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Published in:
Journal of Cranio-Maxillofacial Surgery

DOI:
10.1016/j.jcms.2022.12.006

Journal of Cranio-Maxillo-Facial Surgery 50 (2022) 894–909

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Review

Nasal symmetry after different techniques of primary lip repair for unilateral complete cleft lip with or without cleft of the alveolus and palate: A systematic review

Adity Bansal [a, *], Srinivas Gosla Reddy [b], Ashi Chug [c], Anthony F. Markus [d], Anne Marie Kuijpers-Jagtman [e, f, g]

[a] Department of Dentistry, All India Institute of Medical Sciences, AIIMS, Deoghar, Jharkhand, 814152, India
[b] GSR Institute of Cranio-Maxillofacial and Facial Plastic Surgery, Vinay Nagar Colony, I S Sadan, Saidabad, Hyderabad, Telangana, 500059, India
[c] Department of Dentistry, All India Institute of Medical Sciences, AIIMS, Rishikesh, Uttarakhand, 249203, India
[d] Emeritus Consultant, Maxillofacial Surgeon, Poole Hospital, University of Bournemouth, University of Duisburg-Essen, Trinity College Dublin, India
[e] Department of Orthodontics and Dentofacial Orthopedics, School of Dental Medicine/Medical Faculty, University of Bern, Freiburgstrasse 7, CH-3010 Bern, Switzerland
[f] Department of Orthodontics, University Medical Center Groningen, University of Groningen, Hanzeplein 1, 9713 GZ, Groningen, the Netherlands
[g] Faculty of Dentistry, Universitas Indonesia, Campus Salemba, Jalan Salemba Raya No.4, Jakarta, 10430, Indonesia

ARTICLE INFO

Article history:
Paper received 6 November 2021
Received in revised form
8 November 2022
Accepted 31 December 2022
Available online 5 January 2023

Handling Editor: Prof. Emeka Nkenke

Keywords:
Unilateral complete cleft lip
Nasal deformity
Systematic review
Rotation advancement technique
Triangular technique

ABSTRACT

The aim of this systematic review was to establish the effect of different surgical repairs for the lip on nasal symmetry. PubMed, Scopus, Embase, Cochrane CENTRAL, and Ovid databases search was performed initially for only English-language articles, in patients with unilateral complete cleft lip with or without cleft alveolus and palate (UCCLAP) who were younger than 1 year of age and undergoing cleft lip repair, and are published from the earliest data available up to December 31, 2020. The primary outcome variable was nasal symmetry, with reported complications being secondary variables. A qualitative synthesis was provided. A total of 19,828 records were obtained, and 17 articles were selected for final review. Assessment of the risk of bias of the included randomized controlled trials (RCTs) (N-1) was done with the Cochrane Risk of Bias 2 (RoB-2) tool, and the ROBINS-I tool was used for non-randomized studies (n = 14). Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) was applied to evaluate the quality of the body of evidence. The majority of the included studies compared the triangular repair with the rotation advancement (RA) techniques, and preferred RA or its modifications. In terms of the nasal symmetry, the Fisher repair proved to be superior to the RA technique. Neither RA nor straight line repair was superior to one another. The Delaire technique may be preferred over the modified RA. Also, satisfactory outcomes were observed with simultaneous lip–nose repair. This systematic review examined a plethora of techniques, and the heterogeneity between studies was very high regarding type of surgery, method of nasal symmetry assessment, and length of follow-up, thus producing low-quality evidence; therefore, results should be interpreted with caution. Future research requires RCTs with larger sample sizes and appropriate length of follow-up, and surgeries preferably performed by a single experienced surgeon.

1. Introduction

Unilateral complete cleft lip with or without cleft of the alveolus or palate (UCCLAP) is a common craniofacial abnormality causing deformation of the nose and the upper lip. The incidence of orofacial cleft varies from 3.4 to 22.9 per 10,000 live births globally, unilateral (U/L) clefts being twice as frequent as bilateral (B/L) clefts

* Corresponding author. : Department of Dentistry, All India Institute of Medical Sciences, AIIMS, Deoghar, Jharkhand, 814152, India.
E-mail addresses: aditybansal@rediffmail.com (A. Bansal), goslareddy@gmail.com (S.G. Reddy), ashichug@gmail.com (A. Chug), afmarkus@gmail.com (A.F. Markus), a.m.kuijpers-jagtman@umcg.nl (A.M. Kuijpers-Jagtman).

https://doi.org/10.1016/j.jcms.2022.12.006
1010-5182/

(*Lowry et al., 2009*) The abnormal attachment of orbicularis oris muscle in a unilateral complete cleft of the lip (UCCL) results in forces pulling the cleft-sided lip to the same side. A deviated and shortened columella, displaced alar base, lower lateral cartilage flattening on the cleft-side, and deviated nasal tip are the typical nasal features observed in UCCL (*Roussel* et al., 2015). Owing to its impact on the facial appearance, peer interactions and social perceptions, orofacial clefts are considered a "social pathology" (*Glener* et al., 2017). Therefore, the aesthetic outcomes of the cleft repairs are critical in order to mitigate these psychosocial implications.

Various techniques and philosophies have been developed for UCCL repair, with numerous modifications, thus allowing flexibility in the flap designs for surgeons around the world. Broadly, the philosophies for cleft lip (CL) repair are the Millard rotation advancement; Tennison Randall (geometric principle); straight line techniques (Rose); and Delaire functional technique (Delaire et al., 1988). At present, there is controversy as to whether the cleft–nose should be addressed at the time of the primary lip repair, and also whether a closed or an open approach should be used for the same (*Millard and Morovic, 1998*). Some surgeons believe that improved appearance can be achieved simply by cheiloplasty by aggressive dissection and soft tissue mobilization, which would allow for easier subsequent refinements at later stages (*Salyer* et al., 2003). However, growth might be restricted with time if there is early scarring when nasal repair is done at the primary stage.

Treatment outcome evaluation is crucial for recognizing and implementing the highest possible level of care. Attainment of nasal symmetry is, arguably, one of the most challenging goals and a measure of success of UCCL surgical management, as it is reflected in aesthetic outcome for the midface. Although vital functions are not affected in patients with cleft lip and palate, it directly impacts the identity of the person, that is,i.e.,the face. Management of UCCL requires the attainment of ideal anatomy and morphology of the nasolabial region, thus achieving a natural lip and nasal shape. In terms of the nose, it aims to raise the flattened and drooped down alae, extend the nasal column length, narrow the nasal base, and restore the apex nasi. In addition, the optimal outcome should ideally be acquired in a single surgery, without multiple revisions (*Christofides* et al., 2006). Therefore, this systematic review aims to compare nasal symmetry as a result of the different surgical techniques used in the repair of UCCL with or without unilateral cleft of the alveolus and palate, in patients less than 1 year of age with a minimum follow-up of 1 year.

2. Materials and methods

2.1. Registration and protocol

This systematic review protocol was registered with the International Prospective Register of Systematic Reviews i.e.,PROSPERO (CRD42021228928). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement was followed for the reporting of this review (Page et al., 2021a; 2021b).

2.2. Eligibility criteria

The research question was formulated using the PICOS framework (population, intervention, comparison, outcome, study design). The research question was the degree of nasal symmetry (O) in patients with a UCCLAP (P) receiving primary surgery of the lip with/without the nose before the age of 1 year (I) using different study designs (S). The comparator was not defined in the PICO formulation, as this systematic review aims to evaluate the effect of different surgical techniques for correction of UCCLAP, and thus to avoid restriction in the search.

Studies comparing nasal symmetry attained following techniques involving the repair of UCCL within the first year of life, associated with or without unilateral cleft of the alveolus or palate, with a minimum follow-up of 1 year, were included in this review. Patients undergoing simultaneous rhinoplasty (open or closed) along with cleft lip (CL) surgery were also included. However, patients with incomplete CL, bilateral complete/incomplete CL, microform CL, patients undergoing secondary/revision CL surgeries, and patients with syndromes or congenital deformities were excluded. Literature published until December 31, 2020, was included. Randomized controlled trials (RCT), prospective studies, retrospective studies, observational studies and surveys comparing different techniques for surgical repair of UCCL and correction of nasal asymmetry, with at least 1 year of follow-up, were included. Case reports, case series, book chapters, editorials, animal studies, and cadaver studies were excluded.

