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Outcome of Orthognathic Surgery in Craniofacial Syndrome Patients

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Abstract

Craniofacial Syndrome (CFS) patients often present a great variety of facial malformations with corresponding cephalometric values, which in turn complicate surgery and increase the risk of relapse. In this study, we present a group of consecutive CFS patients treated with orthognathic surgery at a craniofacial center in Sweden. The secondary objective was to identify diagnoses that were unable to be corrected toward normal reference values according to cephalometric measurements. CFS patients included those undergoing orthognathic surgery from 2001 to 2015 following skeletal maturity and with adequate radiological documentation. Patients were grouped according to diagnosis, and pre- and post-operative cephalometric measurements were compared with reference values from normal control patients. Evaluation of 31 CFS patients with Crouzon, Treacher Collins, Apert Saethre-Chotzen, or Pfeiffer syndrome revealed surgical outcomes demonstrating lateral cephalometric progress toward normal values. These findings showed that orthognathic surgery performed on CFS patients improved cephalometric characteristics in all groups. The most difficult rehabilitation was observed in corrections for Treacher Collins syndrome due to the accompanying complexity of skeletal and soft-tissue malformations.

Keywords: Cephalometry; Craniofacial syndromes; Maxillofacial anomalies

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Introduction

Craniofacial Syndromes (CFSs) are a heterogeneous group of developmental disorders that affect the head and neck region. In general, CFSs are associated with complex malformations associated with various genetic mutations. A possible consequence is premature closure of sutures in the cranium and midface, resulting in growth disturbances and a distorted facial appearance [1]. These syndromes may also affect brain development, hearing, vision, musculoskeletal disorders, and/or malformation of internal organs [2]. Furthermore, malformations of the jaws, sometimes associated with orofacial clefts and odontogenic malformations, can cause difficulties with eating and speech and negatively impact patient quality of life, as well as incur increased costs for healthcare systems [3].

To date, studies have described >700 distinct CFSs [4]. The clinical manifestation can range from mild to severe but usually falls into two major categories: Those associated with craniosynostosis [*i.e.*, premature fusion of one or more cranial sutures (Apert, Crouzon, Pfeiffer, and Saethre-Chotzen syndromes] and those associated with clefts [*i.e.*, structural abnormalities involving the lip and/or hard palate (Pierre Robin, Treacher Collins, Nager, and Stickler syndromes] [1].

Apert, Crouzon, Pfeiffer, and Saethre-Chotzen syndromes are among the most prevalent craniofacial disorders [5]. Additionally, although not associated with craniosynostosis, patients with Treacher-Collins syndrome usually require a considerable amount of reconstructive craniofacial operations.

Apert Syndrome

This syndrome is also coined acrocephalosyndactyly. It is one of the most frequent craniofacial anomalies and is characterized by a premature fusion of mainly the coronal sutures, preventing

the skull to grow in sagittal direction and therefor causing the skull to expand to the sides and upwards. This results in a shortening of the head in the anteroposterior direction with a flat back head, also known as brachycephaly. The deficient growth in the midfacial bones leads to a hypoplastic maxilla and a beaked nose.

Crouzon Syndrome

Crouzon syndrome is characterized by calvarial deformities, facial anomalies and exophthalmos. Classical clinical features for Crouzon syndrome are a brachycephalic skull, hypertelorism, strabismus, symmetrical hypoplasia of the orbits, zygomas and maxilla, leading to exorbitism [6]. Mandibular growth is usually not affected. But due to the maxillary hypoplasia, the mandibula may have a prognathic appearance [7]. Both Apert and Crouzon syndrome show narrow and arched palate and dental malocclusion, such as negative overjet, anterior open bite, posterior crossbite and severe dental crowding.

