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Review

Relapse-related factors of Le Fort I osteotomy in cleft lip and palate patients: A systematic review and meta-analysis

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ABSTRACT

A systematic review search was based on the PICOS approach, as follows: population: cleft lip and palate patients; intervention: Le Fort I osteotomy; comparator: different surgical protocols; outcome: stability, recurrence or surgical complications; study designs: only case reports were excluded from the review. No restrictions were placed on language or year of publication. Risk of bias was analyzed, heterogeneity was assessed, and subgroup analysis was performed using a level of significance of 1% ($p = 0.01$).

The search identified 248 citations, from which 29 studies were selected and a total of 797 patients enrolled. The level of agreement between the authors was considered excellent ($k = 0.810$ for study selection and $k = 0.941$ for study eligibility). Our results reported a mean maxillary advancement of 5.69 mm, a mean vertical downward/upward of 2.85/−2.02 mm and a mean clockwise rotation of 4.15°. Greater surgical relapse rates were reported for vertical downward movement (−1.13 mm, 39.6%), followed by clockwise rotation (−1.41°, 33.9%), sagittal (−0.99 mm, 17.4%) and vertical upward (0.11 mm, 5.4%) movements. No relevance was found regarding the type of cleft, the type of Le Fort I osteotomy, concomitant bone grafting, surgical overcorrection, postoperative rigid or elastic intermaxillary fixation, or retention splint.

Study limitations were heterogeneity and the low number of high-quality studies. In spite of reported high relapse rates, Le Fort I osteotomy for maxillary reposition is the first-choice procedure for selected cleft lip and palate patients in whom extensive maxillary movements are not required, because of its safety and its three-dimensional movement versatility in one-step surgery. Otherwise, distraction osteogenesis should be considered as the gold standard treatment.

1. Introduction

It is well documented that patients with a history of cleft lip and/or palate (CLP) exhibit varied degrees of maxillary hypoplasia (Good et al., 2007). Its cause is likely multifactorial, but mainly due to the inherent congenital condition and to the surgeries performed to the middle third of the facial skeleton and surrounding soft tissues (Geraedts et al., 2007; Latief et al., 2009; Shi and Losee, 2015; Tache and Mommaerts, 2020). The typical facial profile of a patient with CLP that may be addressed surgically in terms of orthognathic surgery (OS) involves three-dimensional deficiencies (sagittal, vertical and). Although patients with CLP deformities have essentially normal mandibular growth, the above-mentioned facial mid-third deficiency may produce abnormalities in mandibular growth direction. Therefore, there is commonly a tendency to present with an anterior open bite and a CCW rotation with steep mandibular plane angle, a decrease in posterior facial height, and an increase in anterior facial height, resulting in a prognathic facial appearance (Park et al., 2017).

The reported incidence of need for OS in patients with CLP varies from 14% to 75% depending on cleft severity, but it is generally quoted as approximately 25% of the unilateral cases and 65% of the complete bilateral cases (Rachmiel et al., 2012; Park et al., 2015), which in any case is higher than in the non-cleft population.

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Treatment of maxillary hypoplasia in patients with cleft lip and palate is challenging. On the one hand, handling a maxillary bone with eventual oro-nasal and palatal fistulae, residual lack of alveolar bone, velopharyngeal hypoplasia, and loss of teeth requires an oversight (Harjunpää et al., 2019; Alaluusua et al., 2019, 2020). On the other hand, CLP are more prone to surgical relapse than their non-cleft counterparts (40% versus 20% of sagittal relapse) (Figueroa et al., 2004; Saltaji et al., 2012), since CLP subjects present the following additional instability factors: 1) scarring envelope tissue (lip, gingiva and periosteum) that produces three-dimensional shrinkage; 2) a lack of strong and symmetric skeletal foundation at the level of the cleft alveolar ridge, even if an alveolar graft has been performed, and at the absent palatine suture in the midline that compromises transversal stability; 3) eventual presence of a pharyngeal flap that may pull the maxillary bone backward; and 4) poor dentition that may jeopardize occlusal balance. Several proposals have been suggested in the literature in order to prevent or to solve the above-mentioned relapse tendency: different surgical protocols, innovative surgical techniques with variations in the osteotomy design, surgical overcorrection, stronger fixation methods, and extra postoperative retention devices, among others.

Despite several decades of surgical experience with OS in CLP patients, the literature largely lacks meaningful analysis of the subject of surgical relapse: namely, its causes as well as proposals for its prevention. Although a data review of cleft maxillary osteotomy stability was published in 2012, that review did not assess the effect of different techniques or additional measures taken to improve stability (Saltaji et al., 2012). Additionally, since 2012, new data might have become available.

Therefore, as the published literature is extensive and heterogeneous, our team formulated the following research question: Could skeletal relapse be avoided or diminished after orthognathic surgery in CLP patients? Therefore, the objective of the present report was to systematically review and analyze skeletal relapse causative effects and preventive factors after maxillary surgical reposition in patients with CLP through a meta-analysis.

2. Materials and methods

A systematic review was performed following the standards of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (Liberati et al., 2009), obtaining records from a main database search and other sources (grey literature search and a manual search). As there was no human or animal intervention, no ethics approval was required for this research. The review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number 2018 CRD42018111851. After data extraction, a meta-analysis was performed to evaluate relapse causative effects and preventive factors.

2.1. Search strategy

The search of PubMed and Cochrane Library databases (Table 1) was based on the PICOS approach (Liberati et al., 2009) (population: cleft lip and palate patients; intervention: Le Fort I osteotomy; comparator: different surgical protocols; outcome: stability, recurrence or surgical complications; study designs: only case reports were excluded from the review). No restrictions were placed on language or year of publication, and Boolean operators ("OR" and "AND") were used for the combinations of thesaurus terms related to cleft lip and palate, Le Fort I osteotomy and stability, or surgical complications. Articles focused only on distraction osteogenesis (DO) were not included.

To retrieve studies published in journals not indexed by the major databases or identified with key words not included in MeSH or in the Emtree thesaurus, a grey literature search was designed. For this purpose, the Google Scholar database was searched using MeSH terms and the PICO strategy key words.

The references list of articles obtained on the previous searches were reviewed, and additional relevant papers were hand-searched.

2.2. Records identification, screening and study eligibility

After completion of the systematic database searches, studies were selected independently by two authors (LF and AVO). Through an analysis of titles and abstracts, studies were assessed against the study eligibility criteria (Table 2). Any articles not fulfilling the criteria were excluded. In the case of disagreement between authors, the study was selected for full-text reading and was subsequently evaluated. The kappa statistic (k) was used to evaluate the level of agreement between the authors.

2.3. Data extraction

A data extraction sheet was developed, pilot-tested on five randomly selected studies and refined accordingly. The same two authors independently extracted demographic, methodological, imaging records and analysis, preoperative cleft status, surgical technique and complementary procedures, fixation method, stability outcomes, complications and follow-up time data for analysis. To avoid overlapping reports, author names were juxtaposed, sample sizes and outcomes compared, and corresponding authors were contacted via e-mail when inconsistencies were found across reports.