2.3. Information sources and search strategy

PubMed, Scopus, Embase, Cochrane CENTRAL and Ovid databases searches were performed initially only for English -nguage articles, published from the earliest data available up to December 31, 2020. A combination of free text terms and Medical Subject Headings (MeSH) terms were used for a broad search, using the search strategy depicted in Supplementary Table 1.

Relevant articles were searched in journals such as 'Indian Journal of Plastic Surgery (IJPS)', 'Plastic and Reconstructive Surgery Journal (PRS)', 'Journal of Craniomaxillofacial Surgery (JCMS)', 'Journal of Cleft Lip Palate and Craniofacial Anomalies (JCLPCA)', 'Cleft Palate-Craniofacial Journal (CPCJ)', 'British Journal of Oral and Maxillofacial Surgery (BJOMS)', and 'International Journal of Oral and Maxillofacial Surgery (IJOMS)'. Additional records were inspected in trial registers, conference proceedings, bibliographic databases, grey literature and the reference lists of the included articles were hand searched.

2.4. Study selection

Eligibility assessment was un-blinded and performed independently by the two reviewers (A.B., S.G.R.) based upon the above-mentioned inclusion criteria. Title and abstract screening were carried out initially by the reviewer, followed by the full-text analysis. A third reviewer (A.K.) was approached to discuss and resolve any disagreements if encountered.

2.5. Data collection

The extracted data from the included studies were as follows: author name, year of publication, study location and type, number of eligible patients, age, sex, side of UCCL, surgical technique/philosophy, nasal symmetry, method of nasal symmetry analysis, columellar symmetry, alar symmetry, septal repositioning, nasal tip projection, complications, and follow-up period. The data extraction form was developed and piloted on all records. One reviewer extracted the data, and the same was checked by the second reviewer. Any disagreements were resolved by the third reviewer. Authors were contacted for further information in case confirmation of the data was required.

2.6. Data items

Outcomes were categorized broadly as nasal symmetry and complications. Any method of nasal symmetry assessment and complications reported was considered eligible for inclusion in this review. Studies with at least 1 year of follow-up were eligible, as

this will allow measurement of more persistent effects. No constraints were placed on the number of times at which the measurement of the outcome could be done, but consideration was given to the length of follow-up when the study findings were interpreted.

2.7. Risk of bias of individual studies

Assessment of the risk of bias of the included RCTs was done with the Cochrane Risk of Bias 2 (RoB-2) tool, and the ROBINS-I tool was used for non-randomized studies. Rating was carried out by two reviewers independently (*Sterne* et al., 2019). Conflict, if any, was resolved via discussion with the third reviewer (A.K.). Seven domains are judged in the ROBINS-I tool as having no information or having low, moderate, serious, or critical risk of bias.

2.8. Data analysis

Nasal symmetry was the primary outcome variable. The nasal symmetry was measured as described by the original study in terms of type of method/columellar symmetry/alar symmetry/septal positioning/projection of nasal tip. The complications experienced were listed as secondary outcomes. A qualitative synthesis of the findings from the included studies was provided. If the studies included were sufficiently homogeneous, a quantitative synthesis (meta-analysis) was performed. Otherwise, a descriptive analysis of the data was performed.

2.9. Risk of bias across studies

Methodological heterogeneity was assessed by comparing the variability in study design and RoB results of the individual studies. Type of operation, length of follow-up, and method of analysis of nasal outcome were compared. The clinical heterogeneity assessment considered sample size differences and characteristics of the study groups, the size and similarity of the control group, and the characteristics of the population.

2.10. Synthesis methods

First, we considered heterogeneity between the studies based on population, type of surgery, outcome measurement, and length of follow-up. As heterogeneity between studies was very high, further statistical analysis was deemed not to be appropriate.

2.11. Certainty of the evidence

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) was applied to evaluate the quality of the body of evidence (*Guyatt* et al., 2009). The quality of evidence was rated per outcome, divided into four categories: high, moderate, low, or very low.

3. Results

3.1. Study selection

The PRISMA flowchart is depicted in Fig. 1. A total of 19,828 records were obtained through the database search. Grey literature and other additional sources yielded no records. After manual removal of the duplicates, 5062 records were screened according to title and abstract, which led to the exclusion of 4987 publications for various reasons (see flowchart), resulting in 74 articles for full-text analysis. After full-text screening, a total of 15 articles were included in the review.

3.2. Characteristics of the included studies

Table 1 depicts the characteristics of the studies included. Of the 15 studies included in the review, 6 were retrospective cross-sectional observational studies (*Suchyta* et al., 2020; *Kwong* et al., 2019; Rossell-Perry, 2016, 2020; *Cline* et al., 2014; *Zaleckas* et al., 2011); five were retrospective observational cohort studies (*Freeman* et al., 2013; *Chang* et al., 2010; *Numa* et al., 2006; *Yamada et al., 2002a,b*; Horswell and Pospisil, 1995); three were prospective observational cohort studies (*Morselli* et al., 2012; *Reddy* et al., 2011; *Amaratunga*, 1988); and one was an RCT (*Mølsted* et al., 2017).

Cheiloplasty was performed most commonly at 3 months. Only 5 studies defined the UCCL patients (*Kwong* et al., 2019; *Rossell-Perry*, 2016; *Cline* et al., 2014; *Chang* et al., 2010; *Numa* et al., 2006). Other studies either described UCCL along with palate (7) (*Suchyta* et al., 2020; *Rossell-Perry, 2020*; *Freeman* et al., 2013; *Horswell and Pospisil, 1995*; *Morselli* et al., 2012; *Amaratunga*, 1988; *Mølsted* et al., 2017) or UCCL with palate or alveolus (3) (*Zaleckas* et al., 2011; *Reddy* et al., 2011; *Yamada et al., 2002a,b*). Use of naso-alveolar moulding (NAM) (Cline et al., 2014; *Chang* et al., 2010) or pre-surgical infant orthopaedics (PIO) (*Zaleckas* et al., 2011; *Yamada et al., 2002a,b*) was mentioned in 2 studies each. The included articles observed diverse types of lip repair techniques (Table 2). Maximum follow-up observed was a range of 9–24 years (*Zaleckas* et al., 2011). Eleven studies were associated with simultaneous lip and nasal repair (*Kwong* et al., 2019; *Rossell-Perry, 2016*; *Mølsted* et al., 2017; *Rossell-Perry, 2020*; *Cline* et al., 2014; *Freeman* et al., 2013; *Chang* et al., 2010; *Morselli* et al., 2012; *Reddy* et al., 2011; *Numa* et al., 2006; *Horswell and Pospisil*, 1995*Rossell-*). A wide range of variables were used to define nasal symmetry, such as nasal alae (*Rossell-Perry, 2020*; *Morselli* et al., 2012; *Reddy* et al., 2011; *Numa* et al., 2006; *Yamada et al., 2002a,b*; *Horswell and Pospisil*, 1995; *Amaratunga*, 1988), columella (*Rossell-Perry*, 2020; *Morselli* et al., 2012; *Reddy* et al., 2011; *Yamada et al., 2002a,b*), nasal width (*Rossell-Perry*, 2016; *Cline* et al., 2014; *Chang* et al., 2010), nasal tip (*Morselli* et al., 2012; *Numa* et al., 2006; *Yamada et al., 2002a,b*; *Horswell and Pospisil, 1995*) and general appearance (*Kwong* et al., 2019; *Suchyta* et al., 2020).

