jeon et al., 2017). On the other hand, Lee et al. reported 1–1.6 mm of residual asymmetry at the hard-tissue pogonion and 0.7–0.8 mm at the soft-tissue pogonion (Lee et al., 2013). These results suggest the need for comprehensive preoperative assessment and precise prediction regarding the magnitude of soft-tissue response, in order to avoid secondary correction and achieve the best esthetic outcome from first surgery.

4.3. Future outlook and limitations

Despite a comprehensive assessment of the literature in our review, some limitations need to be addressed. Firstly, studies reporting controlled methodology were limited. A majority of the eligible studies were performed on Asian subjects. Therefore, the findings of the previous studies need to be compared with other populations. Also, the criteria for the assessment of facial asymmetry varied among the different studies, thereby suggesting a need for standardized assessment practice. Secondly, despite current advances in the field of diagnosis and prediction of orthognathic surgery outcomes (Jung et al., 2018; Knoops et al., 2018; Parappallil et al., 2018), our review included a limited number of recently published studies due to the stringent, pre-defined eligibility protocol. Finally, the quality of this review relied on prospective and retrospective studies, because no randomized clinical trials were found. Therefore, the findings of this review should be used with caution.

A medium-term follow-up generally allows postsurgical edema to subside, completion of the healing process, and any relapse to occur. Additionally, soft-tissue resilience varies with the facial landmarks, and this may influence the projection of soft tissues, depending upon the degree of osseous movement (Landes et al., 2002). From the perspective of improving surgical outcomes and facial esthetics in the future, individualized norms for asymmetric and non-asymmetric patients with regard to the magnitude of soft-tissue response would be helpful. Therefore, well-designed prospective studies, addressing region-based soft-tissue responses and

magnitudes, controlling for residual asymmetry during preoperative planning, and applying medium-term follow-up are required.

5. Conclusion

While the methodological variations and the inadequate number of studies limited the evaluation of soft-tissue response, this review highlighted the favorable response of soft tissues following osseous surgery. The following conclusions can be drawn from our analysis:

1. A meticulous 3D assessment of the soft tissue response, especially in the horizontal and anteroposterior directions, is essential for preoperative treatment planning.
2. The soft-tissue response following orthognathic surgery may not be the same in asymmetric and non-asymmetric subjects, and it may vary according to the type of surgery (set-back or advancement) and facial region.
3. In asymmetric patients, the soft-tissue response is more obvious following advancement surgeries. Moreover, correction of hard-tissue menton may facilitate a pronounced soft tissue movement in the lower central facial region.
4. Although the patterns of hard- and soft-tissue change following orthognathic surgery are similar, the magnitude of soft-tissue movement is less compared with that of hard tissue.

The findings presented in this review may help the surgeon to identify the degree and direction of hard- and soft-tissue relative movements required to achieve esthetic treatment goals.

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