2.4. Analysis of risk of bias and quality of evidence of included articles

The assessment of methodological quality was performed using the risk of bias scale for small intervention studies described elsewhere (Haas et al., 2014). Studies were classified as having a low risk of bias if all seven items were present; as having a medium risk of bias if one or two items were missing; and as having a high risk of bias if three or more items were missing. Moreover, included manuscripts were assessed according to the GRADE system in order to evaluate their quality of evidence and strength of recommendation (Guyatt et al., 2008).

2.5. Statistical analysis

Sample size, mean difference and standard deviation (SD) in relation to relapse data were extracted of the clinical studies included in the systematic review to create the meta-analysis. To assess heterogeneity, the random effect model with values for I^2 was used. I^2 was classified as high heterogeneity >75%, medium heterogeneity between 74% and 51% and low heterogeneity <50%. Subgroup analysis was performed due to the different therapeutic methods. The level of significance used in the analyses was 1% ($p = 0.01$).

Statistical analyses were performed using R computer software (R Core Team, 2019: A language and environment for statistical computing. The R Foundation for Statistical Computing, Vienna, Austria).

Table 1
Database search strategy.

DATABASE	KEYWORDS
MEDLINE	(("Cleft Palates" OR "Palate, Cleft" OR "Palates, Cleft" OR "Cleft Palate, Isolated" OR *"Cleft Lips" OR "Lip, Cleft" OR "Lips, Cleft" OR "Harelip" OR "Harelips"*) AND ("Maxillary Osteotomy" OR "Maxillary Osteotomies" OR "Osteotomies, Maxillary" OR "Osteotomy, Maxillary" OR "Osteotomy, Le Fort" OR "Le Fort Osteotomy" OR "Osteotomy, LeFort" OR "LeFort Osteotomy" OR *"Orthognathic Surgery" OR "Orthognathic Surgery" OR "Orthognathic Surgeries" OR "Surgeries, Orthognathic" OR "Surgery, Orthognathic" OR "Maxillofacial Orthognathic Surgery" OR "Maxillofacial Orthognathic Surgeries" OR "Orthognathic Surgeries, Maxillofacial" OR "Orthognathic Surgery, Maxillofacial" OR "Surgeries, Maxillofacial Orthognathic" OR "Surgery, Maxillofacial Orthognathic" OR "Orthognathic Surgical Procedures" OR "Orthognathic Surgical Procedure" OR "Procedure, Orthognathic Surgical" OR "Procedures, Orthognathic Surgical" OR "Surgical Procedure, Orthognathic" OR "Surgical Procedures, Orthognathic")* AND ("Recurrence" OR "Recurrences" OR "Recrudescence" OR "Recrudescences" OR "Relapse" OR "Relapses" OR "Intraoperative Complications" OR "Complication, Peroperative" OR "Complications, Peroperative" OR "Peroperative Complication" OR "Peroperative Complications" OR "Complication, Intraoperative" OR "Complications, Intraoperative" OR "Intraoperative Complication" OR "Injuries, Surgical" OR "Injury, Surgical" OR "Surgical Injury" OR "Surgical Injuries" OR "Postoperative Complications" OR "Complication, Postoperative" OR "Complications, Postoperative" OR "Postoperative Complication")).
COCHRANE LIBRARY	(("Cleft Palate" OR "Cleft Lip") AND ("Orthognathic Surgery" OR "Maxillary Osteotomy" OR "Osteotomy, Le Fort") AND ("Recurrence" OR "Intraoperative Complications" OR "Postoperative Complications"))
GOOGLE SCHOLAR	(("Cleft palate" OR "Cleft lip") AND ("LeFort I Osteotomy" OR "Orthognathic Surgery") AND ("Stability" OR "Recurrence")).

Table 2
Eligibility criteria.

Category	Inclusion criteria	Exclusion criteria
Study design	Intervention study	Case report Review of the literature
Study population	Cleft lip and palate patients	Syndromic patients
Intervention	Le Fort I maxillary osteotomy	Other treatment modalities
Outcome	Stability and/or recurrence data with a minimum of 6-month follow-up	
Other		Languages other than English or Spanish Full text not available

2.6. Surgical protocol and stability data analysis

Timing and protocol of orthodontic treatment, history of pharyngoplasty or pharyngeal flap, previous graft surgeries or any other additional technique were reported.

The type of surgical technique and fixation method were assessed when reported. The presence of residual alveolar clefts, simultaneous graft surgeries, the amount of transverse, sagittal and vertical movement, fixation method, and use of postoperative retention devices or any other additional method to add stability were recorded.

The stability of the surgical procedure in the sagittal, vertical and transverse planes was assessed using the mean and SD of recurrence measured on dental and/or skeletal landmarks in the anterior and posterior segments of the maxilla, between the immediate postoperative period (mean surgical changes − T1) and the last follow-up (mean stability changes − T2).

Some authors did not report the SD of recurrence, but that of the initial and final situations. Therefore, the deviation could be estimated assuming a moderate-to-high degree of correlation between both measures ($\rho = 0.5–0.7$).

To assess heterogeneity, the random effect model with values for I^2 was used. Subgroup analysis was performed due to the different therapeutic methods. The level of significance used in the analyses was 1% ($p = 0.01$).

3. Results

3.1. Database search and references search

The major databases were searched through to March 2021. After title exclusion and abstract review, 42 articles were selected for the eligibility process and full-text reading (Fig. 1). The level of inter-rater agreement was excellent ($k = 0.810$, 95% confidence interval = 0.704–0.879).

3.2. Study eligibility

Finally, 29 articles met eligibility criteria and were included for systematic review (Posnick and Ewing, 1990; Eskenazi and Schendel, 1992; Hochban et al., 1993; Posnick and Taylor, 1994; Cheung et al., 1994; Posnick and Dagys, 1994; Ayliffe et al., 1995; Erbe et al., 1996; Saelen et al., 1998; Bertolini et al., 2000; Hirano and Suzuki, 2001; Mehra et al., 2001; Heliövaara et al., 2001, 2002; Baumann and Sinko, 2003; Thongdee and Samman, 2005; Baek et al., 2007; Chua et al., 2010; Gomes et al., 2013; Kumari et al., 2013; Watts et al., 2014, 2015; Karabekmez et al., 2015; Andersen et al., 2015; Wong et al., 2016; Park et al., 2017; Zheng et al., 2018; Séblain et al., 2018; Marion et al., 2019) (Fig. 1). The inter-rater agreement coefficient was excellent ($k = 0.941$, 95% confidence interval 0.893–0.968).

3.3. Data extraction

Included studies were published between 1990 and 2019; of these, four were prospective and 25 were retrospective, and 24 were considered with a sample of consecutive patients. The total sample of this systematic review is composed of 797 patients with an age range of 16.2–27 years in a proportion of 1.3:1 for males, and the majority presented with unilateral cleft lip and palate (UCLP) as a congenital diagnosis (Table 3).