Half of the studies included used a quantitative method for nasal symmetry analysis (7 studies) (*Rossell-Perry*, 2020; *Rossell-Perry*, 2016; *Cline* et al., 2014; *Freeman* et al., 2013; *Morselli* et al., 2012; *Horswell and Pospisil, 1995*; *Amaratunga, 1988*), followed by qualitative (5 studies) (*Suchyta* et al., 2020; *Kwong* et al., 2019; *Zaleckas* et al., 2011; *Numa* et al., 2006; *Mølsted* et al., 2017); or a combination of the two (3 studies) (*Reddy* et al., 2011; *Chang* et al., 2010; *Yamada et al., 2002a,b*). Facial photographs were used the most, with frontal view being the most common. Varied scales and indices were used, such as an ordinal scale using the Modified Q-sort method (*Mølsted* et al., 2017); Mortier's modified rating scale (*Zaleckas* et al., 2011); a visual analogue scale (VAS) (*Chang* et al., 2010); and the Cleft Lip Component Symmetry Index (CLCSI) (*Amaratunga*, 1988).

3.3. Risk of bias of individual studies

Table 3 and Table 4 depict the RoB of all the studies included. The Cochrane Risk of Bias 2 (RoB-2) tool for RCT (Table 3) shows that blinding of participants and the personnel was unclear in the

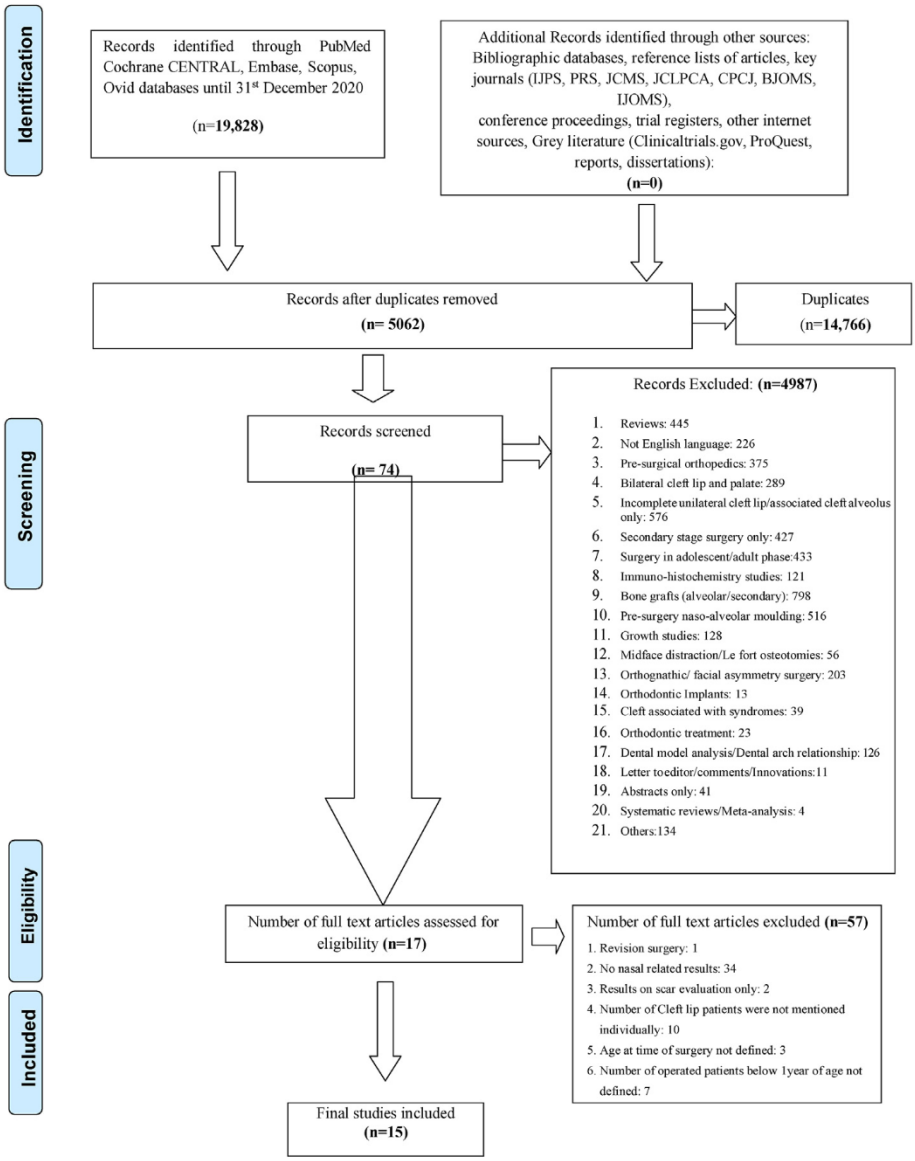

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart depicting the selection process.

study (*Mølsted* et al., 2017). A total of 14 studies were appraised with the ROBINS-I tool for non-randomized studies (Table 4); we observed no information in one study, low risk in two studies, moderate risk in 10 studies, and serious risk in one study.

3.4. Certainty of the evidence

The GRADE tool was used to assess the certainty of evidence for the nasal symmetry and reported complications (Table 5). Evidence obtained was of very low quality for both the outcomes.

3.5. Synthesis of the results

The aim of this research was to establish the effect of different surgical repairs for the lip on nasal symmetry. The heterogeneity between the studies was very high regarding type of surgery, method of nasal symmetry assessment and length of follow-up. For example, in the 15 included studies in this systematic review, 22 different surgical techniques were performed (Table 2). Therefore, a meta-analysis of the data was not possible. A descriptive synthesis of the characteristics of each study is presented in Tables 1 and 6.

3.6. Nasal symmetry

3.6.1. Patients with unilateral complete cleft lip

Five studies with a total of 279 patients were included (*Kwong* et al., 2019; *Rossell-Perry, 2016*; *Chang* et al., 2010; *Numa* et al., 2006; and *Cline* et al., 2014). Study location was the United States in 4 of these studies (*Kwong* et al., 2019; *Rossell-Perry, 2016*; *Numa* et al., 2006; and *Cline* et al., 2014). Three of the studies were cross-sectional (*Kwong* et al., 2019; *Rossell-Perry, 2016*; and *Cline* et al., 2014), and two were cohort studies (*Chang* et al., 2010; and *Numa* et al., 2006). Concomitant rhinoplasty was performed in all of these studies.

Table 1
Characteristics of the included studies.

Author, publication, year	Study location	Study type	Number of eligible patients Type of surgery Control group	Age/sex	Concomitant rhinoplasty procedure (yes/no)
A) Patients with unilateral complete cleft lip					
Kwong et al. (2019)	USA	ROS (cross sectional study)	20 Fisher: 5 MRA: 5 Mohler:5 NC: 5	3–4 mo/ND	Yes
Rossell-Perry (2016)	USA	ROS (cross-sectional study)	150 Group B: 84Reichert-Millard or upper rotation advancement plus double unilimb Z-plasty Group C: 66Upper rotation advancement plus double unilimb Z-plasty or triple unilimb Z-plasty techniques Group A not included in this review as it involved incomplete clefts	3 mo Group B: Technique3: M:24, F:20 Technique 4: M:23, F:17 Group C Technique 5: M:18, F:12 Technique 6:M:23, F:14	Yes
Cline et al. (2014)	USA	ROS (cross-sectional study)	15 MRA: 7 Philtral ridge repair: 8	MRA: 4.1 mo Philtral ridge: 3.2 mo Gender ND for specifically complete clefts	Yes
Chang et al. (2010)	Taiwan	ROS (cohort study)	76 Group I: 23 Primary rhinoplasty alone Group II: 16 NAM alone Group III: 14 NAM plus primary rhinoplasty Group IV: 23 Primary rhinoplasty plus NAM plus over-correction	3 mo/ND	Yes
Numa et al. (2006)	USA	ROS (cohort study)	18 Study group: 9 ABF-SS technique with primary rhinoplasty Control group: 9 MRA with primary rhinoplasty	Study group: Age range: 10.6 mo (10–13) M:7, F:2 Control group: Age: 11.8 mo (3–36 mo) M:5, F:4	Yes
B) Patients with Unilateral complete cleft lip and alveolus/Unilateral complete cleft lip, alveolus and palate					
Zaleckas et al. (2011)	Lithuania	ROS (cross-sectional study)	66 TR: 19 MRA: 20 Olekas: 27	1 mo - 1 y/ND	No
Gosla Reddy et al., 2011	India	POS (cohort study)	158 Group A: 82 Afroze incision without septoplasty Group B: 76 Afroze incision with septoplasty	Less than 1 y Group A: M:51, F:31 Group B: M:44, F:32	Yes
Yamada et al. (2002)	Japan	ROS (cohort study)	171 Group I: 10 Triangular flap (Berstein) Group II: 10 Rotation advancement plus small triangular flap (Onizuka) Control group: 151	3 mo Gender: ND	No
C) Patients with Unilateral complete cleft lip, alveolus and palate					
Suchyta et al. (2020)	USA	ROS (cross sectional study)	29 Fisher: 7 MRA: 7 Mohler:7 NC: 8	3 mo–4 mo/ND	No
Rossell-Perry (2020)	Peru	ROS (cross sectional study)	71 Group I: 25 Modified McComb technique Group II: 22 Potter technique Group III: 24 V–Y-Z method	3 mo Group I: M: 16, F: 9 Group II: M: 12, F: 10 Group III: M: 15, F: 9	Yes
Mølsted et al. (2017)	Denmark Finland Norway Sweden UK	RCT	448 Trial 1: 148 MRA (125), Gothenburg method (23), TR: 0 Trial 2: 151 MRA (114), Gothenburg method (0), TR (37) Trial 3: 149 MRA (149)	3 mo–4 mo Gender: ND	Yes
Freeman et al. (2013)	UK	ROS (cohort study)	120 Group I: 30 MRA with nasal correction Group II: 45 Modified Millard without nasal correction Group III: Controls: 45	3 mo Classical Millard: M: 28, F: 2) Modified Millard: M: 29, F:16) Controls: M: 42, F:3)	Yes
Morselli et al. (2012)	Italy	POS (cohort study)	40 Group A: 20 primary rhinoseptoplasty Group B: 20 Cheiloplasty without primary correction of nasal deformities	Age same in both groups: 8 ± 2 mo Group A: M: 20 Group B: M: 20	Yes
Horswell and Pospisil, 1995	UK	ROS (cohort study)	58 Del: 16 MRA: 17 NC: 25	3–5 mo Del M: 9, F: 7 MRA M: 11, F: 6 NC M: 16, F: 9	Yes

