



Review

Predicting the need for orthognathic surgery in cleft patients: A systematic review

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ABSTRACT

Objectives: A systematic review was performed to determine the predictive factors for orthognathic surgery in the cleft population.

Materials & methods: A systematic search was made in Cochrane, Embase, Pubmed, Scopus, Web of Science and Google Scholar based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The search terms focus on the variables or factors that are associated with or predictive for the later need for orthognathic surgery in patients with cleft lip &/or palate (CLP). Clinical studies published from inception until July 2024 were included. Full text of potentially relevant studies were retrieved and independently examined by two reviewers.

Results: A total of 296 articles were identified. Eighteen studies were eligible for final inclusion. Out of the 1345 patients, unilateral CLP was the most common cleft subtype (64.0 %). All were retrospective in nature and the quality of most studies was moderate. Due to the heterogeneity of the studies, a meta-analysis could not be performed. Factors that were significantly associated with indication for future orthognathic surgery in cleft children were categorised into a) iatrogenic, b) intrinsic and c) cephalometric-based variables. Amongst all the factors in these 3 categories, a lower ANB angle was the most widely mentioned predictive factor for subsequent OGS in CLP patients. The age at which such prediction was derived, ranged from 5 to 11 years old.

Conclusion: Although further well-controlled studies are needed to better provide clinicians with predictive factors of the need for cleft orthognathic surgery, both intrinsic and iatrogenic factors have been shown to influence the overall maxillofacial growth in CLP patients.

1. Introduction

1.1. Background

Up to 25–60 % of cleft lip and/or palate (CLP) patients are at risk of needing orthognathic surgical correction of their dentofacial skeletal deformity (Hathaway et al., 2011). Being the most common birth defects of the human face, CLP affects about 1 in every 700 newborns worldwide. Comprehensive surgical management of these patients span from infancy to adulthood. This includes primary cleft lip repair, primary cleft

palate repair, alveolar bone graft, orthodontics and secondary cleft surgeries. The latter include secondary nasolabial revision, velopharyngeal insufficiency correction, palatal fistula repairs, orthognathic surgery (OGS) and rhinoplasty.

CLP patients commonly present with malocclusion and maxillary hypoplasia due to alterations in their facial growth and development. The disturbance in maxillary development is often associated with the innate facial growth deficiencies and maxillary tissue scarring from previous CLP surgeries. The dentofacial appearance of CLP usually involve skeletal Class III malocclusion with short and retrusive maxilla,

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maxillary arch constriction, mandibular counter-clockwise and vertical overgrowth, dental crossbite, and an overall concave facial profile (Shetye, 2004).

These dentofacial deformities negatively impact mastication, speech, appearance, social interaction and quality of life (Rustemeyer and Gergsen, 2012). While orthodontics can align and level maxilla-mandibular arches, tooth movement alone may not always be sufficient to correct or mask more severe skeletal discrepancies (Lisson and Weyrich, 2014). This limitation is known as the “envelop of discrepancy” (Proffit et al., 2007). Thankfully, maxillary osteotomies offer a surgical solution to improve the form and function of the face and stomatognathic system of these cleft patients (Lisson and Weyrich, 2014; Lin et al., 2018).

Predicting an individual’s likelihood for the need for orthognathic surgical correction of dentofacial deformity may better prepare the patients and families towards treatment acceptance. Unsurprisingly, the anticipated number of surgeries is a major concern for patients and their caregivers (Jacob et al., 2022). Besides the extended duration for complex treatment (Alansari et al., 2014; Hameed et al., 2019), the need for frequent follow-ups, surgical & orthodontic-associated discomfort and pain may induce treatment fatigue in these cleft patients. These associated physical, psychological and economic burden are often also shared by their caregivers (Imani et al., 2021; Celie et al., 2024).

In CLP children, however, it is difficult to pinpoint the specific threshold and considerations for treatment selection between orthodontics or that combined with surgical intervention (Lisson and Weyrich, 2014; Lin et al., 2021). Inappropriate selection of orthodontics alone for surgical cases may result in greater morbidity. These include extended duration spent to reverse the orthodontically compensated dentition, increased clinical visits, higher costs and additional risks associated with extended orthodontic treatment (Lisson and Weyrich, 2014).

This motivates the search for factors with prognostic relevance to further optimise planning and customisation of clinical management for cleft patients. Collection and evaluation of these data may potentially help construct prediction models that help forecast and stratify cleft children according to their risks for adverse dentofacial development and need for orthognathic corrective surgery (Nollet et al., 2008).

1.2. Aim

The purpose of this study is to evaluate the evidence regarding variables that may help predict the need for orthognathic surgery in growing CLP patients.

2. Materials & methods

2.1. Search strategy

The present review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The search was carried out in 6 electronic databases (Cochrane, Embase, Pubmed, Scopus, Web of Science and Google Scholar) to identify published articles from inception till 5 July 2024. In addition, a manual search of reference lists from included studies were also performed.

Based on a population, exposure and outcome (PEO) framework (Table 1), the research question for this study was designed as such, “What are the predictive factors for orthognathic surgery amongst

growing cleft children?”

The search used combination of the following MeSH (Medical Subject Headings) terms as well as other non-MeSH terms that might identify articles directly related to the research area under investigation: “cleft palate”, “cleft lip”, combined with the terms “prediction” OR “prognosis” OR “forecasting” AND “orthognathic surgery”. The electronic search was complemented by a manual search among bibliographic references of the studies picked up from the electronic search, to locate any further articles that the primary search had failed to identify. Titles and abstracts were reviewed independently by 2 reviewers (SJHT, CHJS) and differences resolved through discussion to reach a consensus.

2.2. Eligibility criteria

The inclusion criteria were: (1) full-text publications (2) in English featuring (3) cross-sectional, cohort studies or randomised controlled trials on (4) variables or factors that are associated with or predictive for (5) the need for orthognathic surgery (6) in patients with orofacial cleft (subtypes cleft lip, cleft palate, cleft lip & palate).

The exclusion criteria were: (1) duplicate studies, (2) meta-analyses, reviews, systematic reviews, conference papers and book chapters, (3) abstracts or titles only (absence of full text), (4) case studies, case series, expert opinions, letters, editorials, animal studies, (5) studies with reference only on facial growth & development but lacking explicit association to indication of and assessment for orthognathic surgery in cleft patients.

2.3. Data extraction & synthesis

Data was extracted into a Microsoft excel spreadsheet. A descriptive summary and narrative analysis of the included studies was performed. The collated data include authors, year of publication, country of the study population, study design, purpose of study, cleft subtypes, overall cleft treatment protocol of study population, assessment age for OGS, decision parameter for indication of OGS, evaluated variables that were predictive for &/or correlated with need for OGS and conclusion of study.

Due to the heterogeneity of the published data and study designs, no meta-analysis could be performed. The main reasons for this were that many studies did not report confidence intervals, the non-uniformity in the assessments for the need for OGS and lack of common overall cleft treatment protocol across different centres. Thus, the following descriptive data was extracted from each study: authors, year of publications, country and cleft institution, study design and aim, cleft subtypes, overall cleft treatment protocol, age & method of assessment for need for OGS, factors related to increased need for OGS, conclusion of study.

2.4. Assessment of study quality

The Newcastle Ottawa Scale (NOS) (Wells et al) was used to assess the quality of cohort and case-control studies included in this review. The NOS for both study types consist of eight questions among three domains. Stars are allocated for adequate methodology and a score of good (7 or more stars), fair (4–6 stars) or poor (below 4 stars) will be given for each study.

3. Results

3.1. Selection of studies

A total of 296 citation records were identified from searching of the six databases. After the duplication removals (n = 53), 243 articles remained. Through further exclusions, 18 studies (17 retrospective studies and 1 case-control study) were included in the systematic review. Fig. 1 illustrates the selection process.