All studies reported orthodontic treatment before OS, and only two papers reported results in patients without previous secondary alveolar graft (Erbe et al., 1996) or residual alveolar cleft (Cheung et al., 1994). In 56.2% of the patients, only maxillary osteotomy was performed as surgical treatment. The conventional Le Fort I was the most prevalent type of osteotomy (79.3%); four authors reported overcorrection as treatment plan, and only three studies did not report a rigid internal fixation (RIF) method. Alveolar graft during the surgical treatment was reported in 50% of the studies. In the postoperative period, only one study did not use intermaxillary

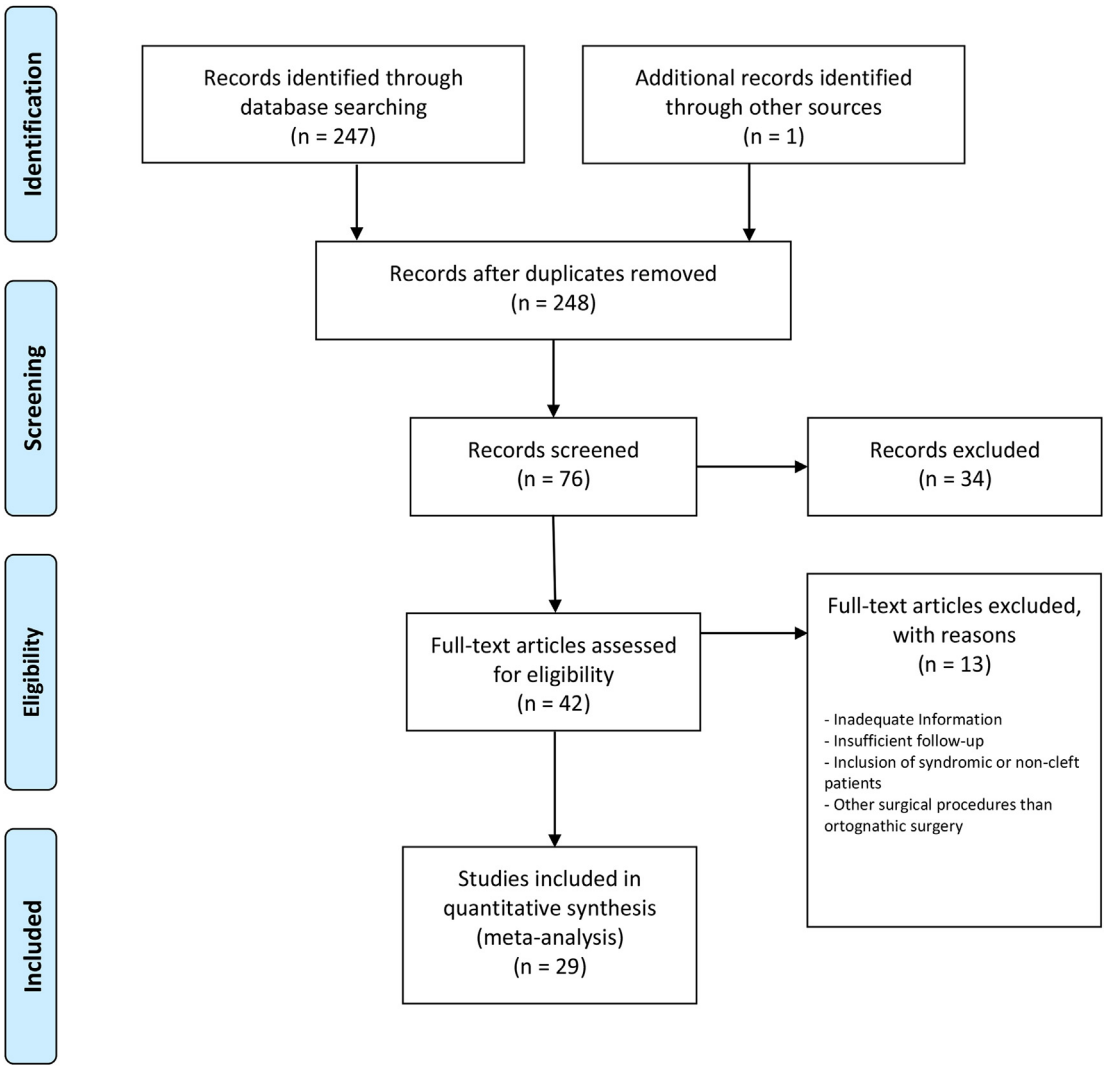

Fig. 1. Flow chart of the systematic review.

fixation, and five papers did not report the method used. Thus 79.3% of the studies used some intermaxillary fixation, either rigid or semi-rigid; at least 41.4% left the final splint during a period of 2–8 weeks (Table 4).

All the stability analysis were done in two-dimensional methods, namely, lateral radiographs and postero-anterior radiographs.

3.4. Analysis of stability: meta-analysis

All the studies included evaluated only maxillary advancement as main surgical procedure, with eventual vertical (downward or upward) and rotation (only CW) movements.

The meta-analysis was able to evaluate the general amount of maxillary advancement and the general amount of maxillary relapse.

3.5. Maxillary advancement: general

The mean maxillary advancement was 5.69 mm ± 0.27 mm (range 5.16–6.23, $p < 0.001$) (Fig. 2). The mean maxillary relapse was −0.99 ± 0.14 mm (17.4% of mean advancement) (−1.27 to −0.72, $p < 0.001$) (Fig. 2). Both had a strong heterogeneity, with 97.1% ($I^2 = 0.971$) and 90.2% ($I^2 = 0.902$), respectively, among the studies (Supplementary Material 1). After correlating advancement and relapse data through a meta-regression, a mean of −0.27 mm (−0.42 to −0.12, $p < 0.001$) of relapse can be expected for each 1 mm of advancement (26.8%).

Considering the strong heterogeneity among the studies, a subgroup analysis was done to evaluate the vertical maxillary displacement associated to advancement: downward, upward and rotation.

3.6. Maxillary advancement and downward

The meta-analysis showed a mean maxillary downward movement of 2.85 mm (2.39–3.32, $p < 0.001$) (Fig. 3) and a mean relapse of −1.13 mm (39.6%) (−1.55 to −0.70, $p < 0.001$) (Fig. 3). Both had no heterogeneity 0% ($I^2 = 0.0$) (Supplementary Material 2). Through a meta-regression correlating vertical movement and relapse, a mean of −0.18 mm (−0.27 to −0.08, $p < 0.001$) of relapse can be expected for each 1 mm of downward movement (17.5%).

Table 3
Study characteristics and demographic data for the included reviews.