Table 1 (*continued*)

Author, publication, year	Study location	Study type	Number of eligible patients Type of surgery Control group	Age/sex	Concomitant rhinoplasty procedure (yes/no)
Amaratunga (1988)	Sri Lanka	POS (cohort study)	100 MRA: 50 LeMesurier: 50	Below 9 mo MRA M: 40, F: 10 LeMesurier M: 34, F: 16	No

ROS: Retrospective observational study; MRA: Millard rotation advancement; mo: months; y: years; ND: not defined; NC: Non-cleft controls; RCT: Randomized controlled trial; TR: Tennison Randall; M: males; F: females; L: Left; R: Right; NLA: Nasolabial advancement; LA: Labial advancement; avg: average; POS: Prospective observational study; NAM: Naso-alveolar molding; ABF-SS: Alar base flap and suspending suture technique; NNC: no nasal correction group; PNC: primary nasal correction group; Del: Delaire cheiloplasty; MRA: Modified rotation advancement technique.

Table 2
Types of UCCL repair techniques observed in the systematic review.

Rotation advancement techniques	Triangular techniques	Straight line repairs	Quadrangular repair	Lateral advancement flap	Functional repair	Anatomical sub-unit approximation techniques	New techniques	Rhinoplasty techniques
Conventional MRA	Old triangular flap (Berstein)	Philtral ridge repair technique	LeMesurier	Malaigne and Mirault	Delaire	Fisher's	Afroze incision	Mc Comb technique
Mohler technique	New triangular flap (Onizuka)	Olekas technique						Potter technique
Reichert Millard technique	Tennison Randall (TR)							V–Y-Z technique
Modified Nakajima concept i.e., use of single upper RA with double lower unilimb Z-plasty								Gothenburg method
Single upper RA with Triple unilimb Z-plasty								
Mulliken's modification of RA								
Noordhoff modification of RA								
Alar-base flap with suspending suture (ABF-SS)								

MRA: Millard rotation advancement technique; RA: Rotation advancement technique.

Table 3
Cochrane risk of bias 2 (RoB-2) tool for randomized controlled trials (RCTs).

Article	Selection Bias		Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	
Mølsted et al., 2017	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk

Table 4
ROBINS-I tool for risk assessment of non-randomized studies.

Study		Pre-intervention		At intervention		Post-intervention			Overall risk of bias
First author	Year	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of intervention	Bias due to deviations from inten ded interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Low/moderate/ serious/critical/no information
Suchyta	2020	Low	Low	Low	Low	Low	Low	Low	Low
Kwong	2019	Low	No information	Low	Low	Low	Low	Low	No information
Rossell-Perry	2020	Low	Low	Low	Low	Low	Serious	Low	Serious
Rossell-Perry	2016	Low	Moderate	Low	Low	Low	Low	Low	Moderate
Cline	2014	Low	Moderate	Low	Low	Low	Moderate	Low	Moderate
Freeman	2013	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Morselli	2012	Low	Low	Low	Low	Low	Low	Low	Low
Zaleckas	2011	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Gosla Reddy	2011	Low	Moderate	Low	Low	Low	Low	Low	Moderate
Chang	2010	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Numa	2006	Low	Moderate	Low	Low	Low	Low	Low	Moderate
Yamada	2002	Low	Low	Low	Low	Low	Moderate	Low	Moderate
Horswell	1995	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Amaratunga	1988	Low	Moderate	Low	Low	Low	Low	Low	Moderate

Table 5
Results of certainty of the evidence (GRADE assessment).

Outcome	No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Overall score
Nasal symmetry	15	Randomized controlled trial and observational studies	Serious	Serious	No serious indirectness	Serious	None	⊕◯◯◯
Complications	6	Observational studies	Serious	Serious	No serious indirectness	Serious	None	⊕◯◯◯

4 ⊕⊕⊕⊕ **High** = This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different is low.
3 ⊕⊕⊕◯ **Moderate** = This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different is moderate.
2 ⊕⊕◯◯ **Low** = This research provides some indication of the likely effect. However, the likelihood that it will be substantially different is high.
1 ⊕◯◯◯ **Very low** = This research does not provide a reliable indication of the likely effect The likelihood that the effect will be substantially different is very high.

None of the studies had similar study groups or number of patients. Three studies compared rotation advancement or its modifications, but none of the studies had similar groups (*Rossell-Perry, 2016*; *Chang* et al., 2010; *Numa* et al., 2006). One study compared rotation advancement (RA) techniques with anatomical sub-unit technique (*Kwong* et al., 2019), and another compared conventional RA technique with modified straight line repair (Cline et al., 2014).

The most common technique in these studies was the MRA technique or its modifications. The Fisher technique yielded better results, followed by the Mohler technique and MRA technique, with maximum scar severity observed in MRA (*Kwong* et al., 2019). A statistically significant difference was found between cleft and non-cleft side for nasal base width when using Reichert-Millard or upper rotation advancement with either double unilimb Z-plasty or triple unilimb Z-plasty technique (*Rossell-Perry, 2016*). However, the upper rotation advancement plus double unilimb Z-plasty has a limited ability to properly repair cleft lips with severe tissue deficiency. *Cline* et al. (2014) revealed similar ratings of symmetry between the two repair types, namelyi.e.,MRA and philtral ridge repair. *Chang* et al. (2010) concluded that primary rhinoplasty along with NAM and overcorrection resulted in overall best assessment. ABF-SS technique showed statistically significant improved degree of symmetry when compared to MRA (*Numa* et al., 2006).

Three studies used photographs as their method of analysis (*Chang* et al., 2010; *Cline* et al., 2014; and *Numa* et al., 2006), while the other two studies used eye-tracking technology (*Kwong* et al., 2019) and anthropometry (*Rossell-Perry, 2016*) as their mode of analysis.

Only two studies used pre-surgical NAM (*Chang* et al., 2010; *Cline* et al., 2014). None of the studies defined columellar symmetry and septal repositioning, although concomitant rhinoplasty was performed in all of the studies. Alar symmetry and nasal tip projection were defined in only one study (*Numa* et al., 2006). The maximum follow-up period reported was 6 years (*Kwong* et al., 2019).