Table 1
PEO framework of review.

PEO Framework	
Population (P)	Patients with cleft lip &/or palate
Exposure (E)	Variables associated with/predictive of
Outcome (O)	Need for future orthognathic surgery

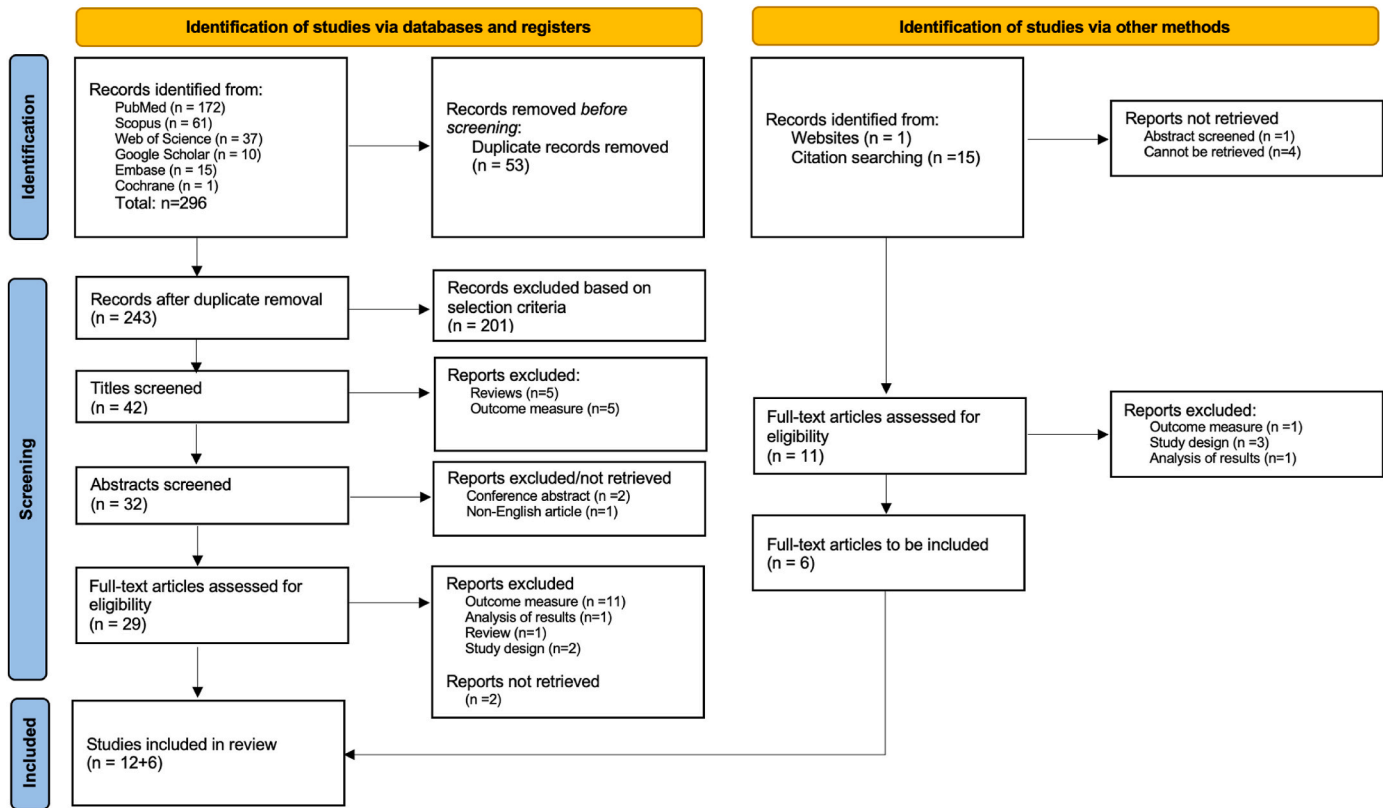


Fig. 1. PRISMA flowchart.

3.2. Quality of studies

The selected studies were evaluated and tabulated for qualitative analysis (Table 2). After quality assessment via the NOS, it was observed that 17 of the studies were of “good” quality and 1 was of “moderate” quality.

3.3. Cleft subtypes

The total number of CLP patients was 1345 (Table 3). The number of patients from each cleft subtypes are as follows: 862 with unilateral cleft lip and palate (UCLP), 170 with bilateral cleft lip and palate (BCLP), 75 with cleft lip and alveolus (of which 33 were unilateral, 7 bilateral and 35 unspecified), 229 with isolated cleft palate, 10 with isolated cleft lip

and 35 with isolated cleft alveolus. Nine studies restricted their cleft population (total n = 533) to patients with UCLP. One study (Antonarakis et al., 2015) was solely on patients with cleft palate (n = 189) and another study (Heliövaara et al., 2013) was conducted only on patients with BCLP (n = 38). The rest of the seven studies included children of various cleft subtypes (Table 3).

3.4. Overall cleft treatment protocol

3.4.1. Cleft lip repair

10 out of the 18 included studies reported on the technique used for cheiloplasty (Table 5). The two techniques reported in the studies are the straight-line repair technique (Kamata et al., 2023) and that of Millard’s technique (Nollet et al., 2008; Liao et al., 2010; Heliövaara and

Table 2
Quality assessment of included studies using the Newcastle Ottawa Scale.

No	Author	Year	Selection	Comparability	Outcome	Quality Score
1	Nollet et al	2008	****	**	***	High
2	Oberoi et al	2008	***	**	**	High
3	Liao et al	2010	****	**	***	High
4	Heliövaara et al	2011	****	**	***	High
5	Heliövaara et al	2013	****	**	***	High
6	Lee et al	2014	****	-	**	Moderate
7	Antonarakis et al	2015	****	*	**	High
8	Meazzini et al	2015	****	**	***	High
9	Park et al	2015	***	**	**	High
10	Yun-Chia et al	2017	****	**	***	High
11	Dalle et al	2017	****	*	***	High
12	Heliövaara et al	2021	****	**	***	High
13	Lim et al	2021	****	**	***	High
14	Lin et al	2021	****	*	***	High
15	Yu et al	2021	****	**	***	High
16	Lau et al	2022	****	*	**	High
17	Kamata et al	2023	***	*	***	High
18	Lim et al	2023	****	*	***	High

Table 3
Details of the included studies.