AUTHOR, yEAR, COUNTRY	DATA cOLLECTED	SAMPLE sELECTION	SAMPLE sIZE	PATIENT GENDER	PATIENT aGE	TYPE OF cLEFT
ESKENAZI, 1992, USA	Retrospective	Consecutive	24	NR	27	20 UCLP/4 BCLP
CHUA, 2010, CHINA	Prospective	Random	25	NR	>16	25 CLP
BAEK, 2007, SOUTH KOREA	Retrospective	NR	14	13 M/1 F	21.7	14 CLP
HIRANO, 2001, JAPAN	Retrospective	Consecutive	58	30 M/28 F	19.8	42 UCLP/16 BCLP
Gomes et al. (2013), BRAZIL	Retrospective	NR	48	NR	24.7	48 CLP
BAUMANN, 2002, AUSTRIA	Retrospective	NR	15	10 M/5 F	21.4	8 UCLP/6 BCLP/1 CP
WATTS, 2015, CANADA	Retrospective	Consecutive	30	NR	18.2	30 UCLP
HOCHBAN, 1993, GERMANY	Retrospective	Consecutive	14	8 M/6 F	26.1	14 UCLP
Erbe et al. (1996), NETHERLANDS	Retrospective	Consecutive	11	7 M/4 F	19	9 UCLP/2 BCLP
SEBLAIN, 2018, FRANCE	Retrospective	Consecutive	18	8 M/10 F	16.2	13 UCLP/5 BCLP
WATTS, 2014, CANADA	Retrospective	Consecutive	30	14 M/16 F	18.3	30 UCLP
BERTOLINI, 2000, ITALY	Retrospective	Consecutive	10	6 M/4 F	21.1	10 UCLP
POSNICK, 1994A, CANADA	Retrospective	Consecutive	14	NR	19	14 CP
HELIÖVAARA, 2002, FINLAND	Retrospective	Consecutive	25	12 M/13 F	23.7	11 BCLP/14 CP
HELIÖVAARA, 2001, FINLAND	Retrospective	Consecutive	40	27 M/13 F	23.7	40 UCLP
WONG, 2016, AUSTRALIA	Retrospective	Consecutive	21	11 M/10 F	20	NR UCLP/CP
ANDERSEN, 2015, DENMARK	Retrospective	Consecutive	7	4 M/3 F	16.7	7 CLP
SAELEN, 1998, NORWAY	Retrospective	NR	20	11 M/9 F	19.8	20 CLP
KUMARI, 2013, INDIA	Prospective	Consecutive	9	4 M/5 F	17.2	7 UCLP/2 BCLP
THONGDEE, 2005, CHINA	Prospective	Consecutive	30	9 M/21 F	18.4	30 UCLP
AYLIFFE, 1995, UK	Retrospective	Consecutive	61	34 M/27 F	20.6	46 UCLP/15 BCLP
CHEUNG, 1994, CHINA	Prospective	Consecutive	46	27 M/19 F	22	30 UCLP/16 BCLP
PARK, 2017, SOUTH KOREA	Retrospective	Consecutive	21	17 M/4 F	23.5	17 UCLP/4 BCLP
POSNICK,1994B, CANADA	Retrospective	Consecutive	35	NR	18	35 UCLP
POSNICK, 1990, CANADA	Retrospective	Consecutive	30	NR	18	30 UCLP
KARABEKMEZ, 2015, TURKEY	Retrospective	Consecutive	15	11 M/4 F	18	8 UCLP/6 BCLP/1 CP
ZHENG, 2018, CHINA	Retrospective	Consecutive	58	38 M/20 F	18.4	58 UCLP
MEHRA, 2001, USA	Retrospective	Consecutive	17	NR	NR	17 CLP
MARION, 2019, FRANCE	Retrospective	Consecutive	54	NR	NR	NR UCLP/UCL

NR, not reported; M, male; F, female; UCLP, unilateral cleft-lip and palate; BCLP, bilateral cleft-lip and palate; CLP, cleft-lip and palate; CP, cleft palate; UCL, unilateral cleft-lip.

3.7. Maxillary advancement and upward

The maxillary upward movement averaged −2.02 mm (4.39 to −0.36, p = 0.09) (Fig. 4) and presented a mean relapse of 0.11 mm (5.4%) (−1.32 to 1.54, p = 0.9) (Fig. 4), both with no heterogeneity 0% ($I^2 = 0.0$).

3.8. Maxillary advancement with rotation

It was possible to analyze results from data obtained only with CW rotation, since CCW was not reported in any study. The CW results showed an average of 4.15° (2.70−5.61, p < 0.001) (Fig. 5) and a mean relapse of −1.41° (33.9%) (−1.86 to −0.95, p < 0.001) (Fig. 5) with heterogeneity of 91.1% ($I^2 = 0.911$) and 72.1% ($I^2 = 0.721$), respectively (Supplementary Material 3). Through a meta-regression correlating CW movement and relapse, a mean of 0.14° (−0.34 to 0.05, p < 0.001) of relapse can be expected for each 1° of CW movement (14%).

3.9. Meta-regression of stability-related factors

Results from the analysis of stability related factors and its effect on horizontal, vertical and rotational movements are summarized in Table 5.

Moreover, although there were no significant differences regarding the year of publication, it appears that for each additional year (from 1990 to 2018), and for the same amount of average advancement, the recurrence increased by 0.02 mm (p < 0.001).

3.10. Analysis of methodological quality

Methodological quality of the studies included in this systematic review was considered to be low, because only two of them (Chua et al., 2010; Zheng et al., 2018) were judged to have medium risk of bias, and the remaining were categorized as having high risk of bias (Table 6). Regarding the quality of evidence assessment according to GRADE system, all studies were considered of low-quality evidence, since all of them were observational studies without serious modifying factors (Table 7).

Three major problems were encountered: randomization, comparison between treatments, and blind assessment. Only one study included sample randomization (Chua et al., 2010); two studies compared cleft patients with no cleft patients (Gomes et al., 2013; Zheng et al., 2018); and blinded observer was found in one study (Gomes et al., 2013).

4. Discussion

Maxillary surgical reposition using conventional Le Fort I osteotomy is the mainstay for correcting maxillary hypoplasia due to its positive impact on oro-facial function and aesthetics, and therefore on patients' psychosocial health. However, our results suggest that most authors perform a cautious maxillary displacement in CLP patients, reporting a mean maxillary advancement of 5.69 mm, a mean vertical downward/upward of 2.85/−2.02 mm and mean CW rotation of 4.15°.

There is controversy in the literature in relation to intraoperative skeletal movement and higher relapse rates (Houston et al., 1989; Posnick and Ewing, 1990; Hochban et al., 1993; Thongdee and Samman, 2005; Watts et al., 2015). Our analysis suggests that for every 1 mm of maxillary advancement achieved with surgery, an average of 0.23 mm of recurrence is expected (p = 0.007); and for every 1 mm of maxillary vertical descent, a mean recurrence of 0.13 mm is expected (p = 0.039). In this context, DO has been proposed when wider range of movements is required, since it is described as a more stable method (Chua et al., 2010; Ansari et al., 2015). A recent meta-analysis compared horizontal relapse rates in CLP patients for Le Fort I osteotomy with rigid

Table 4
Orthognathic surgery characteristics.