The overall risk of bias as assessed by ROBINS-I tool was moderate in 4 studies (*Rossell-Perry, 2016*; *Chang* et al., 2010; *Numa* et al., 2006; and *Cline* et al., 2014). No information was available on the bias in the selection of participants in one study (*Kwong* et al., 2019). There was moderate risk in two studies each for bias in measurement of outcomes (*Rossell-Perry, 2016*; *Cline* et al., 2014) and participant selection (*Cline* et al., 2014; *Numa* et al., 2006). Certainty of evidence of all these studies was very low for nasal symmetry and complications.

3.6.2. Patients with unilateral complete cleft lip and alveolus/ unilateral complete cleft lip, alveolus and palate

Three studies were included with patients with either UCCL with alveolus or UCCLAP. These studies did not discriminate between patients in each category (*Zaleckas* et al., 2011; *Gosla Reddy* et al., 2011; and *Yamada et al., 2002a,bGosla*). The total number of patients was 395. Study location was different in all three studies. Two of the studies were cohort studies (*Gosla Reddy* et al., 2011; and *Yamada et al., 2002a,b*), while one was a cross-sectional study (*Zaleckas* et al., 2011). Concomitant rhinoplasty was performed in only one study (*Gosla Reddy et al., 2011*).

The number of patients and the study groups were u-comparable in any of the two studies. *Zaleckas* et al. (2011) compared three techniques, i.e., Tennison Randall (TR), MRA and straight line repair (Olekas), while *Yamada et al. (2002a,b)* studied two triangular techniques (Berstein and Onizuka). A new technique, 'Afroze,' was compared with and without septoplasty in the study by *Reddy* et al. (2011).

The most common technique in the included studies was RA and triangular repair (*Zaleckas* et al., 2011; and *Yamada et al., 2002a,b*). *Zaleckas* et al. (2011) concluded that scar severity was minimal and that the nose looked most aesthetic after the Olekas technique. Afroze incision with septoplasty showed significantly lower asymmetry (*Reddy* et al., 2011). *Yamada* et al. (2002) observed nasal asymmetry in both groups (triangular repair, and RA with small triangular flap i.e., Onizuka); however, this deformity was evident at a much earlier stage in the triangular repair. Also, the nasal and nostril shape was deemed better in the RA group.

Photographs were analyzed in two studies (*Zaleckas* et al., 2011; *Gosla Reddy et al., 2011*), although the methods to analyze them were different: i.e., Mortier rating scale (*Zaleckas* et al., 2011) and Mommaerts and Nagy method (*Reddy* et al., 2011). A three-dimensional optical scanner was used in the third study (*Yamada et al., 2002a,b*).

PIO was used in two studies (*Zaleckas* et al., 2011; *Yamada et al., 2002a,b*). Septal repositioning, complications and disadvantages were not defined in any of the studies. Columellar symmetry was defined by two studies (*Reddy* et al., 2011; *Yamada et al., 2002a,b*). Lower asymmetry was noted in Afroze incision with septoplasty (*Reddy* et al., 2011), and no significant difference was observed between the groups in the other study (*Yamada et al., 2002a,b*). Alar symmetry was also defined by the above two studies, in which better results were obtained in Afroze incision with septoplasty (*Reddy* et al., 2011), while the alar width with respect to the cleft side was seen to be increased in both groups as compared to the control group (*Yamada et al., 2002a,b*). Nasal tip projection was defined in only one study, in which nasal protusion showed a decrease at 1.5 years of age in the triangular group (*Yamada et al., 2002a,b*). *Zaleckas* et al. (2011) showed maximum follow-up (range: 9–24 years).

Risk assessment by the ROBINS-I tool revealed moderate risk of bias in all three studies. Risk was moderate for selection participants in two studies (*Zaleckas* et al., 2011; *Reddy* et al., 2011), for bias due to confounding in one study (*Zaleckas* et al., 2011), and for

Table 6
Depicting descriptive analysis of the included studies.

Author	Name of surgical technique	Nasal symmetry	Methods of analysis used	PIO or NAM	Columellar symmetry	Alar symmetry	Septal repositioning	Nasal tip projection	Complications (if any reported)	Disadvantages (if any)	Follow- up period
A) Patients with unilateral complete cleft lip											
Kwong et al. (2019)	Fisher Millard Mohler	**Likert score** Fisher: 6.91 ± 0.11 Millard: 5.60 ± 0.14 Mohler: 6.47 ± 0.13 Control: 9.07 ± 0.11 **Fixation duration** Fisher: 51.9% Mohler: 54.4% Millard: 58.3% Controls: 47.3%	Likert scale: 1−10 Eye tracking Measured eye fixation duration	No	ND	ND	ND	ND	**Scar severity:** Millard >Mohler >Fisher	ND	4-6 y
Rossell-Perry (2016)	Group B: Reichert-Millard or upper rotation advancement plus double unilimb Z-plasty Group C: Upper rotation advancement plus double unilimb Z-plasty or triple unilimb Z-plasty techniques Primary rhinoplasty in all patients using technique by Potter (a composite V−Y advancement flap)	Group B: Statistically significant differences between cleft and non cleft side wrt nasal base width when Group C: Statistically significant difference between cleft and non cleft side for nasal base width when using upper rotation advancement plus double unilimb Z-plasty technique	Anthropometry under general anaesthesia using Castroviejo caliper	No	ND	ND	ND	ND	ND	The upper rotation advancement plus double unilimbZ-plasty has a limited ability to properly repair cleft lips with severe tissue deficiency	1 y or later or at the age of 1.5-2y
Cline et al. (2014)	MRA Philtral Ridge Repair (modified straight line repair)	No statistically significant difference in nasal vestibular width and alar base height, height of alar rim dome, Cupid's peak height post-operatively between the two groups Subjective analysis also revealed similar ratings of symmetry between the two repair types.	Frontal and standard basilar view photographs	NAM	ND	ND	ND	ND	ND	ND	Rotation advancement: avg: 47 mo (range: 12 −120 mo) Philtral ridge: avg: 58 mo (range: 13 −129 mo)
Chang et al. (2010)	Modified rotation advancement with Mohler incision Vermilion reconstructed with Noordhoff vermilion flap Group I and III: lower lateral cartilage dissection using bilateral rim incisions, followed by placement of	Nostril height, nostril width, one-fourth medial part of nostril height, nasal sill height, nostril area, inner nostril height-to-width ratio **Nostril height:** group IV had nostril height that was most comparable with non cleft side Group I had lowest	Standard basilar view photograph Measurements using Photoshop VAS scale	NAM	ND	ND	ND	ND	ND	ND	5 y

(*continued on next page*)

Table 6 (*continued*)

Author	Name of surgical technique	Nasal symmetry	Methods of analysis used	PIO or NAM	Columellar symmetry	Alar symmetry	Septal repositioning	Nasal tip projection	Complications (if any reported)	Disadvantages (if any)	Follow- up period
	interdomal sutures to relocate the displaced cleft side lower cartilage Group II: no cartilage dissection of the lower lateral cartilage Group IV: a rim incision on non cleft side, and Tajima inverted U-Incision on cleft side	nostril height **Nostril width:** all groups showed wider nostril than non-cleft side. Group IV had narrowest nostril **One-fourth medial part of nostril height:** Group IV and III showed a statistically difference from the other groups **Nasal sill height:** group II, III, and IV had statistically significant improved nasal sill height **Nostril area:** Group III and group IV had statistically significant different areas from group I and II **Inner nostril height to width ratio:** group IV demonstrated more rounded cleft side nostril **Group IV had the best overall assessment**									
Numa et al. (2006)	Study group: ABF-SS technique with primary rhinoplasty Control group: MRA with primary rhinoplasty	ABF-SS technique showed statistically significant improved degree of symmetry in nostril size, nostril shape, nostril symmetry	Photographs: frontal, lateral and standard basilar views Visual analogue ordinal scale ranging from 0 to 4	No	ND	ABF-SS technique showed statistically significant improved symmetry in alar base	ND	ABF-SS technique showed statistically significant improved symmetry in nasal tip/ dome	None	ND	1y −2 y post lip repair Study group: 14 mo (6−28 mo) Control group: 19 mo (9−60 mo)
B) Patients with unilateral complete cleft lip and alveolus/Unilateral complete cleft lip, alveolus and palate											
Zaleckas et al. (2011)	1. TR 2. MRA 3. Olekas (modified G. Pfeifer or wave incision with a small triangular flap above the red lip)	**NOSE RATING** (mean ± SD TR: 2.25 ± 0.32 MRA: 2.48 ± 0.5 Olekas: 1.89 ± 0.2 Scars and nose looked best after Olekas technique	Photographs: en face, right and left profile, standard basilar view Modified rating scale by Mortier et al.	PIO	ND	ND	ND	ND	ND	ND	9 y- 24 y Mean age at the time of evaluation: TR:20.5 ± 3.2 MRA: 15.2 ± 2.7 Olekas:10.5 ± 1.2
Gosla Reddy et al., 2011	Group A: Afroze incision without septoplasty Group B: Afroze incision with septoplasty	Nostril height, and nostril gap area: Group B showed significantly lower asymmetry For both groups, nostril height shows the	Photograps:standard basilar view and frontal Photographic analysis as described by Mommaerts and Nagy	No	Columella-to-Cupid's bow distance: Group B showed significantly lower asymmetry	For alar base-to-inter-pupillay line distance, better asymmetry in Group B	ND	ND	ND	ND	2 y