Pfeiffer Syndrome

Various skull deformities have been described in the literature as Pfeiffer´s syndrome. However, it is in general classified into three different types. The main diagnostic features in the clinical subtypes are broad and deviated thumbs and big toes with or without incomplete syndactyly in combination with some kind of craniosynostosis. In type I, brachycephaly is present as a result of premature synostosis of both coronal sutures. This subtype is characterized by midface hypoplasia, finger and toe abnormalities in terms of broad and deviated thumbs and big toes. In type II, pansynostosis of the skull is present, meaning craniosynostosis of all calvarial sutures have taken place. Pansynostosis is also referred to as cloverleaf skull and is, within type II, accompanied by hydrocephalus and brain dysfunction. Besides, this group fall victim to severe exorbitism and ankylosis of the elbows. Type III is similar to type II but without a cloverleaf skull [1]. These patients have prominent eyes with hypertelorism and with a downward slant of the eyelid, irregularly placed teeth due to a small retrognathic maxilla with high palate, soft tissue syndactyly such as between the second and third toes bilaterally, broad thumbs and toes and a flat nasal bridge.

Saethre-Chotzen Syndrome

The phenotype of Saethre Chotzen syndrome (also known as acrocephalosyndactyly type III) shows a variability in this population and is partially characterized by craniosynostosis [8]. The coronal suture is most frequently affected. The patients suffer from facial asymmetry (especially those with unicoronal synostosis), small and low set ears, hearing loss, low frontal hairline, strabismus, drooping upper eyelids (ptosis), syndactyly and a depressed nasal bridge. Significant is also deformities of the maxilla, sometimes in company with a bifid uvula and a narrow and/or cleft palate.

Treacher Collins Syndrome

Treacher Collins Syndrome (TCS) patients have a convex profile with hypoplasia of several facial structures such as the zygoma and mandible. Typically, the mandible is small and down-tilted, which can compromise the airways and this may result in tracheostomy. Furthermore, TCS is characterized by coloboma of the lower eyelids and show downward slanting of the palpebral fissures. External- and middle-ear malformation with hearing loss, cleft palate, abnormal hairline and malocclusion are also typical findings in TCS [1].

Treatment of CFSs

Various surgical techniques are employed for correcting CFSs, including Le fort I, II, and III osteotomies; bilateral sagittal split osteotomy; intra- and extra-oral vertical ramus osteotomy; and genioplasty, with these collectively referred to as orthognathic surgery [9-12]. Surgical intervention aims to improve function, facial appearance, breathing, and intermaxillary interactions, as well as anatomical deviations otherwise too complicated to correct with orthodontic treatment or surgical camouflage [13-15]. Indications for treatment were cephalometric assessments outside reference values and functional or aesthetic demands from the patients.

Each syndrome introduces a different set of potential complications and requires a unique approach for management and surgical reconstruction. Meticulous interdisciplinary planning and radiological evaluations usually precede surgical intervention. Lateral cephalometric analysis is a helpful diagnostic tool for determining the surgical treatment for patients with CFS. This method allows analysis of the intermaxillary, dental, and skeletal relationships, thereby allowing determination of treatment needs and evaluation of surgical outcomes [4,16]. In this study, we present cephalometric measurements before and after orthognathic surgery in patients with CFS in order to demonstrate their utility in assessing surgical outcomes.

Materials and Methods

Patients

The study included CFS patients diagnosed with Crouzon, Pfeiffer, Apert, Saethre-Chotzen, or Treacher Collins syndrome and who underwent orthognathic surgery after skeletal maturity. Patients underwent surgery from 2001 to 2015 at the Craniofacial center at Sahlgrenska University Hospital, Gothenburg, Sweden, with surgical outcomes analyzed by pre- and post-operation lateral cephalometry. Patients were eligible for study inclusion upon meeting the following criteria: 1) completion of orthognathic surgical treatment and 2) availability of a complete set of pre- and post-operative lateral cephalometric radiographs.

Capturing the lateral cephalogram

Lateral cephalometric radiography was performed at the Specialist Clinic for Oral Radiology, Västra Götalandsregionen, Gothenburg, Sweden. A standardized technique was performed with the patients in a natural head position (*i.e.*, a reproducible position with the head in an upright posture and eyes focused on a point in the distance at eye level with a horizontal visual axis). The cephalostat features two posts that are placed in the external auditory meatus. The sagittal plane of the patient is then positioned parallel to the X-ray film, with the teeth in centric occlusion, and the Frankfort plane (auriculo-infraorbital plane) positioned horizontally [17,18].