AUTHOR, yEAR	PRIOR ALVEOLAR BONE GRAFTING	ORTHODONTICS PRE/POST-OP	BIMAXILLARY OR mONOMAXILLARY	TYPE OF LE FORT i	MAXILLARY SEGMENTATION	ALVEOLAR gRAFT	MAXILLARY RIF	IMF POST-OP	sPLINT POST-OP
ESKENAZI [13]	18 patients	Yes	2 B/22 M	High	NR	NR	4 miniplates	12 R/12 S	No
CHUA [14]	All patients	Yes	24 B/1 M	Conventional	13 patients	No	4 miniplates	0 R/25 S	NR
BAEK [12]	NR	Yes	NR	Conventional	NR	NR	NR	NR	NR
HIRANO [15]	17 patients	Yes	28 B/30 M	Conventional	NR	No	4 miniplates	All patients R/S	NR
GOMES [16]	All patients	Yes	NR	Conventional	NR	No	Miniplates	All patients R/S	NR
BAUMANN [36]	All patients	Yes	11 B/4 M	Conventional	NR	No	4 miniplates	0 R/15 S	Yes (6w)
WATTS [39]	All patients	Yes	17B/13 M	Conventional	NR	Yes	4 miniplates	Not used	Yes (8w)
HOCHBAN [18]	NR	Yes	0 B/14 M	Conventional	NR	Yes	4 miniplates	All patients R/S	Yes (4/6w)
ERBE [17]	No	Yes	1 B/21 M	Conventional	All patients	Yes	3 miniplates	All patients R	Yes (3/8w)
SEBLAIN [19]	NR	Yes	9 B/9 M	Minimally Invasive	10 patients	Yes	4 miniplates	0 R/18 S	No
WATTS [35]	All patients	Yes	16 B/14 M	Conventional	19 patients	Yes	4 miniplates	0 R/30 S	Yes (6/8w)
BERTOLINI [20]	NR	Yes	NR	Conventional	NR	Yes	Miniplates	All patients R/S	Yes (6/8w)
POSNICK [21]	Not Applicable	Yes	4 B/10 M	Conventional	NR	Not Applicable	4 miniplates	All patients R	Yes (6/8w)
HELIÖVAARA [37]	5 patients	Yes	NR	Conventional	NR	Yes	Miniplates	0 R/25 S	Yes
HELIÖVAARA [34]	33 patients	Yes	4 B/36 M	Conventional	NR	Yes	Miniplates	0 R/40 S	No
WONG [33]	All patients	Yes	10 B/11 M	Conventional	No	Yes	4 miniplates	0 R/21 S	NR
ANDERSEN [23]	All patients	Yes	NR	Conventional	NR	NR	NR	0 R/7 S	NR
SAELEN [32]	All patients	Yes	8 B/12 M	Conventional	No	No	4 miniplates	7 patients R/S	NR
KUMARI [26]	All patients	Yes	0 B/9 M	High	1 patient	No	Miniplates	0 R/9 S	No
THONGDEE [27]	All patients	Yes	14 B/16 M	Conventional	21 patients	No	4 miniplates	All patients S	No
AYLIFFE [24]	All patients	Yes	26 B/35 M	Conventional	NR	No	Miniplates	NR	NR
CHEUNG [28]	No	Yes	23 B/23 M	Conventional	NR	Yes	4 miniplates	All patients S	Yes (6w)
PARK [5]	NR	Yes	21 B/0 M	Conventional	NR	NR	NR	NR	NR
POSNICK [29]	NR	Yes	11 B/24 M	Conventional	No	Yes(10)/No(25)	4 miniplates	All patients R	Yes (8w)
POSNICK [30]	NR	Yes	8 B/22 M	Conventional	17 patients	Yes	4 miniplates	25 R/4 S	NR
KARABEKMEZ [22]	All patients	Yes	9 B/6 M	Quadrangular	No	NR	4 miniplates	NR	NR
ZHENG [31]	NR	Yes	30 B/28 M	High Ladder-Shaped	NR	Yes(24)/No(34)	Miniplates	0 R/58 S	Yes (2w)
MEHRA [38]	NR	NR	17 B/0 M	Ladder-Shaped	All patients	NR	4 miniplates	NR	NR
MARION [25]	31 patients	Yes	17 B/37 M	Conventional	24 patients	Yes(19)/No(35)	4 miniplates	All patients S	Yes (6w)*
SYSTEMATIC REVIEW, 2019		82.5% Yes	43,8% B/56,2% M	79,3% Conventional					

NR, not reported; B, bimaxillary surgery; M, monomaxillary surgery; RIF, rigid internal fixation; IMF, intermaxillary fixation; R, rigid intermaxillary fixation; S, semi-rigid intermaxillary fixation; w, weeks; *, 33 patients of N = 54.

internal fixation (RIF) (20%), Le Fort I distraction osteogenesis (DO) (12%) and anterior maxillary DO (12%) (Jiang et al. (2020)). However, DO implies some drawbacks: it is a longer and less comfortable procedure; two surgical procedures are required for placement and removal of the distraction devices; and distraction vectors may be difficult to control accurately. Thus, when extensive maxillary movements are not required, OS is advisable (Baek et al., 2007; Chua et al., 2010; Andersen et al., 2015). Therefore, we focused our review on Le Fort I osteotomy procedures while excluding the DO procedures in order to try to identify the surgical key points to optimize results of Le Fort I osteotomy in selected patients in whom limited amounts of maxillary movements are required.

All reviewed studies included patients with a mean age over 16 years, which is important to rule out "pseudorelapse" secondary to mandibular growth in adolescent patients. According to the reviewed literature, greater surgical relapse rates have been reported for vertical downward movement (−1.13 mm, 39.6%), followed by CW rotation (−1.41°, 33.9%), sagittal (−0.99 mm, 17.4%) and vertical upward (0.11 mm, 5.4%) movements. It is important to note that one article reported a continued postoperative downward movement instead of upward relapse. Its authors attribute that to the use of elastic traction during the postsurgical orthodontics (Andersen et al., 2015).

Indeed, it has been widely reported that vertical relapse (for downward and CW movements) is higher than horizontal due to

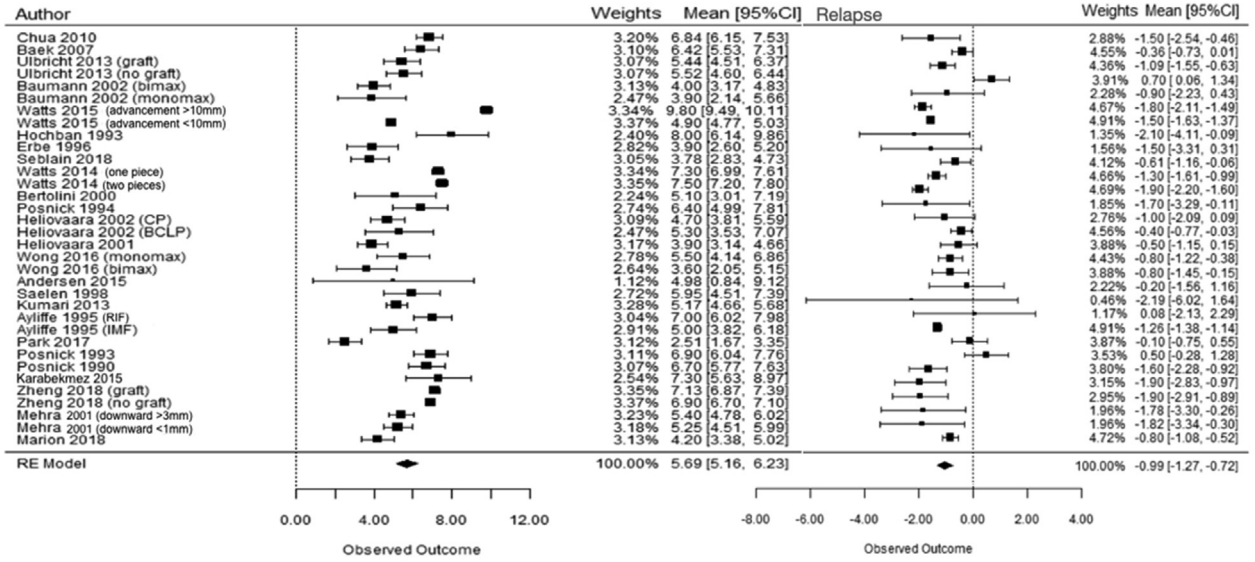

Fig. 2. Maxillary advancement (mean ± SD) and maxillary advancement relapse (mean ± SD).