		largest aymmetry of all variables	Indirect anthropometry on digital photographs in Photoshop								
Yamada et al. (2002)	Group I: Triangular flap surgical method: "old method": Bernstein): size of triangular flap: 4 mm Group II: Rotation advancement plus small triangular flap surgical method ("new method": Onizuka) size of triangular flap: 2 mm	Asymmetry of the nostrils in both groups. Asymmetry of the superior point of the nostril (antero-posteriorly and vertically) was most obvious In the triangular group, this deformity was evident at an earlier stage already (3 mo after surgery) Shape of the nose and the nostril better in rotation group	3D optical scanner 3D anthropometry	PlO	Base of columella deviated towards normal side in both groups (±8 mm before surgery, and 2–3 mm after surgery); no difference between the groups	Wider alar width in both groups when compared with normal Alar width at the cleft side increased in both groups	ND	Protusion of the nasal tip has decreased in the triangular group at 1.5 years of age	ND	ND	18 mo
C) Patients with unilateral complete cleft lip, alveolus, and palate											
Suchyta et al. (2020)	Fisher repair Millard Mohler repair	**Nasal symmetry** No statistical significant difference: Fisher: 2.61 ± 0.41 Millard: 2.65 ± 0.51 Mohler: 2.66 ± 0.28 Control images: 3.82 ± 0.14 **General appearance** No significant difference Fisher: 3.30 ± 0.45 Millard 3.18 ± 0.31 Mohler: 4.46 ± 0.16 **Average satisfaction of respondents:** Fisher: 60.2 ± 15.7% Millard: 58 ± 11.8% Mohler:57 ± 13.3% Control: 91.4 ± 2.20%	Photographs: Asher-McDade scale Likert scale: 1-5	No	ND	ND	ND	ND	**Scar severity:** Millard >Mohler >Fisher	ND	4y-6y
Rossell-Perry (2020)	Group I: modified McComb technique Group II: Potter technique Group III: V–Y-Z method	In group I: statistically significant differences were observed between the cleft and non cleft sides for nostril dome height	Anthropometry using Castroviejo caliper	No	In group I: significant differences between cleft and non cleft sides for columella length	In all three groups, statistically significant differences between the cleft and non cleft sides for alar base width	ND	ND	McComb technique: greater nasal deformity recurrence Potter technique: turned-up nose and scar V–Y-Z technique: recurrence, but less as compared to above two	McComb technique: greater recurrence	Group I: 14.36 mo (range: 12 mo–19 mo) Group II: 15.09 mo (range: 12 mo–20 mo) Group III: 14.41 mo (12 mo –18 mo)
Mølsted et al. (2017)	Trial 1: MRA, Gothenburg method, TR Trial 2: MRA, Gothenburg method, TR Trial 3: MRA	**Nasal form and deviation and nasolabial profile** Statistically significant differences between trials 1 and 3, and trials 2 and 3 Score were best in trial 2 for nasal form and	Photographs: Frontal view, cleft-side profile view, and standard basilar view Scored using 5-point ordinal scale using Modified Q-sort method described by Mercado et al.	No	ND	ND	ND	ND	ND	ND	5 y of age

(*continued on next page*)

Table 6 (*continued*)

Author	Name of surgical technique	Nasal symmetry	Methods of analysis used	PIO or NAM	Columellar symmetry	Alar symmetry	Septal repositioning	Nasal tip projection	Complications (if any reported)	Disadvantages (if any)	Follow- up period
		deviation Better outcome was seen in trials 1 and 2 for nasolabial profile MRA preferred by all surgeons in all trials									
Freeman et al. (2013)	Classic Millard with nasal correction: 30 Modified Millard without nasal correction: 45	Percentage nasal asymmetry was measured for three parameters: front perimeter, base perimeter, and nostrils FRONT PERIMETER Control group more symmetry than other two No significant difference between the two cleft groups BASE PERIMETER Significant more asymmetry in modified Millard than classic Millard and control group, and significant more asymmetry in classic Millard than control NOSTRIL Modified Millard having highest asymmetry, followed by classic Millard, and then control group TOTAL Modified Millard had more asymmetry than classic Millard and control	Symnose, a computer-assisted technique Facial photographs in frontal and standard basilar view	No	ND	ND	ND	ND	ND	ND	10 y
Morselli et al. (2012)	Group A: primary rhinoseptoplasty Group B: Cheiloplasty without primary correction of nasal deformities	**Minimum and Maximum nostril diameter** Group A: 9.60 mm and 5.50 mm on cleft side, and 9.70 mm and 5.40 mm on the contra-lateral side. Group B: 12.10 mm and 6.0 mm on the cleft side, and 9.75 mm and 6.50 mm on the contra-lateral side Perfect symmetry of nostril thickness was	Anthropometry, by using a caliper Morphologic and functional evaluation by nasal endoscopy	No	**Columella length** Group A: 6.10 ± 1.17 mm Group B: 7 ± 1.41 mm **Columella width** Group A: 5.70 ±1.03 mm Group B:6.25 ± 1.48 mm	**Mean value of nasal ala thickness** Group A: 3.20 mm on cleft side, and 3.40 mm on the contra-lateral side Group B: 5.75 mm on the affected side, and 4.25 mm on the contra-lateral side	ND	**Nasal tip protusion** Group A:11.8 ± 1.44 Group B:13.3 ± 2.03	Group B: 60% of patients have bone spurs, 70% had turbinate hypertrophy	ND	Group A: mean age: 6.2 ± 0.5 y Group B: 8.1 ± 0.3 y

		significantly higher in Group A vs B **Nasal width mean value** Group A: 28.60 ± 1.6 mm Group B: 30.50 ± 1.96 mm **Nasolabial angle** Group A: 101.25 ± 8.35° Group B:94.50 ± 6.86°									
Horswell and Pospisil, 1995	MRA: 17 Del: 16	Less nasal protusion in proportion to nasal height and width in the MRA group compared with Del and NC Nostril length less on cleft side in MRA group when compared to Del. The mean difference between the cleft and non-cleft sides in each group tended to be less for nostril length in Del group	Frontal and standard basilar view photographs Anthropometric measurements	No	ND	Mean difference between cleft and non cleft sides in each group tended to be less for alar-base width and alar length in Del group	ND	MRA leads to more asymmetrical noses, greater tip deviation, and are shorter, wider with less anterior projection	ND	ND	4-5 y of age
Amaratunga, 1988	Group I: MRA Group II: LeMesurier	**Nostril height:** Better in Millard Millard: 81.7 ± 2.14 LeMesurier: 67.3 ± 3.52 **Nostril width** Not significantly different in any Millard: 109.8 ± 7.16 LeMesurier:98.2 ± 9.36 LeMesurier gives a symmetrical nasal floor	Measurements with a vernier caliper. Cleft Lip Component Symmetry Index (CLCSI)	No	ND	Ala more in position in Millard	ND	ND	More contracture with Millard than LeMesurier	ND	1 y