No.	Authors (Year)	Country/Centre	Study Design	Aim	Cleft Subtypes	Age of Assessment for OGS	Conclusion
1	Nollet et al. (2008)	Netherlands [Nijmegen Cleft Palate Craniofacial Unit]	Retrospective cohort	To evaluate the craniofacial development of patients with a complete UCLP and to develop prediction models for cephalometric outcome at adulthood.	Complete UCLP (n = 43)	18 years old	Correct prediction from cephalometric parameter at age 9 at 85 %
2	Oberoi et al. (2008)	USA [University of California, San Francisco, Centre for craniofacial Anomalies]	Case control	To delineate factors that may contribute to maxillary hypoplasia requiring maxillary advancement surgery in UCLP patients.	UCLP (n = 32)	NR	The need for OGS can be determined as early as 10–12 years of age by the degree of jaw size discrepancy (as measured by mandibular/maxillary unit length difference and the anterior-posterior position of the maxilla). Compared to the non-surgical patients, there was a significantly higher incidence of missing maxillary teeth and greater average number of surgical procedures (primarily secondary palatoplasty and fistula repairs)
3	Liao et al. (2010)	Taiwan [Chang Gung Craniofacial Centre, Taipei]	Retrospective cohort	To investigate if stage of palate repair, one-stage versus two-stage repair, had a significant effect of facial growth in patients with UCLP.	UCLP (n = 72)	20 years old	A significantly greater percentage of cleft patients who underwent one-stage palatoplasty required Le Fort I advancement/distraction as compared to those who underwent two-stage palatoplasty.
4	Heliövaara and Rautio (2011)	Finland [Cleft Palate and Craniofacial Centre, Helsinki University Central Hospital]	Retrospective cohort	To compare 6-year-old children with UCLP and children with unilateral cleft lip and a separate cleft palate, cephalometrically and to evaluate the need for orthognathic surgery later in life.	UCLP (n = 67) Unilateral CL + CP (n = 40)	Mean: 18.1 years old (15.6–20.5 years old)	At 6 years of age, UCLP children with ANB <0° should have orthodontic treatment planned for preparation for OGS. UCLP patients, of the same age, with ANB >4.5° do not seem to need OGS.
5	Heliövaara et al. (2013)	Finland [Cleft Palate and Craniofacial Centre, Helsinki University Central Hospital]	Retrospective cohort	To assess 6-year-old children with BCLP to determine the need for orthognathic surgery later in life and to cephalometrically compare the craniofacial morphology of those needing orthognathic with those not needing surgery.	BCLP (n = 38)	Mean: 18.2 years old (15.5–20.2 years old)	At 6 years of age, BCLP children with ANB <7° will likely need OGS when they are older.
6	Lee et al. (2014)	USA [University of California Los Angeles Craniofacial Clinic]	Retrospective cohort	To investigate the institutional experience with canine substitution and in cleft lip and palate patients and their need for orthognathic surgery.	CP (n = 10) UCLP (n = 65) BCLP (n = 20)	Mean: 18.1 years old (older than 15 years old)	A strong association is seen between orthodontic canine substitution (dental agenesis) with maxillary hypoplasia and subsequent OGS.
7	Antonarakis et al. (2015)	Canada [The Hospital for Sick Children, Toronto]	Retrospective cohort	To determine the frequency of need for orthognathic surgery among non-syndromic patients with isolated cleft palate repaired during infancy	CP (n = 189)	Minimum 15 years old	Higher tendency for the need for OGS in cleft patients of Asian descent (although not significant)
8	Meazzini et al. (2015)	Italy [University of Milan, Centre for Cleft Lip and Palate]	Retrospective cohort	To evaluate the craniofacial morphology at 5 and 10 years old and at the completion of growth, the need for orthognathic surgery and the orthodontic burden in patients with UCLP.	Complete UCLP (n = 62)	At the end of growth	At 5 years of age, UCLP patients with ANB smaller than 2° have a higher risk of need for OGS
9	Park et al. (2015)	South Korea [Seoul National University Hospital and Dental Hospital]	Retrospective cohort	To determine the cephalometric variables that can predict the future need for orthognathic surgery or distraction osteogenesis in Korean cleft males.	CLA (n = 35) UCLP (n = 56) BCLP (n = 40)	Mean: 17.3 years old (minimum of 15 years old)	A total of 10 cephalometric variables at the mean age of 9.3 yo (before alveolar bone graft) were selected as effective predictors of the future need for OGS (weighted classification accuracy was 77.3 %).
10	Yun-Chia Ku et al. (2018)	Taiwan [Craniofacial Research Centre, Chang Gung Memorial Hospital, Taoyuan]	Retrospective cohort	To predict the need for orthognathic surgery in patients with UCLP in the early permanent dentition	Complete UCLP (n = 61)	Mean: 15 years old (16.9–22.63 years old)	8 cephalometric variables were significantly different between group needing OGS and group that does not. At age of 11 yo: ANB </ = -0.45°, Overjet </ = -2 mm, maxillary length </ =

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Table 3 (continued)

No.	Authors (Year)	Country/Centre	Study Design	Aim	Cleft Subtypes	Age of Assessment for OGS	Conclusion
11	Dalle Ore et al. (2017)	USA [Rady Children's Hospital San Diego & University of California]	Retrospective cohort	To determine if timing of primary palate repair and primary lip repair contributed significantly to subsequent orthognathic surgery in a cohort of cleft patients.	UCLP (n = 32) BCLP (n = 20) Unilateral cleft lip (n = 8) Cleft palate (n = 11)	NR	47.25 mm (selected as the minimum number of discriminators needed to obtain an accuracy of 86.9 % in prediction for future need for OGS) Primary cleft lip repair before age of 3 months old was associated with increased incidence of later orthognathic surgery.
12	Heliövaara and Leikola (2021)	Finland [Cleft Palate and Craniofacial Centre, Helsinki University Central Hospital]	Retrospective cohort	To evaluate if dental arch relationships at 6 years of age can categorise treatment outcome and predict later need for orthognathic surgery in children with UCLP	Complete UCLP (n = 47)	16–18 years old	The use of 5-years-old index may help to predict treatment outcome and the clinical need for OGS in early adulthood
13	Lim et al. (2021)	Japan [Osaka University Hospital]	Retrospective cohort	To determine the prognostic factors for orthognathic surgery in children with cleft lip and/or palate using artificial intelligence systems.	BCLP (n = 19) BCLA (n = 5) UCLP (n = 71) UCLA (n = 20) CP (n = 11)	15 years old	The prognostic factors for OGS determined by artificial intelligence systems were the number of clefts in the lip and alveolus, the method of palatal repair, male gender and other cephalometric variables.
14	Lin et al. (2021)	South Korea [Seoul National University Children's Hospital & Seoul National University Dental Hospital]	Retrospective cohort	To determine the cephalometric predictors of the future need for orthognathic surgery in patients with repaired UCLP using machine learning.	UCLP (n = 56)	At or above 15 years old	At 6 years of age, it was possible to predict the future need for correction of sagittal skeletal discrepancy in patients with UCLP via cephalometric predictors (ANB, PP-FH, CF and FCA) with a good accuracy.
15	Yu et al. (2021)	South Korea [Seoul National University Children's Hospital & Seoul National University Dental Hospital]	Retrospective cohort	To investigate the cephalometric predictors of the future need for orthognathic surgery in Korean patients with UCLP despite long-term use of facemask with miniplat.	UCLP (n = 53)	Mean: 18.68 years old (minimum of 15 years old)	Math formula (see Table 10) A total of 6 cephalometric variables at the age of 10 years were selected as effective predictors of the future need for OGS.
16	Lau et al. (2020)	USA [University of the Pacific School of Dentistry, Orthodontic Clinic]	Retrospective cohort	To determine the soft tissue & skeletal cephalometric predictors for future orthognathic surgery in the mixed dentition phase of cleft lip and/or palate patients.	Isolated CP (n = 3) Isolated CL (n = 2) UCLP (n = 19) BCLP (n = 7)	13.77±2.24 years old	Upper lip to E-plane and lower lip to E-plane are the soft tissue variables with highest predictive value for OGS Frequency of surgery in patients with BCLP was significantly higher than those with UCLP.
17	Kamata et al. (2023)	Japan [Keio University Hospital]	Retrospective cohort	To reveal factors inhibiting maxillary growth and inducing later orthognathic surgery.	Complete UCLP (n = 32) Incomplete UCLP (n = 7) BCLP (n = 13)	At the end of growth	Palatal fistulae and repeated lip revision surgeries (of more than twice) were significant risk factors associated with later OGS.
18	Lim et al. (2023)	Japan [Osaka University Hospital]	Retrospective cohort	To determine dental and palatal morphology in children with cleft lip and/or palate and identify morphological prognostic factors for orthognathic surgery.	BCLP (n = 13) BCLA (n = 2) UCLP (n = 47) UCLA (n = 13) CP (n = 5)	15 years old	At the age of 7, "shrinkage of palate" (vertical shallowing, transverse narrowing of posterior maxilla and left-side asymmetry of anterior maxilla) derived from 3D digital models of these cleft patients (pre-orthodontics) was found to be a predictor of the clinical decision to perform OGS at a later age.