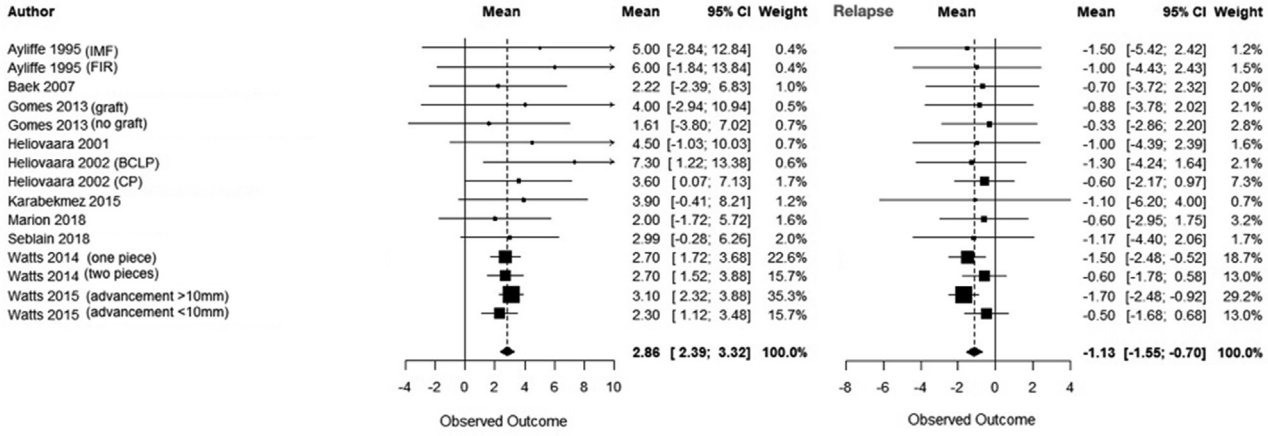

Fig. 3. Maxillary downward movement (mean ± SD) and maxillary downward movement relapse (mean ± SD).

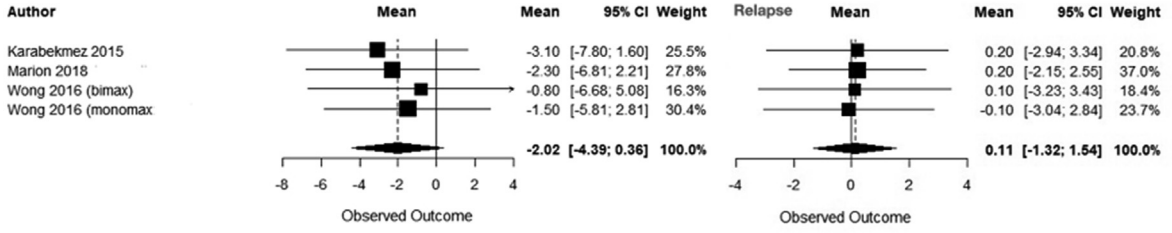

Fig. 4. Maxillary upward movement (mean ± SD) and maxillary upward movement relapse (mean ± SD).

the lower jaw impaction and masticatory muscles pull, which are even stronger when intermaxillary fixation is carried out (Willmar, 1974). However, transverse surgical stability may be even more jeopardized in CLP patients due to the above-mentioned lack of palatine suture and weakened alveolar ridge at the cleft level. Consequently, the cleft maxillary segment may rotate medially, resulting in a crossbite, which is especially relevant in those patients in whom the alveolar cleft is still patent (Rahpeyma and Khajehahmadi, 2015). Unfortunately, most stability and relapse studies in CLP patients have focused their attention on the horizontal and vertical dimensions, and available evidence regarding transverse movements in the literature is very low; this emphasizes the requirement for comprehensive three-dimensional analysis to corroborate this assumption (Cheung et al., 1994; Erbe et al., 1996; Thongdee and Samman, 2005).

In spite of a smaller amount of maxillary advancement, relapse rates in these patients are high when compared with their counterpart non-cleft patients in whom reported sagittal, vertical and

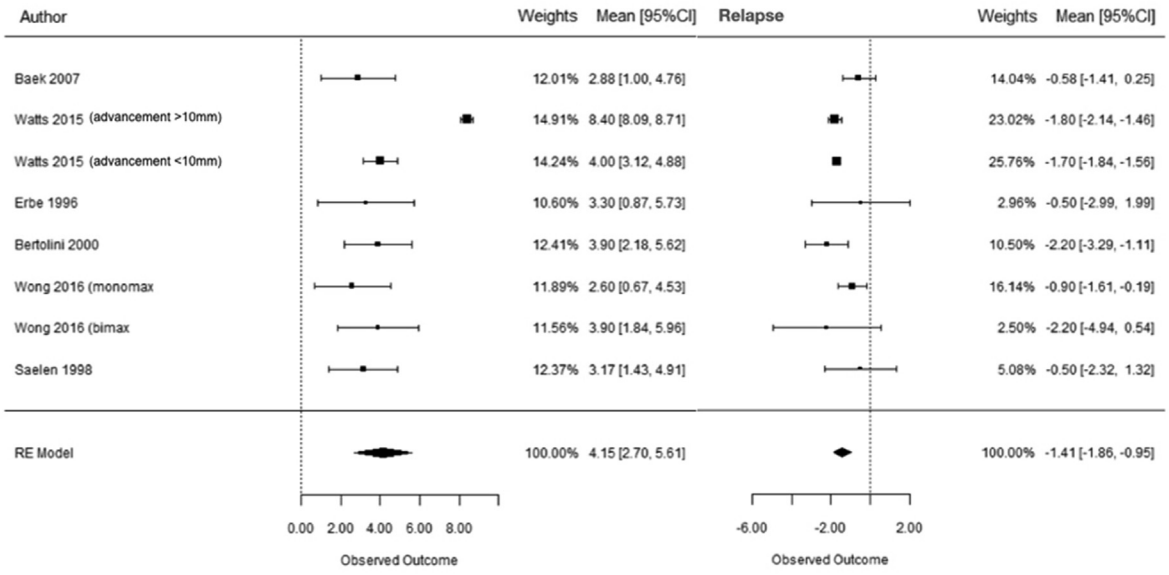

Fig. 5. Maxillary clockwise rotation (mean ± SD) and maxillary clockwise rotation relapse (mean ± SD).

Table 5
Relapse related variables.