Lateral cephalometric analysis

Craniofacial morphology was evaluated based on the cephalometric landmarks and lines used in Bergen analysis (Figure 1) [17]. Cephalometric reference points and planes (*i.e.*, landmarks) were identified on cephalograms using software (Sectra PACS; Sectra Imtec AB, Linköping, Sweden) and employed to construct lines, planes, and angles to allow measurement of angular values. The following cephalometric variables were extracted from the lateral cephalograms: Sella-Nasion-A-point (SNA), Sella-Nasion-B-point (SNB), Nasion-Sella Line/nasal Line (NSL/NL), and Mandibular

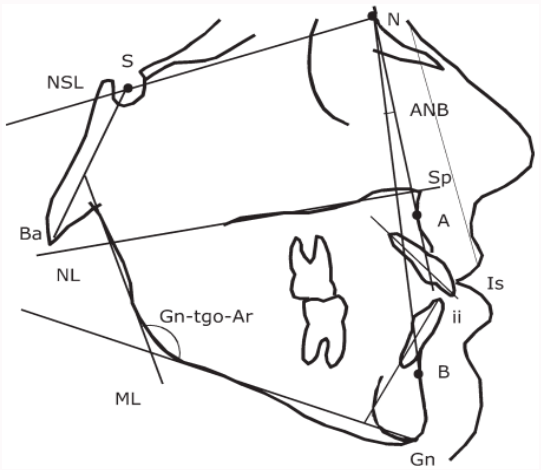

Figure 1: Cephalometric landmarks and lines used in Bergen analysis: N: Nasion; S: Sella; Ba: Basion; A-point; B-point; Gn: Gnathion; Sp: Anterior Nasal Spine; Is: Incision superius; Ii: Incision inferius; NSL: Nasion Sella Line; NL: Nasal Line; and ML: Mandibular Line. Maxillofacial measurements of interest: SNA: Sella-Nasion-A-point; SNB: Sella-Nasion-B-point; NSL/NL: Nasion-Sella Line/Nasal Line; and ML/NL: Mandibular Line/Nasal Line [6].

Line/Nasal Line (ML/NL). All variables were measured by the same investigator (HL), who is a specialist in maxillofacial radiology. Postoperative cephalometric measurements were compared with those from control values [19].

Statistical analyses

Normality assumption was controlled using the Shapiro-Wilk test, and a Gaussian distribution was confirmed for the evaluated variables. Descriptive data (*i.e.*, mean and standard deviation) are presented for the SNA, SNB, NSL/NL, and ML/NL angles before and after surgical treatment. Calculations were performed using SPSS software (v.26; IBM Corp., Armonk, NY, USA).

Ethics

The study was conducted according to the principles outlined in the Declaration of Helsinki and approved by the Gothenburg Ethics Committee (Dnr. 784-11).

Results

A total of 31 patients (12 females, 19 males) with CFS were included in this study. The two most common diagnoses were Crouzon syndrome (39%; 12/31) and Treacher Collins syndrome (22.5%; 7/31), accounting for 19 of 31 patients (61%). The remaining 12 patients had the following diagnoses: Apert syndrome (16%; 5/31), Saethre-Chotzen syndrome (13%; 4/31), and Pfeiffer syndrome (9.5%; 3/31). A summary of patient gender, age, and diagnosis is presented in Table 1. Surgeries performed included Le Fort I in one or up to six pieces, Le Fort II, sagittal split osteotomy and/or segmental osteotomy of the mandible, chin plasty or chin implant, or a combination of these. Some patients had previously undergone Le Fort III or monobloc procedures during childhood.

Assessment of the SNA angle prior to surgery revealed that all groups, except those diagnosed with Saethre-Chotzen syndrome, showed a low mean SNA, demonstrating a skeletal maxillary anteroposterior deficiency (also known as maxillary retrognathism). However, after surgery, all patient groups showed mean SNA values comparable with that of the control group, demonstrating successful

Table 1: Summary of patient characteristics.