Rautio, 2011; Heliövaara et al., 2013; Antonarakis et al., 2015; Park et al., 2015; Yu et al., 2021; Heliövaara and Leikola, 2021; Lim et al., 2023). Majority of the reported cheiloplasty techniques are that of the original and modifications of the Millard's rotation and advancement flap technique. In most of the studies, primary cleft lip was repaired from 3 months old and above (Heliövaara and Rautio, 2011; Heliövaara et al.,

2013; Antonarakis et al., 2015; Park et al., 2015; Yun-Chia Ku et al., 2018; Heliövaara and Leikola, 2021; Lin et al., 2021; Yu et al., 2021; Kamata et al., 2023) with the exception of Nollet et al. (2008) and Liao et al. (2014) at 6–8 months and 4.8–14.4 months of age respectively.

Table 4

Determination for orthognathic surgery in included studies.

No.	Study	Cephalometric Parameters	Occlusal Parameters	Facial Aesthetic Parameters	Others
1	Nollet et al. (2008)	Overjet Incisal inclination Position of skeletal bases Soft tissue profile	When orthodontic treatment alone could not provide a functional occlusion Dental crowding	When orthodontic treatment alone could not provide a positive facial appearance	–
2	Oberoi et al. (2008)	–	–	–	–
3	Liao et al. (2010)	–	–	–	–
4	Heliövaara and Rautio (2011)	Maxillary hypoplasia - negative overjet - anterior crossbite - concave profile	Transverse deficiency - deficient maxillary arch width of lateral segments - posterior cross bite	Poor facial harmony Unbalanced profile Vertical deficiency - edentulous appearance - inadequate smile line	–
5	Heliövaara et al. (2013)	Maxillary hypoplasia - negative overjet - anterior crossbite - concave profile	Transverse deficiency - deficient maxillary arch width of lateral segments - posterior cross bite	Poor facial harmony Unbalanced profile Vertical deficiency - edentulous appearance - inadequate smile line Facial asymmetry Occlusal cant Bimaxillary retrusion	–
6	Lee et al. (2014)	–	–	–	Team recommendation
7	Antonarakis et al. (2015)	Apparent Class III skeletal relationship 1) ANB angle of $</ = -3^\circ$ 2) Wits appraisal of $</ = -5$ mm 3) Harvold unit difference (CoGn-CoANS) $>/ = 34$ mm Apparent Class II skeletal relationship 1) ANB angle of $>/ = 7^\circ$ 2) Harvold unit difference $</ = 15$ mm or smaller 3) Wits appraisal of 7 mm or larger	–	–	–
8	Meazzini et al. (2015)	Skeletal discrepancy Incisal inclination Soft tissue thickness	–	–	–
9	Park et al. (2015)	ANB $</ = -3^\circ$ Wits appraisal of $</ = -5$ mm Harvold unit difference $>/ = 34$ mm	–	–	–
10	Yun-Chia Ku et al. (2018)	Skeletal and dentoalveolar discrepancies Molar relationship Dental compensation	–	Facial profile	–
11	Dalle Ore et al. (2017)	–	–	–	–
12	Heliövaara and Leikola (2021)	Maxillary hypoplasia - severe AP discrepancy	–	Poor facial harmony Unbalanced profile Vertical deficiency - edentulous appearance - inadequate smile line Facial asymmetry Occlusal cant Bimaxillary retrusion & poor aesthetics	–
13	Lim et al. (2021)	ANB $>/ = 0^\circ$ or $< 0^\circ$ Wits appraisal $</ = -5$ mm Harvold unit difference $>/ = 34$ mm	–	–	Clinical recommendations by orthodontists
14	Lin et al. (2021)	ANB $</ = -3^\circ$ Wits appraisal of $</ = -5$ mm Harvold unit difference $>/ = 34$ mm	–	–	–
15	Yu et al. (2021)	ANB $</ = -3^\circ$ Wits appraisal of $</ = -5$ mm Harvold unit difference $>/ = 34$ mm	–	–	–

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Table 4 (continued)

No.	Study	Cephalometric Parameters	Occlusal Parameters	Facial Aesthetic Parameters	Others
16	Lau et al. (2020)	–	–	–	Clinical recommendations by 2 orthodontists and 2 oral & maxillofacial surgeons based on T2 patient records (13.77 ±2.4 years old)
17	Kamata et al. (2023)	–	–	–	Clinical recommendation by 2 orthodontists
18	Lim et al. (2023)	ANB >/ = 0° or < 0° Overjet >/ = 0 mm or < 0 mm at 15 years old		–	Clinical recommendations

3.4.2. Cleft palate repair

15 out of the 18 included studies reported on their palatoplasty protocol (Table 5). Cleft children underwent one-stage palatoplasty in a majority of 11 studies (Oberoi et al., 2008; Heliövaara and Rautio, 2011; Heliövaara et al., 2013; Antonarakis et al., 2015; Park et al., 2015; Yun-Chia Ku et al., 2018; Heliövaara and Leikola, 2021; Yu et al., 2021; Kamata et al., 2023; Lim et al., 2023; Lim et al., 2023) while the rest underwent a two-stage palatoplasty in 2 other studies (Nollet et al., 2008; Meazzini et al., 2015). In one study (Liao et al., 2010), a comparison was made between cleft patients that had undergone one-stage versus two-stage palatoplasty.

The range of age for 1 stage palatoplasty was between 7.2 months and 22.8 months. In the 2-stage palatoplasty studies, the range of ages for soft palate closure was 6–14 months. However, the range of age for hard palate closure, was more dispersed at 30.5 months old, 5.6 years old and 9–11 years old (Nollet et al., 2008; Meazzini et al., 2015; Liao et al., 2010).

With respect to 1-stage palatoplasty, the techniques reported included Furlow's (Oberoi et al., 2008; Park et al., 2015; Lim et al., 2023; Yu et al., 2021; Lim et al., 2023), VY's (Heliövaara and Rautio, 2011; Heliövaara et al., 2013; Antonarakis et al., 2015; Heliövaara et al., 2013; Yu et al., 2021), 2 flap (Liao et al., 2010; Antonarakis et al., 2015; Yun-Chia Ku et al., 2018; Kamata et al., 2023), von Langenback (Antonarakis et al., 2015) and other techniques not mentioned.

3.4.3. Alveolar bone graft

Majority of the studies (Table 5) performed secondary alveolar bone graft (ABG) during the mixed dentition phase. Of note, secondary ABG was performed together with the hard palate closure at 9–11 years old in 1 study. In 2 other studies, early SABG was conducted at 30.5 mths (about 2.5 years) in Meazzini et al. (2015) while late primary GPP at 12–18 mths followed by SABG at mixed dentition phase in Lin et al. (2021).

3.4.4. Orthodontics

Only 4 studies (Table 5) reported of the use of dental orthopaedics during infancy (Nollet et al., 2008; Liao et al., 2010; Antonarakis et al., 2015; Meazzini et al., 2015). This is presumably for optimisation prior to primary cheiloplasty. At the pre-ABG phase, maxillary arch expansion, if needed, were mentioned in 6 studies (Park et al., 2015; Yun-Chia Ku et al., 2018; Heliövaara and Leikola, 2021; Yu et al., 2021; Kamata et al., 2023; Lim et al., 2023). During pubertal phase, 3 studies reported the use of maxillary protraction (Park et al., 2015; Lim et al., 2023; Yu et al., 2021).