PIO: Pre-surgical infant orthopedics; NAM Naso-alveolar molding; MRA: Millard Rotation-advancement technique; ND: not defined; AR: alar surface area obtained by 'Cleft alar surface area divided by non-cleft alar surface area'; 3D: Three-dimensional; mo: months; y:year; Min: Minimum; TR: Tennison Randall technique; 2-D: Two dimensional; NLA: Naso-labial advancement; LA: Labial advancement; CPH: Cupid's peak height; CBH: Columella base height; NBH: Nasal alar base height; sn-cphi: sub-nasale to peak of cupid's bow; sbal-cphi: peak of cupid's bow to subalare; SR: Symmetry ratio = cleft counts divided by non-cleft counts; sbal-ch: chelion to subalare; vh: vermillion height; wrt: with respect to; avg: average; VAS: visual analogue scale; Del: Delaire's cheiloplasty; ABF-SS: Alar base flap and suspending suture technique; NNC: no nasal correction group; PNC: primary nasal correction group; MRA: Modified rotation advancement technique.

bias in measurement of outcomes in one study (*Yamada et al., 2002a,b*). GRADE assessment observed very low evidence for nasal symmetry and complications in all of the studies.

3.6.3. Patients with unilateral complete cleft lip, alveolus and palate

Seven studies with a total of 866 patients were included (*Suchyta* et al., 2020; *Rossell-Perry, 2020*; Mølsted et al., 2017; *Freeman* et al., 2013; *Morselli* et al., 2012; *Horswell and Pospisil, 1995*; and *Amaratunga, 1988*). Study location was variable for all the studies, except for two studies which were carried out in the United Kingdom (*Freeman* et al., 2013 and *Horswell and Pospisil, 1995*), and one study was multicentric (*Mølsted et al., 2017*). Four studies were cohort studies (*Freeman* et al., 2013; *Morselli* et al., 2012; *Horswell and Pospisil, 1995*; and *Amaratunga, 1988*), two were cross-sectional studies (*Suchyta* et al., 2020; *Rossell-Perry, 2020*), and one was an RCT (*Mølsted et al., 2017*). Rhinoplasty was carried out along with the primary lip repair in all except two studies (*Suchyta* et al., 2020 and *Amaratunga, 1988*).

The study groups were not comparable in any of the studies. *Freeman* et al. (2013) compared RA or its modifications. *Suchyta* et al. (2020), *Mølsted et al. (2017)*, *Horswell and Pospisil (1995)* and *Amaratunga (1988)* compared RA techniques with the Fisher anatomical sub-unit technique, triangular repair, Delaire functional repair, and LeMesurier quadrangular technique, respectively. *Rossell-Perry (2020)* compared three techniques of rhinoplasty, namely, the., modified McComb, Potter and V–Y-Z technique. *Morselli* et al. (2012) compared primary cheiloplasty with or without rhinoseptoplasty.

RA or its modifications was the main technique observed in this study (*Suchyta* et al., 2020; *Mølsted et al., 2017*; *Freeman* et al., 2013; *Horswell and Pospisil, 1995*; and *Amaratunga, 1988*). *Suchyta* et al. (2020) reported maximum average respondent satisfaction in the Fisher technique, followed by the MRA and Mohler technique. *Rossell-Perry (2020)* reported that the V–Y-Z technique was better when compared to the Potter and modified McComb technique. MRA was the most commonly preferred technique, as shown by *Mølsted et al. (2017)*. More asymmetry was observed in nasal base perimeter and in the nostrils when compared with the MRA technique as reported by *Freeman* et al. (2013). There was a significantly higher nostril thickness symmetry when primary rhinoplasty was performed along with cheiloplasty (*Morselli* et al., 2012). The Delaire functional technique was considered better than the MRA technique, as less nasal protrusion, along with a shorter nostril length on the cleft side, was seen in MRA techniques (*Horswell and Pospisil, 1995*). The MRA technique was observed better than LeMesurier technique in terms of nostril height and nasal alar positioning, but the latter was considered superior in terms of nasal floor and scar contracture (*Amaratunga, 1988*).

Photographs were used for nasal symmetry analysis in three of the studies (*Suchyta* et al., 2020; *Mølsted et al., 2017*; *Freeman* et al., 2013), while anthropometry was used in two methods (*Rossell-Perry, 2020*; *Morselli* et al., 2012). *Horswell and Pospisil (1995)* used both photographic assessment and anthropometry. The Cleft Lip Component Symmetry Index (CLCSI) was used in the study by *Amaratunga (1988)*.

PIO or naso-alveolar molding was not used in any of the studies. Septal repositioning and disadvantages were not defined in any of the studies. Columellar symmetry was defined in two studies (*Rossell-Perry, 2020* and *Morselli* et al., 2012). Significant differences were observed between cleft and non-cleft sides for the modified McComb technique (*Rossell-Perry, 2020*). The columellar was more symmetrical in patients undergoing primary rhinoseptoplasty along with primary cheiloplasty (*Morselli* et al., 2012). Alar symmetry was defined by four studies (*Rossell-Perry, 2020*; *Rossell-Perry, 2020*; *Horswell and Pospisil, 1995* and *Amaratunga, 1988*). *Rossell-Perry (2020)* observed no significant difference between cleft and non-cleft side for alar base width. Superior results were obtained for alar symmetry by primary rhinoseptoplasty along with primary cheiloplasty (*Morselli* et al., 2012). The Delaire technique resulted in better alar symmetry when compared to MRA (*Horswell and Pospisil, 1995*). MRA led to better alar positioning than the LeMesurier technique (*Amaratunga, 1988*). Two studies defined nasal tip projection (*Morselli* et al., 2012 and *Horswell and Pospisil, 1995*). The LeMesurier technique resulted in more asymmetrical noses than MRA (*Horswell and Pospisil, 1995*), as well as primary rhinoseptoplasty (*Morselli* et al., 2012). Complications were defined by four studies (*Suchyta* et al., 2020; *Rossell-Perry, 2020*; *Morselli* et al., 2012 and *Amaratunga, 1988*). The maximum follow-up period seen was 10 years (*Freeman* et al., 2013).

Risk assessment of the non-randomized studies via ROBINS-I tool revealed moderate risk in three studies (*Freeman* et al., 2013; *Horswell and Pospisil, 1995* and *Amaratunga, 1988*), low in two studies (*Suchyta* et al., 2020; *Suchyta* et al., 2020) and serious risk in one study (*Rossell-Perry, 2020*). Risk assessment of RCTs by the Cochrane Risk of Bias 2 (RoB-2) tool showed unclear risk in blinding of participants and personnel.

3.7. Reported complications of lip surgery

3.7.1. Lip scar formation/scar contracture

Hypertrophic scar formation with respect to the lip was reported by three studies (*Suchyta* et al., 2020; *Kwong* et al., 2019; and *Amaratunga, 1988*), all of which observed greater severity of scar in MRA technique when compared to the Mohler and Fisher technique (*Suchyta* et al., 2020; *Kwong* et al., 2019) and the LeMesurier technique (*Amaratunga, 1988*).

The upper part of the scar was reported to be closer to the nose after MRA, while the lower part of the scar was closer to the lip after the TR technique (*Kwong* et al., 2019). Also the modified Mohler technique resulted in one longitudinal and one transverse scar, while TR resulted in a Z-shaped scar above white roll on the cleft-side (Rossell-Perry, 2020).

3.7.2. Nasal deformity and its recurrence

Turned-up nose was noted in the Potter technique (Rossell-Perry, 2020). Nasal deformity recurrence was reported in only one study, with the McComb technique resulting in a greater recurrence when compared to the Potter technique or V–Y-Z technique (Rossell-Perry, 2020).

3.7.3. Other complications

Of the 11 included studies concerning concomitant rhinoplasty, only one study reported complications; namely,i.e.,in patients undergoing cheiloplasty without primary rhinoplasty, nasal bone spurs were observed in 60% of the patients, and turbinate hypertrophy in 70% of the patients (*Morselli* et al., 2012). No complications were reported if the patient was undergoing primary lip repair with either the alar base flap and suspending suture (ABF-SS) technique or MRA technique, along with primary rhinoplasty (Numa et al., 2006).