Patient characteristics:				
Gender	[F]		[M]	
	12		19	
Syndromes	[No.]		[%]	
A. Crouzon	12		39	
B. Treacher Collins	7		22.5	
C. Apert	5		16	
D. Saethre-Chotzen	4		13	
E. Pfeiffer	3		9.5	
Age [years]	**Before treatment**		**After treatment**	
	mean	**range**	**mean**	**range**
A. Crouzon	15	7-20	20	18-24
B. Treacher Collins	12	3-17	22	11-25
C. Apert	14	13-15	22	17-24
D. Saethre-Chotzen	17	15-20	20	17-22
E. Pfeiffer	12	7-11	16	11-21

Table 2: Lateral cephalometric analysis for Crouzon, Treacher Collins, Apert, Saethre-Chotzen, and Pfeiffer syndromes, respectively.

	Before treatment	**After treatment**	**Reference values***
A. Crouzon	Unit°		
SNA	69 ± 6.6	81.1 ± 8.4	82.7 ± 3.7
SNB	81.2 ± 7.1	83.2 ± 7.7	80.6 ± 2.9
NSL/NL	7 ± 9.1	4.6 ± 6.6	6.8 ± 2.5
ML/NL	28.9 ± 10	26.4 ± 7.2	21.9 ± 4.5
B. Treacher Collins	Unit°		
SNA	76.3 ± 4.8	79.5 ± 5.7	82.7 ± 3.7
SNB	66.3 ± 6.7	72.5 ± 5.2	80.6 ± 2.9
NSL/NL	16.2 ± 10.8	17.1 ± 7.8	6.8 ± 2.5
ML/NL	41 ± 10.7	34.6 ± 6.9	21.9 ± 4.5
C. Apert	Unit°		
SNA	64.7 ± 4.8	81.4 ± 5.1	82.7 ± 3.7
SNB	76.2 ± 4.3	76.9 ± 6.5	80.6 ± 2.9
NSL/NL	3.2 ± 7.9	8.6 ± 2.4	6.8 ± 2.5
ML/NL	38.8 ± 13.2	30 ± 4.6	21.9 ± 4.5
D. Saethre-Chotzen	Unit°		
SNA	79.4 ± 4.3	79.8 ± 4.1	82.7 ± 3.7
SNB	79 ± 3.4	77.8 ± 2.1	80.6 ± 2.9
NSL/NL	9.9 ± 3.2	8.9 ± 1.7	6.8 ± 2.5
ML/NL	27.8 ± 4.5	28.7 ± 5.3	21.9 ± 4.5
E. Pfeiffer	Unit°		
SNA	74.3 ± 1.2	80.9 ± 4.4	82.7 ± 3.7
SNB	79.4 ± 1.7	82.6 ± 0.9	80.6 ± 2.9
NSL/NL	7.7 ± 3.5	4.3 ± 2.3	6.8 ± 2.5
ML/NL	27.1 ± 12.6	32 ± 10.7	21.9 ± 4.5

Data are presented as the mean ± standard deviation.
*Cephalometric reference values were obtained from healthy patients with normal occlusion used as a control group. Reference values are given for each syndrome.
ML/NL: mandibular line/nasal line; NSL/NL: nasion-sella line/nasal line; SNA: sella-nasion-A-point; SNB: sella-nasion-B-point.

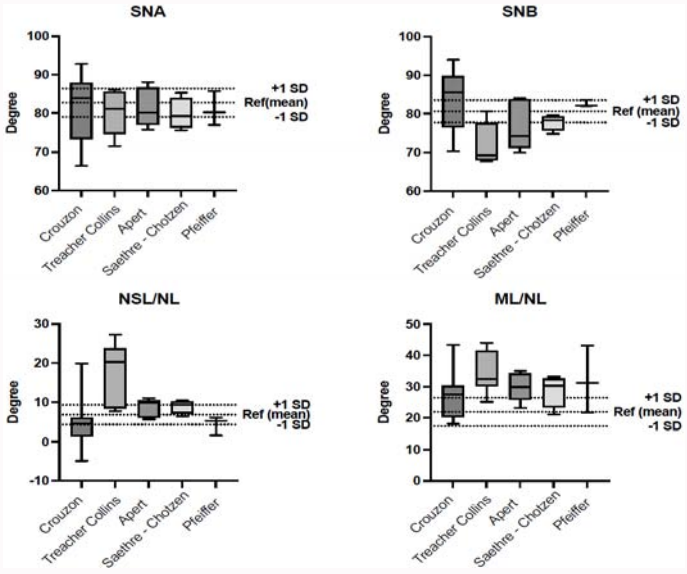

Figure 2: Box plot of cephalometric postoperative measurements for the different patient groups. Data are presented as mean values relative to control (normal) cephalometric values. Treacher Collins syndrome showed a larger deviation from control values for SNB, NSL/NL, and ML/NL as compared with other syndromes.

treatment outcomes according to the orthognathic anteroposterior position of the maxilla (Figure 2).