3.5. Determination of OGS (age)

The pooled mean age where the need for OGS was assessed was 17.01 years old (Table 3). 2 studies did not report of the age of assessment for OGS (Oberoi et al., 2008; Dalle Ore et al., 2017) while 2 other studies only stated as it as "at the end of facial growth" (Meazzini et al., 2015; Kamata et al., 2023). Overall, the most common age of assessment for the need of OGS was 15 years and above. The outlier was a study by Lau et al. (2020), whereby the mean was 13.77± 2.24 years old.

3.6. Determination of OGS (assessment)

The parameters evaluated for the decision making for OGS (Table 4) were predominantly via analysis of lateral cephalometric radiographs followed by clinical assessment. Three studies did not specify their decision-making parameters for OGS while two merely reported that it was based on recommendation from the clinical team. A majority of four studies used three bony cephalometric parameters: (1) ANB ≥0° or < 0°, (2) Wits appraisal ≤ −5 mm and (3) Harvold unit difference ≥34 mm to decide on the need for OGS.

Besides hard tissue (bone and teeth) cephalometric factors, two studies (Nollet et al., 2008; Meazzini et al., 2015) included soft tissue counterparts (soft tissue thickness and profile) as part of their assessment for the indication of OGS. In addition to cephalometric assessment, Nollet et al. (2008) included clinical evaluation such as dental crowding and the lack of functional occlusion that can be attained with orthodontic treatment alone. Two other studies included assessment of dental crowding, transverse deficiency manifesting as cross bites, facial aesthetics and harmony of facial profile. This same author in three of the included studies (Heliövaara and Rautio, 2011; Heliövaara et al., 2013; Heliövaara and Leikola, 2021) included aesthetic assessment of frontal view parameters, namely incisal show, smile line, occlusal cant and facial asymmetry.

3.7. Predictive iatrogenic factors

A predilection for orthognathic surgery was noted in cleft patients associated with these iatrogenic factors (Table 6): orthodontic cleft closure via canine substitution (Lee et al., 2014), lip revision surgery more than twice (Kamata et al., 2023), earlier age where one received primary lip procedure (Dalle Ore et al., 2017), palatal fistulae after palate repair (Kamata et al., 2023), had undergone palatal repair via the push-back technique (Lim et al., 2021) and had received a 1-stage palate repair (Liao et al., 2010).

3.8. Predictive intrinsic factors

Other intrinsic or congenital-based variables (Table 7) that were found to have correlation with an increased need for cleft OGS include dental agenesis (Oberoi et al., 2008; Lee et al., 2014), number of missing teeth (Lim et al., 2021), number of clefts in the lip & alveolus (Lim et al., 2021), severity of cleft (Park et al., 2015; Lau et al., 2020) and gender (Lim et al., 2021).

3.9. Predictive cephalometric factors

Across the eighteen studies, we have identified nine studies which proposed cephalometric markers during childhood that can predict future need for OGS (Tables 8 and 9). Eight of which were based on the UCLP population at the ages of 5 years old (Meazzini et al., 2015; Heliövaara and Leikola, 2021), 6 years old (Heliövaara and Rautio, 2011; Lin et al., 2021), 9 years old (Nollet et al., 2008), 10 years old (Yu et al., 2021), 11 years old (Yun-Chia Ku et al., 2018) and range of 10–12 years old (Oberoi et al., 2008). 1 study (Heliövaara et al., 2013) was based on the BCLP population at age 6 years old. Four studies presented

Table 5

Cleft treatment protocol in included studies.

No.	Study	Cleft Lip Repair	Cleft Palate Repair	Alveolar Bone Grafting	Orthodontics/Orthopaedics Treatment
1	Nollet et al. (2008)	<u>6-8 mths old</u> Millard technique	<u>12-14 mths old</u> Soft-palate closure by modified von Langenback technique <u>9-11 years old</u> Hard palate closure	<u>9-11 years old</u> Together with hard palate closure	<u>Infancy</u> Pre-surgical orthopaedic treatment (Hotz method) <u>12-15 years old</u> Fixed orthodontics <u>19-21 years old</u> Pre- and post- surgical fixed orthodontics
2	Oberoi et al. (2008)	NR	<u>Before 1 year old</u> Predominantly Furlow's Z plasty	NR	NR
3	Liao et al. (2010)	<u>4.8-14.4 mths old</u> Modified rotation- advancement technique	<u>1 years old</u> 1 stage palatoplasty with 2-flap technique, palatal mucoperiosteal flaps 1st stage of 2-stage palatoplasty with Widmaier technique <u>5.6 years old</u> 2nd stage of 2-stage palatoplasty with vomerine mucoperiosteal flap	<u>Mixed dentition phase</u> Secondary ABG	<u>Infancy</u> Passive infant orthopaedics
4	Heliövaara and Rautio (2011)	<u>3-6 mths old</u> Modified Millard I & II technique	<u>1-1.9 years old</u> Veau-Wardill-Kilner VY push back or Cronin modification	None	None
5	Heliövaara et al. (2013)	<u>3-6 mths old</u> Modified Millard I & II technique	<u>1-1.9 years old</u> Veau-Wardill-Kilner VY push back or Cronin modification	None	None
6	Lee et al. (2014)	NR	NR	NR	NR
7	Antonarakis et al. (2015)	<u>3-4 mths old</u> Millard technique	<u>12 months old</u> von Langenbeck, 2-flap palatoplasty or Veau-Wardill-Kilner VY techniques	None	<u>Infancy</u> infant orthopaedics
8	Meazzini et al. (2015)	<u>6 mths old</u>	<u>6 mths old</u> Soft palate closure <u>30.5 mths old</u> Hard palate closure	<u>30.5 mths old</u> Early secondary ABG	<u>Infancy/Pre-cheiloplasty</u> Intraoral plate with extraoral wires (no nasal molding)
9	Park et al. (2015)	<u>3-5 mths old</u> Millard rotation & advancement flap	<u>12-18 mths old</u> Furlow double opposing Z plasty	<u>Mixed dentition phase</u> Secondary ABG	<u>Pre-ABG</u> Maxillary arch expansion (if need) <u>Puberty</u> Facemask for maxillary protraction <u>Permanent dentition phase</u> Fixed orthodontics
10	Yun-Chia Ku et al. (2018)	<u>3-6 mths old</u>	<u>9 to 12 mths old</u> 2-flap palatoplasty	<u>9 to 11 years old</u> Secondary ABG	<u>Pre-ABG</u> Optional orthodontic treatment performed to align maxillary anterior teeth
11	Dalle Ore et al. (2017)	NR	NR	NR	NR
12	Heliövaara and Leikola (2021)	<u>3-6 mths old</u> Modified Millard I & II technique	<u>0.6-1.9 years old</u> Veau-Wardill-Kilner VY push back or Cronin modification	<u>9 to 11 years old</u> Secondary ABG	<u>Pre-ABG</u> Orthodontic treatment
13	Lim et al. (2021)	NR	NR	NR	NR
14	Lin et al. (2021)	<u>3-5 mths old</u> Rotation & advancement flap	<u>12 to 18 mths old</u> Furlow double opposing Z plasty	<u>12 to 18 mths old</u> Late primary gingivoperiostealplasty <u>Mixed dentition phase</u> Secondary ABG	<u>Pre-ABG</u> Maxillary arch expansion (if needed) <u>Puberty</u> Facemask with bone-anchored miniplates for maxillary protraction <u>Permanent dentition phase</u> Fixed orthodontics
15	Yu et al. (2021)	<u>3-5 mths old</u> Millard rotation & advancement flap	<u>X</u> Furlow double opposing Z plasty or V-Y push back	<u>Mixed dentition phase</u>	<u>Pre-ABG</u> Maxillary arch expansion (if needed) <u>Pre-pubertal phase</u> If patients had moderate-to-severe maxillary hypoplasia: facemask with miniplates <u>Permanent dentition phase</u> Fixed orthodontics
16	Lau et al. (2020)	NR	NR	NR	NR
17	Kamata et al. (2023)	<u>3 mths old</u> Straight line repair	<u>12-15 mths old</u> 2-flap technique	<u>Mixed dentition phase</u> Secondary ABG	<u>Pre-ABG</u> Maxillary arch expansion (if needed) <u>Permanent dentition phase</u> Fixed orthodontics
18	Lim et al. (2023)	NR	<u>NR</u> Push-back, Furlow's, other techniques	NR	<u>7 years old</u> First-phase orthodontics <u>At or after 15 years old</u> Second-phase orthodontics

Table 6

Iatrogenic factors associated with prediction of need for future orthognathic surgery in cleft children.