Complications were not defined in nine of the included studies (Mølsted et al., 2017; Rossell-Perry, 2016; Cline et al., 2014; Freeman et al., 2013; Zaleckas et al., 2011; Gosla Reddy et al., 2011; Chang et al., 2010; Yamada et al., 2002a,b; Horswell and Pospisil, 1995).

4. Discussion

This SR mainly focused on nasal symmetry after UCCLAP repair in patients less than 1 year of age. Although this SR included many different philosophies for repair, it included only one RCT (*Mølsted* et al., 2017), with the rest being cohort studies and non-randomized cross-sectional studies. This RCT favored the MRA technique, as a greater reduction was observed in the cleft-side nasal width when compared with TR (*Mølsted* et al., 2017). However, the outcome assessment varied widely between studies, and therefore it is very difficult to draw conclusions about the effectiveness of one lip repair procedure compared to another. Also, the papers published to date have evaluated the results without long-term outcomes, without considering the change in the soft tissue landmarks with the growth of the patient, and without defining the exact sub-type of the cleft patients being included, and without variables such as width of the cleft, severity of the nasal dome collapse, extent of the septal deficiency and deformity, and difference in the alveolar height, which can affect the nasal symmetry.

4.1. Nasal symmetry

Overall, RA was the most frequently encountered technique, although the literature reveals that MRA has limited effectiveness in UCCL repair due to its inability to lengthen the lateral lip segment, and thus appears to be useful mainly in patients with incomplete UCL with minimal tissue deficiency (*Rossell-Perry*, 2016). In this review, incomplete CL were excluded, so no conclusion can be drawn about the effectiveness of MRA in these types of clefts. Most of the studies in this review comparing the triangular repair with the RA techniques preferred RA or its modifications; however, nasal flattening, columellar deviation, peaking and notching were higher in the MRA group due to the vermilion's straight line closure (*Suchyta* et al., 2020). The Fisher repair proved to be superior to the RA technique or its modifications in our review, with improved quality of scar and greater symmetry restoration, with fewer revision surgeries (*Suchyta* et al., 2020). Neither RA nor straight line repair was superior to the other according to our review. Our review also observed that a straight line repair (Olekas) gave improved nasal results and better scars when compared to MRA or TR (*Zaleckas* et al., 2011).

Based on the results of this SR, the Delaire technique may be preferred over the modified RA (MRA), as the latter results in more asymmetrical noses in patients with more tip deviation, and also in wider and shorter noses with less anterior projection. However, evidence is limited, as it arose from one retrospective cohort study with a small sample size (N = 16) (*Horswell and Pospisil, 1995*). No significant difference was noticed when MRA and quadrangular techniques were compared. Although nostril height was better in MRA along with alar position, the Le Mesurier quadrangular technique gave a more symmetrical nasal floor in one prospective cohort study (sample size N = 50) (*Amaratunga, 1988*).

4.1.1. Concominant rhinoplasty or septoplasty

Some protocols for cleft lip nose correction suggest the use of NAM or primary rhinoplasty to obtain better surgical outcomes. However, primary rhinoplasty might interfere with nasal development, leading to the functional impairment (*Rossell-Perry*, 2020). This SR observed satisfactory outcomes with simultaneous lip–nose repair (*Morselli* et al., 2012). Patients who underwent rhinoseptoplasty had eight times greater chances of getting significantly higher symmetry of nostril thickness than those who underwent only cheiloplasty (*Morselli* et al., 2012). *Latham* hypothesized that the nasal septum is the key factor for the attainment of the height and facial anteroposterior dimensions (*Latham, 1969*), equivalent to *Reddy* et al., who concluded that primary septoplasty showed significant better alar height and nasal symmetry (*Reddy* et al., 2011).

4.1.2. Methods of nasal symmetry analysis

Although clefts are the most common craniofacial anomaly, a tool for post-operative aesthetic outcome is yet to be found. It can be assessed by direct clinical examination, videographic assessment, two-dimensional clinical photographs, or by three-dimensional (3D) methods. Quantitative methods were used by the majority of the studies in this review, with only one study using a 3D optical scanner (*Yamada et al., 2002a,b*). Focus should be placed on emerging 3D technology (*Loon* et al., 2011), the 3dMD Face system (*Perdanasari* et al., 2020), and 3D Rugle V software (*Matsunaga* et al., 2016). These are recommended for more effective and reproducible results.

Although improvement in nasal symmetry was observed in all types of UCCLAP repair, this outcome might be substantially different from the estimated result, as the GRADE showed very low quality of evidence for the nasal outcome. A total of 15 studies were included, but meta-analysis could not be accomplished due to the high level of heterogeneity among the studies. Risk of bias was moderate in 10 studies, with serious risk in one study; hence the results should be interpreted with discretion.

4.2. Complications

Of the 15 studies, only six studies reported complications. The most common complication encountered in this SR is the formation of the hypertrophic scar on the lip, and the most common associated technique responsible was MRA. Although, nasal deformities are reported in abundance in literature after UCCLAP repair, they are observed to be minimal in this SR. Good outcomes were obtained in patients undergoing primary lip repair with rhinoplasty, and only one study reported bony spurs and turbinate hypertrophy as complications.

The quality of evidence as assessed by GRADE was very low for complications. Limitations, inconsistency and imprecision were serious in all studies that reported complications. No two studies had similar variables to compare, and hence meta-analysis could not be performed.

4.3. Limitations of the study

This systematic review was hampered by the lack of high-quality studies concerning the effects of cleft surgery on nasal shape in patients with UCCLAP. Only one RCT could be included, and most studies were non-randomized retrospective comparative studies. Other issues that complicated this SR were unclear definition of a CL in many studies; samples with a wide age range with an undefined number of children below 1 year of age; use of NAM or PIO not specified; variability in follow-up; and surgeries performed by a number of surgeons with different or unspecified levels of expertise. Additionally, some authors evaluated results after cleft palate repair, and some before their repair. Furthermore, photographic evaluation lacked standardization, and methods to assess nasal symmetry were diverse, with outcomes being

measured by nonblinded assessors. Also, there was a bias towards English-language articles, as other languages were excluded.

The methodological and clinical heterogeneity of the studies included complicated the comparison of their results and prevented a combined quantitative synthesis in the form of a meta-analysis. The quality of the evidence was rated as very low for observational studies, and moderate for RCT according to the GRADE assessment, which means that clinical applicability must be interpreted with caution.

5. Conclusion

The present SR included a plethora of techniques for the correction of UCCL in an effort to produce a "perfect repair." The results may point to the RA technique being superior to its modifications and the triangular technique in terms of nasal symmetry. However, RA was equivalent to straight line repair and quadrangular repair and inferior to the Fisher and Delaire repair. Therefore, these results should be considered with caution due to the wide heterogeneity of the study. The majority of the studies used soft tissue landmarks for determining short-term symmetry; however, long-term changes should be assessed as well, as growth may lead to significantly different outcomes.

Future research that examines the effects of surgical protocols on the shape of the nose requires RCTs with larger sample sizes and appropriate length of follow-up, and surgeries preferably performed by a single experienced surgeon. The global cleft community should agree on a minimum core outcome set of standardized documentation to enable inter-center comparisons to obtain results with a high quality of scientific evidence, thus providing an improved guide for the surgeon's clinical decision-making.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Source of support/Funding sources

None.

CRediT author statement

Adity Bansal: Conceptualisaton, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualisation, Roles/writing: Original draft, Srinivas Gosla Reddy: Conceptualisaton, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualisation, Supervision, Writing: review and editing, Ashi Chug: Conceptualisaton, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualisation, Supervision, Writing: review and editing, Anthony F Markus: Conceptualisaton, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualisation, Supervision, Writing: review and editing, Anne Marie Kuijpers-Jagtman: Conceptualisaton, Data curation, Formal analysis, Investigation, Methodology, Validation, Visualisation, Supervision, Writing: review and editing.

Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcms.2022.12.006.

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