Variable		Mean (SD)	p
Type of cleft	Horizontal	0.80 (0.28)	**0.005**
	Vertical	0.19 (0.28)	0.498
	CW Rotation	NA	NA
Bone-graft	Horizontal	−0.63 (0.31)	0.041
	Vertical	0.05 (0.28)	0.836
	CW Rotation	NA	NA
Type of osteotomy	Horizontal	−0.42 (0.30)	0.165
	Vertical	−0.28 (0.31)	0.371
	CW Rotation	0.80 (0.85)	0.349
Post-operative rigid intermaxillary fixation (IMF)	Horizontal	−0.05 (0.26)	0.846
	Vertical	0.15 (0.26)	0.562
	CW Rotation	−0.08 (0.62)	0.891
Post-operative elastic (IMF)	Horizontal	0.32 (0.37)	0.856
	Vertical	0.34 (0.33)	0.305
	CW Rotation	0.17 (0.76)	0.821
Splint	Horizontal	−0.13 (0.35)	0.699
	Vertical	−0.24 (0.41)	0.553
	CW Rotation	NA	NA
Overcorrection	Horizontal	−0.28 (0.34)	0.406
	Vertical	−0.19 (0.40)	0.629
	CW Rotation	NA	NA

NA: not aplicable

transverse (in patients who had undergone three-segmented osteotomy) maximum relapse rates are −0.1 mm, −0.8 mm and 0 mm, respectively (Haas Junior et al., 2017). Therefore, several surgical tips and strengthening techniques have been proposed in order to improve postoperative balance, as discussed below.

Regarding prior alveolar bone grafting, one-piece maxilla surgery is advisable for transverse stability as well as for improving paranasal area symmetry and alar base support. Moreover, alveolar bone graft is a sine qua non requirement for canine and lateral incisor eruption in cleft alveolar ridges (Weissler et al., 2016). Conversely, when faced with a non-grafted alveolar cleft, bone graft may be placed concomitantly with maxillary surgery (either maintaining the alveolar gap or reducing it by lesser maxillary fragment repositioning) (Tideman et al., 1980; Erbe et al., 1996; Watts et al., 2014). Similarly, re-grafting of the cleft alveolar ridge and the osteotomy gap between segments during the maxillary osteotomy is a common procedure to increase long-term stability and to improve paranasal symmetry and alar base support (Gomes et al., 2013; Power and Matic, 2017). Cranial, iliac or mandibular bone as well as xenogenic bone can be used for this purpose (Mehra et al., 2001; Gomes et al., 2013; Zheng et al., 2018). Although no comparative studies regarding their respective long-term volume gain have been reported in the literature, the latest avoids donor site morbidity and is less time consuming.

When evaluating the use of bone grafts to fill Le Fort I osteotomies in this meta-analysis, the results suggested more stability in cases in which bone grafts were not used; however, this information should be carefully addressed, because it was observed that the amount of maxillary advancement was greater in patients with bone grafts than in patients without bone grafts. This means that the relapse is related to the amount of maxillary advancement, and that when bone grafts were used, surgeons are more encouraged to

Table 6
Quality assessment of the included studies.

Study	Randomization	Comparison between treatments	Blind assessment	Validation of measurements	Statistical analysis	Defined inclusion and exclusion criteria	Report of follow-up (at least 12 months)	Risk of bias
Eskenazi [13]	No	No	No	No	Yes	No	Yes	**High**
Chua [14]	Yes	No	No	Yes	Yes	Yes	Yes	**Medium**
Baek [12]	No	No	No	No	Yes	No	No	**High**
Hirano [15]	No	No	No	No	Yes	No	Yes	**High**
Gomes [16]	No	Yes	Yes	No	Yes	Yes	No	**High**
Baumann [36]	No	No	No	Yes	Yes	No	Yes	**High**
Watts [39]	No	No	No	Yes	Yes	Yes	Yes	**High**
Hochban [18]	No	No	No	Yes	Yes	No	Yes	**High**
Erbe [17]	No	No	No	No	No	No	Yes	**High**
Seblain [19]	No	No	No	No	Yes	No	Yes	**High**
Watts [35]	No	No	No	Yes	Yes	Yes	Yes	**High**
Bertolini [20]	No	No	No	No	No	No	Yes	**High**
Posnick [21]	No	No	No	No	Yes	No	Yes	**High**
Heliövaara [37]	No	No	No	Yes	Yes	Yes	Yes	**High**
Heliövaara [34]	No	No	No	No	Yes	Yes	Yes	**High**
Wong [33]	No	No	No	Yes	Yes	Yes	Yes	**High**
Andersen [23]	No	No	No	Yes	Yes	Yes	Yes	**High**
Saelen [32]	No	No	No	Yes	Yes	No	No	**High**
Kumari [26]	No	No	No	No	No	No	Yes	**High**
Thongdee [27]	No	No	No	Yes	Yes	Yes	Yes	**High**
Ayliffe [24]	No	No	No	No	Yes	Yes	Yes	**High**
Cheung [28]	No	No	No	Yes	No	No	Yes	**High**
Park [5]	No	No	No	Yes	Yes	Yes	Yes	**High**
Posnick [29]	No	No	No	No	Yes	No	Yes	**High**
Posnick [30]	No	No	No	No	Yes	No	Yes	**High**
Karabekmez [22]	No	No	No	No	Yes	No	Yes	**High**
Zheng [31]	No	Yes	No	Yes	Yes	Yes	Yes	**Medium**
Mehra [38]	No	No	No	No	Yes	Yes	Yes	**High**
Marion [25]	No	No	No	Yes	Yes	Yes	Yes	**High**

Risk of bias assessment: High: 0 to 4 Yes - Medium: 5 to 6 Yes - Low: 7 Yes.

aggressively treat the maxillary hypoplasia. However, some studies suggest that concomitant bone grafting increases infection rates, and recommend performing the alveolar bone graft at least 6 months before the Le Fort I osteotomy, or afterward for paranasal symmetrization purposes (Bittermann et al., 2020).

There have been several Le Fort I osteotomy designs described (Tideman et al., 1980; Eskenazi and Schendel, 1992; Kumari et al., 2013; Karabekmez et al., 2015; Zheng et al., 2018) in order to increase surgical balance and to address a wider area of midface deficiency, although none of them have demonstrated better stability outcomes. Our meta-regression results suggested that there is no reason for overcorrection. A minimally invasive approach has shown enhanced outcomes related to complication rates, but not for those related to relapse (Séblain et al., 2018).

Regarding the surgical protocol, the preservation of masticatory muscles attached to the mandible in single-jaw surgery has been documented as a relapse-favorable situation, in contrast to the weakness that results from bimaxillary surgery (Willmar, 1974; Bauman and Sinko, 2003). Mandibular surgery in CLP cases is usually indicated when a mandibular retrusion or deviation coexists or a major occlusal plane change is required; however, mandibular setback is inadvisable to compensate for a major maxillary advancement.

RIF, in terms of miniplates, has been widely demonstrated to be more stable than vintage wires (Posnick and Ewing, 1990; Eskenazi and Schendel, 1992; Ayliffe et al., 1995). Furthermore, the pull exerted by suspension wires may contribute to vertical relapse. Usually 4 miniplates are placed vertically to fix the maxilla, and one miniplate can be placed horizontally to bridge the grafted area and to increase the transverse stability of the lesser fragment (Erbe et al., 1996).