Iatrogenic Factors			
Study	Factor	Odds Ratio	Comments
Lee et al. (2014)	Orthodontic cleft closure via canine substitution	6.48	
Dalle Ore et al. (2017)	Primary lip procedure performed below 3 months of age	10.9	
Liao et al. (2010)	1-stage palate repair	NA	
Lim et al. (2021)	Push-back method (palatal repair)	9.039	
Kamata et al. (2023)	Lip revision surgery performed more than twice	43.4	
Kamata et al. (2023)	Palatal fistulae after palatal repair	22.3	

Table 7

Intrinsic factors associated with prediction of need for future orthognathic surgery in cleft children.

Intrinsic Factors			
Study	Factor	Odds Ratio	Comments
Oberoi et al. (2008)	Missing maxillary teeth (majority were lateral incisors on the cleft side)	NA	
Lee et al. (2014)	Missing teeth outside the cleft	4.94	
Park et al. (2015)	Dental agenesis		
	Cleft subtypes/severity	NA	BCLP > UCLP > CLA BCLP > CLA (P < 0.05)
Lim et al. (2021)	Number of clefts in the lip & alveolus (at 7 yrs old)	6.692	
Lim et al. (2021)	Number of clefts in the lip & alveolus (at 10 yrs old)	13.644	
Lim et al. (2021)	Number of missing teeth (at 7 years old)	1.712	
Lim et al. (2021)	Male gender (at 7 years old)	3.958	
Lau et al. (2020)	Cleft subtypes/severity	NA	BCLP > UCLP

numerical thresholds to stratify the need for cleft OGS at different ages (Table 9). Overall, ANB angle (°) was the most highly reported metric used (Nollet et al., 2008; Oberoi et al., 2008; Heliövaara and Rautio, 2011; Heliövaara et al., 2013; Meazzini et al., 2015; Yun-Chia Ku et al., 2018; Lin et al., 2021; Yu et al., 2021). A lower ANB angle, in CLP patients, was the most widely cited predictive factor for later need of OGS.

4. Discussion

To our knowledge, this is the first systematic review looking at the prediction of the need for OGS in CLP patients. From this review, we categorised predictive variables associated with a greater need for OGS in CLP patients were into (1) iatrogenic factors, (2) intrinsic factors and (3) cephalometric factors. Amongst the factors in these 3 categories, a lower ANB angle was the most widely reported factor used in prediction of subsequent OGS in CLP patients (age range: 5–11 years old).

4.1. Determination of OGS: timing

From our findings, the need for OGS was assessed was at a pooled mean age of 17.01 years old. Overall, the most common age of assessment for the need of OGS was 15 years old and above. This corresponds

Table 8

Cephalometric factors associated with prediction of need for future orthognathic surgery in cleft children.

Study	Cephalometric Variables	Explanation
Nollet et al. (2008)	At age 9: s-n-ss (SNA) s-n-pg sss-ns-sms sss-ns-pgs	Found to be significant predictors for the need for OGS at age 18 (85 %)
Oberoi et al. (2008)	Difference between the mandibular unit length (Co-Pg) and maxillary unit length (Co-ANS) >30 mm ANS Significantly smaller ANB Wit's analysis Upper lip position	
Heliövaara and Rautio (2011)	At 6 years old (UCLP patients): ANB < −1°	None of the children whose ANB >4.5° needed OGS
Heliövaara et al. (2013)	At 6 years old (BCLP patients): ANB <7°	
Meazzini et al. (2015)	At 5 years old (UCLP patients): SNA (significantly lower than non-surgical group) At 5 years old (UCLP patients): ANB <2°	Identified 45 % of cleft patients that needed OGS
Park et al. (2015)	At T0 (mean age of 9.3 yo): ANB, IMPA, AB to mandibular plane, APDI, Wits, Overjet, Harvold unit difference (P < 0.05) At T1 (mean 17.3 yo): APDI, ODI, Harvold unit difference, Wits appraisal, AB to mandibular plane angle, gonial angle, ANB, overjet, A to N perpendicular and IMPA	These 7 cephalometric variables shown significant differences between the surgical and non-surgical groups These 10 cephalometric variables were selected as predictors for OGS
Yun-Chia Ku et al. (2018)	At 11 years old (UCLP patients): ANB </ = −0.45° Overjet </ = −2.00 mm Maxillary length </ = 47.25 mm Other variables: L1-MP, SNB, Go-Gn, overbite, SN	3 cephalometric variables were selected as the minimum number of discriminators required to obtain optimum discriminant effectiveness for OGS prediction
Heliövaara and Leikola (2021)	At age 6 years old (UCLP patients): 5-year-olds index • ANB (significantly lower values) • anb (significantly lower values)	
Lim et al. (2021)	At age 10 years old: smaller length of the maxilla (A-Ptm)	Odds ratio: 1.823
Lim et al. (2021)	At age 7 years old: Greater mandibular prominence (SNB)	Odds ratio: 1.739
Lin et al. (2021)	At age 6 years old (UCLP patients): ANB, PP-FH, CF, FCA	
Yu et al. (2021)	At age 10.45 years old (UCLP patients): ANB, anteroposterior dysplasia indicator, Wits-appraisal, mandibular body length, Harvold unit difference, overjet	
Lau et al. (2020)	At mixed dentition: Soft tissue convexity, soft tissue profile, upper lip to E-plane, lower lip to E-plane, overjet	
Lau et al. (2020)	At permanent dentition: Soft tissue convexity, soft tissue profile, upper lip to E-plane, lower lip to H-plane, soft tissue	

(continued on next page)

Table 8 (continued)

Study	Cephalometric Variables	Explanation
Lim et al. (2023)	facial angle, nasal prominence, maxillary depth	At early mixed dentition: “Shrinkage of palate” that comprises vertical shallowing and transverse narrowing of posterior maxilla & cleft-side asymmetry of the anterior maxilla
	Palatal Morphology/ Geometrics	

SNA-Sella-nasion-subspinale/A point; SNB- Sella-nasion-point B; s-n-pg- Sella-nasion-pogonion; ss-ns-sms- Soft tissue subspinale (A point)-Soft tissue nasion-Soft-tissue supramentale; ss-ns-pgs- Soft tissue subspinale (A point)-Soft tissue nasions-Soft-tissue pogonion; Co-condylion; Pg: Pogonion; ANS-anterior nasal spine; ANB-point A-nasion-point B; IMPA-incisor mandibular plane angle; APDI-Anterior posterior dysplasia indicator; ODI-Overbite depth indicator; L1-MP-angle between lower central incisor and mandibular plane; Go-Gn-Gonion-gnathion; PP-FH-inclination of palatal plane in relation to the FH plane; CF-combination factor (skeletal size of maxilla and mandible); FCA-facial convexity angle (intermaxillary relationship between maxilla and mandible).

with existing literature where the age of 15 was regarded as a time where reasonable assessment can be made in cleft patients (Daskalogiannakis and Mehta, 2009). By the age of 15, 98 % of facial growth is usually completed in females. For males, this is delayed till age 17 or 18 (Broadbent et al., 1975; van der Linden, 1986). At this phase of development, the discrepancy of sagittal skeletal relationships and stabilised occlusion can thus be better evaluated for the need for orthognathic surgical correction in relation with the patients’ concerns (Shetye and Gibson, 2023).

4.2. Determination of OGS: Methods of assessment

While the broad principle for the need of cleft OGS points towards the correction of the retruded midface and associated malocclusion, the specific threshold for surgical indication varied amongst the studies. This is testament to the subjective aspect of judgement for the need for orthognathic surgery and lack of universal consensus (Choi et al., 2021). Among the twelve studies that included cephalometric evaluation, there was no consensus in this aspect. In terms of numerical cephalometric

values, the cut-off value was ANB $\leq 3^\circ$ (Antonarakis et al., 2015; Park et al., 2015; Lin et al., 2021; Yu et al., 2021) in four studies, while other investigators fixed it at ANB $\geq 0^\circ$ or $< 0^\circ$. Five studies shared the same cut-off Wits appraisal at $</ = -5$ mm (Antonarakis et al., 2015; Park et al., 2015; Lim et al., 2021; Lin et al., 2021; Yu et al., 2021) and Harvold unit difference of ≥ 34 mm.

Of note, radiographic cephalometric evaluation were applied only to the lateral profile of patients. Clinical assessment of frontal profile was limited to 3 studies (Heliövaara and Rautio, 2011; Heliövaara et al., 2013) with considerations for: facial asymmetry, occlusal cant, vertical maxillary deficiency and associated unesthetic incisal show. Indeed, lateral cephalograms alone may not allow for consideration of facial parameters from the other dimensions (Lim et al., 2023). Including cephalometric variables from a frontal facial analysis would increase the predictive power of the model (Lau et al., 2020) as CLP patients may also present with occlusal cants, transverse discrepancies, maxilla-mandibular asymmetries (Choi et al., 2013; Yang et al., 2016; Paknahad et al., 2018; Akarsu-Guven et al., 2021; Salinero et al., 2024).

4.3. Predictive iatrogenic factors: palatoplasty-associated

From this review, three studies (Liao et al., 2010; Lim et al., 2021; Kamata et al., 2023) noted significant impact of palatoplasty-related factors on the need for future OGS. Liao et al. (2010) reported that patients who underwent 1-stage palate repair had higher “risk” of needing future OGS as compared to that of 2-stage palate repair. An earlier study supports this notion by suggesting how a later palatal repair (done in the second stage) defers any interference with maxillary development to an older age when less growth remains (Liao and Mars, 2006). On the contrary, two systematic reviews (Kappen et al., 2018; Salgado et al., 2019) have found inconclusive and opposing evidence regarding maxillary growth between patients who underwent 1- and 2-stage palatoplasty.

Interestingly, Lim et al. (2021) also observed that UCLP, CLP and CP patients who underwent the 1-step palatal push-back repair had greater tendency to display an anterior crossbite at 15 years of age. Theoretically, surgical techniques, such as the von Langenbeck and 2-flaps techniques, that minimise scarring (Shetye and Gibson, 2023) from the denudation of palatal bone, attenuate the impairment of maxillary growth as compared to that with the push-back technique (Lee and Liao, 2013). However, the existing evidence remains regarding the impact of

Table 9
Overview of prediction variables for cleft orthognathic surgery based on developmental Phase.

Study/Age	Developmental Phase							
	Primary Dentition	Mixed Dentition						Permanent Dentition
	Pre-puberty	Puberty						At/Near Skeletal Maturity
	5 yrs old	6 yrs old	9 yrs old	10 yrs old	11 yrs old	12 yrs old	15 yrs old	And Beyond
Meazzini et al (2015)	[UCLP] ANB $< 2^\circ$						Preparation for & Execution of Cleft Orthognathic Surgery	
Heliövaara et al (2021)	[UCLP] 5-year-old index score ≥ 4							
Heliövaara et al (2011)		[UCLP] ANB $< -1^\circ$						
Heliövaara et al (2013)		[BCLP] ANB $< 7^\circ$						
Lin et al (2021)		[UCLP] ANB, PP-FH, CF, FCA						
Nollet et al (2008)			[UCLP] s-n-pg, ss-ns-sms, ss-ns-pgs					
Yu et al (2021)				[UCLP] ANB, ADPI, Wits, Mandibular body length, Harvold unit difference, Overjet				
Yun-Chia et al (2017)					[UCLP] ANB $< -0.45^\circ$, Overjet ≤ -2 mm, Maxillary length ≤ 47.25 mm			
Obero et al (2008)				[UCLP] Difference of 32 mm between mandibular unit length and maxillary unit length				

various palatoplasty techniques on maxillary growth and jaw relationship remains inconclusive (Lee and Liao, 2013).

4.4. Predictive iatrogenic factors: cheiloplasty-associated

Cheiloplasty-associated factors were also reported as a predictive variable for increased need for OGS in two studies. One of which highlighted the increased chance for need of OGS in patients with primary lip procedure performed below 3 months of age (Dalle Ore et al., 2017). An explanation to this is that surgical insult inflicted in a younger infant, during a period of rapid growth, may induce a relatively greater degree of scarring and earlier onset of tension on the repaired lip and maxillary complex, thus retarding subsequent facial development (Liao and Mars, 2005; Friede, 1998). However, studies have suggested that scarring from the cleft lip repair alone (Mars and Houston, 1990; Celie et al., 2024) is unlikely or insufficient to be the predominant reason for development of midfacial hypoplasia. An explanation for this seemingly contradictory finding is that patients with isolated cleft lip are the minority in Dalle Ore et al. (2017) study. Hence, facial growth might have been influenced by the effect of cleft palatoplasty performed in the majority of their subjects.

Overall, complications from primary cleft surgeries (Kamata et al., 2023) that resulted in “palatal fistulae” and “repeated lip revision” were associated with an increased likelihood for OGS in later age.

4.5. Predictive intrinsic factors: cleft severity & subtypes

In three of the included studies (Park et al., 2015; Lim et al., 2021; Lau et al., 2020), CLP patients with more severe cleft subtypes were found to have a greater need for subsequent OGS correction of dentofacial deformity. This is in agreement with a systematic review (Choi et al., 2021) whereby the rate of OGS intervention was found to be the highest for patients with BCLP followed by UCLP, isolated cleft palate and isolated cleft lip. The presumption is that the severity or size of a cleft is dependent on the innate tissue deficiency (Daskalogiannakis and Antonarakis, 2015). Going by this proposition, patients with more severe cleft subtypes or larger clefts will face less favourable maxillofacial growth and dental arch relationships (Smahel and Brejcha, 1983; Chiu et al., 2011). Nevertheless, controversial evidence on the association between severity of cleft and the extent of maxillary deficiency have also been reported (Meazzini et al., 2011; Antonarakis et al., 2015; Lacerda and Vieira, 2023). This was shown in a study (Lisson and Weyrich, 2014) which revealed an equal need for maxillary surgical advancement in both UCLP and BCLP patients.

Indeed, it may hard to isolate the individual impact of iatrogenic or intrinsic factors on the restriction of maxillary growth. For instance, as compared to a unilateral cleft palate, the repair of a bilateral cleft palate may necessitate raising of larger mucoperiosteal flaps and exposure of greater area of denuded palatal bone (Chiu et al., 2011). In the latter case of a larger cleft defect, there will understandably be an increased likelihood for greater scarring, future contracture and greater tension of tissues (Chiu et al., 2011). Thus, this may result in a greater predisposition for impairment of maxillary growth and need for OGS correction in these patients.