Postoperative maxillomandibular rigid fixation has also been associated with relapse, mostly for vertical downward movement and, to a lesser extent, for sagittal advancement (Saltaji et al., 2012; Rahpeyma and Khajehahmadi, 2015). Thus, although no statistical differences were found in our analysis, functional training with light guiding elastics has been proposed as a less detrimental procedure (Cheung et al., 2006; Marion et al., 2019). Apart from proper morphological and functional final occlusion, some authors support long-term containment by dental retention as well as a palatal plate or satellite device (Thongdee and Samman, 2005).

Finally, it is important to note that Le Fort I osteotomy has been demonstrated to be a safe procedure (Hwang et al., 2019). Only 8 of 157 (5%) cases of velopharyngeal insufficiency have been assessed by 7 authors in the present review, and none have reported maxillary necrosis or oro-nasal fistula. Palatine pedicle preservation in CLP patients is considered essential, because their maxillary vascular supply is unpredictable and usually impaired due to previous surgeries and scars (Drommer, 1979; Yamaguchi et al., 2016; Hwang et al., 2019).

Regarding our analysis, we based our methodological quality assessment according to Haas et al. because it has been proved effective and user-friendly for smaller intervention studies when the systematic review includes different types of studies and not only randomized clinical trials. This methodological quality assessment has been used for many years by our research group and other groups since it was originally published in 2014; it is an adaptation of another published tool where we added two more criteria (comparative effect among groups and blinding). On the other hand, GRADE is an important tool to show the quality of evidence and strength of recommendation; however, it is most useful when the systematic review includes only randomized

Table 7
Quality of evidence and strength of recommendation according to GRADE system.

AUTHOR, YEAR, COUNTRY	STUDY LIMITATIONS	INCONSISTENCY OF RESULTS	INDIRECTNESS OF EVIDENCE	IMPRECISION	PUBLICATION BIAS	LARGE MAGNITUDE OF EFFECT	pLAUSIBLE CONFOUNDING, WHICH WOULD REDUCE A DEMONSTRATED EFFECT	DOSE-RESPONSE GRADIENT	QUALITY OF EVIDENCE
ESKENAZI, 1992, USA	−1	−1	NA	0	0	+1	0	+1	LOW
Chua et al. (2010), CHINA	−1	0	−1	0	0	+1	0	+1	LOW
Baek et al. (2007), SOUTH KOREA	−1	0	0	0	0	+1	0	+1	LOW
HIRANO, 2001, JAPAN	−1	0	NA	0	0	+1	0	+1	LOW
GOMES, 2013, BRAZIL	−1	0	NA	0	0	+1	0	+1	LOW
BAUMANN, 2002, AUSTRIA	−1	0	NA	0	0	+1	0	+1	LOW
WATTS, 2015, CANADA	−1	0	NA	0	0	+1	0	+1	LOW
HOCHBAN, 1993, GERMANY	−1	0	NA	0	0	+1	0	+1	LOW
ERBE, 1996, NETHERLANDS	−1	0	NA	0	0	+1	0	+1	LOW
SEBLAIN, 2018, FRANCE	−1	0	NA	0	0	+1	0	+1	LOW
WATTS, 2014, CANADA	−1	−1	NA	0	0	+1	0	+1	LOW
BERTOLINI, 2000, ITALY	−1	0	NA	0	0	+1	0	+1	LOW
POSNICK, 1994A, CANADA	−1	0	NA	0	0	+1	0	+1	LOW
HELIÖVAARA, 2002, FINLAND	−1	0	NA	0	0	+1	0	+1	LOW
HELIÖVAARA, 2001, FINLAND	−1	0	NA	0	0	+1	0	+1	LOW
WONG, 2016, AUSTRALIA	−1	0	NA	0	0	+1	0	+1	LOW
ANDERSEN, 2015, DENMARK	−1	−1	NA	−1	0	+1	0	+1	LOW
SAELEN, 1998, NORWAY	−1	0	NA	0	0	+1	0	+1	LOW
KUMARI, 2013, INDIA	−1	0	NA	−1	0	+1	0	+1	LOW
THONGDEE, 2005, CHINA	−1	0	NA	0	0	+1	0	+1	LOW
AYLIFFE, 1995, UK	−1	0	NA	0	0	+1	0	+1	LOW
CHEUNG, 1994, CHINA	−1	0	NA	0	0	+1	0	+1	LOW
PARK, 2017, SOUTH KOREA	−1	0	NA	0	0	0	0	+1	LOW
POSNICK,1994B, CANADA	−1	0	NA	0	0	+1	0	+1	LOW
POSNICK, 1990, CANADA	−1	0	NA	0	0	+1	0	+1	LOW
KARABEKMEZ, 2015, TURKEY	−1	0	NA	0	0	+1	0	+1	LOW
ZHENG, 2018, CHINA	−1	0	NA	0	0	+1	0	+1	LOW
MEHRA, 2001, USA	−1	0	NA	0	0	+1	0	+1	LOW
MARION, 2019, FRANCE	−1	0	NA	0	0	+1	0	+1	LOW

clinical trials and good-quality clinical papers. There is only one randomized study in this systematic review, and the methodological quality assessment regarding orthognathic surgery stability in cleft patients was considered to be medium to low. This is an acknowledged limitation, and we recognize the need for better methodological quality clinical studies.

Some limitations were present in this study. First, although horizontal relapse rates were addressed by all included articles, vertical, transverse and rotational vectors were less reported. Second, only three studies with sample randomization (Chua et al., 2010) or comparison (Gomes et al., 2013; Zheng et al., 2018) were eligible for inclusion, and most studies were retrospective. Third, the heterogeneity was considered high when maxillary advancement in general was analyzed, but with the subgroups analysis in upward or downward surgical movements, the authors were able to reduce the I^2 to 0%. Thus, the related heterogeneity was clinical, and it was solved with the methods used.

A lack of homogeneous data in the present review regarding cleft type selection is likely relevant, particularly when it is suggested that relapse is more significant in bilateral cleft patients (Hirano and Suzuki, 2001; Heliövaara et al., 2002). Controversially, our results showed that for the same amount of advancement, the studies that mixed unilateral and bilateral cases reported less recurrence than those that included only unilateral cases. However, the first group reported a lesser amount of maxillary advancement. Similarly, it has been found that for each additional year of publication and for the same amount of average advancement, the recurrence increases by 0.02 mm ($p < 0.001$), which is inconsistent with evolution of fixation materials and surgical techniques. This inconsistency might be a consequence of recent publications reporting greater amounts of maxillary advancement, which is directly related to the amount of relapse ($p = 0.007$). Therefore, there is an array of inevitable confounding factors and variables that may have reduced the validity of the results to a certain extent. Thus, the call for homogeneous and high methodological quality

papers is imperative. If, otherwise, one presumes that the studied factors are indeed irrelevant, the design of innovative techniques to improve stability would be required.

5. Conclusion

In conclusion, within the limitations of this systematic review and meta-analysis, our results suggest that Le Fort I osteotomy for maxillary reposition is the first-choice procedure for selected CLP patients in whom extensive maxillary movements are not required, because of its safety and its three-dimensional movement versatility in one-step surgery, even though it is associated with high relapse rates.

Ethical approval

Not required.

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Declaration of competing interest

None declared.

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Appendix A. Supplementary data

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