4.6. Predictive intrinsic factors: Missing dentition

In three studies, missing teeth was found to significantly predisposed cleft children for future OGS (Oberoi et al., 2008; Lee et al., 2014; Lim et al., 2021). This aligns with an association reported between the frequency of dental anomalies and adverse maxillofacial growth outcomes in UCLP and BCLP (Lacerda and Vieira, 2023). One of type of “dental anomalies” is dental agenesis (Lacerda and Vieira, 2023).

Complete UCLP patients with more than one congenitally missing permanent maxillary tooth reportedly have a greater tendency to develop a reduced facial height and Class III profile (Lai et al., 2015).

Likewise, analysis of lateral cephalograms by Wu et al. (2013) reported that an increasing number of missing maxillary teeth was found to be accompanied by a decrease in anterior facial height, maxillary dental arch length and incisal overjet in UCLP children. These findings are in agreement with how the absence of a permanent lateral incisor is almost consistently found in syndromic cleft patients (Binder syndrome, holoprosencephaly) and thus suggestive of an association with the congenitally hypoplastic state of maxillary tissues (Meazzini et al., 2011). Hence, the combination of cleft and dental agenesis may predispose patients to a greater need for orthodontic intervention and future orthognathic surgery as compared to CLP patients without missing teeth (Lai et al., 2015).

4.7. Predictive cephalometric factors

A list of predictive factors and formulae based on cephalometry has been compiled (Tables 9 and 10) but are to be interpreted with caution. Firstly, they are derived based on data and context of specific cleft centre's patients and must be customised to individual CLP child. In addition, one should be cognisant of the few limitations of lateral cephalometry. At a younger age, the permanent central incisors may remain unerupted and this precludes cephalometric assessment for incisal overjet and related parameters (Meazzini et al., 2015; Antonarakis et al., 2015). In addition, the lack of cooperation in younger children to remain in resting position during radiographic examination coupled with the different interpretation of what “resting” is may also affect the soft tissue cephalometric values and measurements (Mølsted et al., 1992).

Lastly, while cephalometric values serve as a common quantitative factor for reference and comparison, they are neither independent of facial growth nor of the effects from previous surgeries or dental treatment (Nollet et al., 2008). Both of which are the widely known “intrinsic” and “iatrogenic” factors that are hypothesized to be responsible for the development of hypoplastic maxillae.

4.8. Implications

Mathematical modelling may lead to development of prediction formulas (Table 10) for prognostication and implementation of appropriate treatment to “minimise risk” of later need for OGS. In addition, these formulas may guide clinicians in the optimisation of conditions for certain “high risk” CLP children and better prepare them for OGS later in life. By knowing the dentofacial developmental trajectory of a cleft child and his/her need for future OGS, there are four potential benefits.

Firstly, it may allow for mental and financial preparation for the patients and caregivers (Nollet et al., 2008) especially in cases where OGS will likely be needed. Secondly, stratification of “risks” for cleft OGS can help guide clinical decision in terms of reducing the risks of deterioration or iatrogenically worsening facial growth in cleft patients (Lim et al., 2021). This can be useful in reducing the overall clinical burden of cleft (WHO, 2020). In addition, clinicians can customise and plan for specific orthodontic treatment and timing according to the patient's predisposition for cleft OGS. An example of which include delaying any orthodontic treatment till further maxillofacial growth for “high risk” patients instead of extended duration for ineffective attempts at orthodontic camouflage (Yun-Chia Ku et al., 2018; Lin et al., 2021). Alternatively, orthodontic treatment in these “high risk” patients can be limited to only dental alignment without excessive dental compensations (Meazzini et al., 2015) while awaiting final assessment of need for OGS after skeletal maturity of their dentofacial complex. Lastly, having a better understanding of predictive factors can aid in calculation and optimisation of resources (Miteff et al., 2018) needed for comprehensive treatment of these CLP patients.

Table 10
Prediction formulae/model for cleft orthognathic surgery from included studies.

No	Study	Prediction Formula	Derivation Method	Accuracy
1	Park et al. (2015)	URL provided in publication: http://bikechild.iptime.org:8838/orthodontics/	Feature wrapping method	Adjusted classification accuracy of 77.3 % Sensitivity: 99.0 % Specificity: 74.1 %
2	Yun-Chia Ku et al. (2018)	At 11 years old: ANB $\leq -0.45^\circ$ Overjet ≤ -2.00 mm Maxillary length ≤ 47.25 mm	Receiver operating characteristic (ROC) analysis and logistics regression A score of 2 or 3 (cephalometric variables) were possible candidates for future OGS A score of 2 indicated the best combination of sensitivity & specificity	Accuracy: 86.9 % Sensitivity: 90.0 % Specificity: 83.9 %
3	Lin et al. (2021)	URL provided in publication: http://147.47.41.53:8890	Boruta method & XGBoost algorithm-based machine learning model	10-fold cross-validation accuracy of 87.4 % Sensitivity: 97.83 % Specificity: 90.00 %
4	Yu et al. (2021)	$D = 5.288 + [0.268 \times \text{ANB } 9 (\text{deg})] + [0.049 \times \text{APDI } (\text{deg})] - [0.084 \times \text{Wits appraisal (mm)}] - [0.148 \times \text{mandibular body length (mm)}] - [0.022 \times \text{Harvold unit difference (mm)}] + [0.154 \times \text{overjet (mm)}]$	Discrimination analysis Non-surgical group: $D = 0.412$ (centroids) Orthognathic surgery needed: $D = -0.680$ (centroids)	Accuracy: 69.8 % Sensitivity: 69.7 % Specificity: 70.0 %
5	Lau et al. (2020)	$Y = (-0.91) (\text{Upper lip-E plane}) + (0.60) (\text{Lower Lip-E plane}) - 4.2$ $e^Y = \text{odds ratio (Odds ratio (OR)} > 1 \text{ implies that the condition/event is more likely to occur in the group)}$	Backwards stepwise regression Y denotes the co-efficient Odds of orthognathic surgery needed is derived from e to the power of Y	–

5. Limitations

The main limitation of this review lies in the heterogeneity of studies in terms of racial groups, treatment protocols and timing of each surgical intervention and assessment for orthognathic surgery. This is exemplified in Europe alone, where there are 194 unique surgical treatment protocols amongst 201 institutions (Shaw et al., 2001). This complicates proper comparisons and control for confounders across studies. While most of the studies in this review are of moderate quality, details of the cleft treatment protocol were excluded in some papers. This precludes comparison and limits the applicability of their findings.

In addition, decision for orthognathic surgery was largely determined by objective and subjective assessment from the clinicians. No consideration of patient's subjective needs was included. Some of these

motivations to undergo orthognathic surgery may stem from the desire to improve facial profile and appearances &/or elevate chewing or speech function due to dentoalveolar arch & skeletal discrepancies. For “borderline cases” (mild to moderate skeletal discrepancy) especially, the selection of either modality may then be more dependent on the patient's preference (Alhammadi et al., 2022). Lastly, all the included studies were retrospective in nature and may be prone to potential bias.

6. Conclusion

In conclusion, a comprehensive overview of the predictive factors for the need for OGS in CLP patients have been categorised into iatrogenic, intrinsic and cephalometric variables. Few cephalometric values and predictive formulae have been published but warrants judicious application. Further high-quality and well-controlled studies are needed to develop better prediction models that can be catered to patients of specific cleft subtypes and cleft treatment protocol.

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