In all patient groups, the mean SNB values pre-surgery was equal to or lower than that of the control group, suggesting that the mandible was orthognathic or retrognathic. After surgery, patients with Crouzon, Apert, Saethre-Chotzen, or Pfeiffer syndrome presented mean SNB values comparable with that of the control group, demonstrating that the mandible was orthognathic. In the Treacher Collins group, the mean SNB value remained lower than that in the control group despite a 6.2° improvement in the mean SNB value post-surgery. Consequently, the mandible remained retrognathic, making it impossible to achieve an orthognathic mandible in these patients.

The NSL/NL angle showed diverse values across patient groups prior to surgery. However, the majority of patient groups (Crouzon, Saethre-Chotzen, and Pfeiffer syndromes) presented mean NSL/NL values comparable with that of the control group, indicating normal maxillary inclination. For patients diagnosed with Crouzon, Saethre-Chotzen, or Pfeiffer syndrome, the mean NSL/NL values post-surgery remained comparable with that of the control group. Additionally, for patients with Apert syndrome, we found that it was possible to achieve NSL/NL values comparable with that of the control group. However, in the Treacher Collins group, the mean NSL/NL value post-surgery increased relative to that of the control group, demonstrating a greater posterior inclination of the maxilla relative to the control group (Figure 2).

Prior to treatment, mean ML/NL values were higher in the Crouzon, Treacher Collins, and Apert groups, indicating a higher intermaxillary angle (also assessed as a skeletal vertical open bite). After surgery, the mean ML/NL values in the Treacher Collins and Apert groups remained higher relative to that of the control group. The Saethre-Chotzen and Pfeiffer groups showed similar outcomes, indicating a skeletal vertical open bite. The Crouzon group exclusively demonstrated a mean ML/NL value similar to that of the control group, suggesting an appropriate vertical relationship between the mandible and the maxilla post-surgery (Figure 2).

Discussion

This study evaluated treatment outcomes of orthognathic surgery using cephalometry in patients with craniofacial genetic disorders, such as Crouzon, Treacher Collins, Apert, Saethre-Chotzen, and Pfeiffer syndromes. Evaluation included examining changes in the mean SNA, SNB, NSL/NL, and ML/NL angles to determine relationships between the upper and lower jaw in both sagittal and vertical dimensions.

Cephalometric analyses showed significant variation in pre-surgical measurements between the different groups. The mean SNA values in the Crouzon and Apert groups were significantly lower than those in other groups and the control group. Therefore, higher mean SNA values did not influence the possibility of achieving an orthognathic maxilla postoperatively. The Treacher Collins group showed a mean SNB value that deviated most significantly from that of the control group, indicating a greater retrognathism of the mandible and, consequently, increased difficulty in achieving orthognathism. The mean NSL/NL and ML/NL values showed significant variations between groups both pre- and post-surgery; therefore, we were able to draw no clear conclusion from the results. Notably, the Apert and Treacher Collins groups showed significantly higher mean ML/NL values pre-surgery relative to the other groups, indicating a greater skeletal open bite. After surgery, these values decreased in both groups but remained higher than that of the control group, suggesting improvements in the open bite, although still deviating from normal values.

Overall, the results of cephalometric analyses showed improved skeletal relationships in all patient groups post-surgery. The Crouzon group, which was the largest, presented the best surgical outcomes according to the four cephalometric measurements. The Treacher Collins group was the most difficult to treat, which agreed with previous studies [20,21]. However, it is worth noting the potential difficulties with cephalometric analysis owing to the displacement of anatomical landmarks in CFS patients, which can be accompanied by significant individual variation. The SN reference line between the Sella (S) and the Nasion point (N) frequently used in cephalometric analysis is not

always possible to define correctly in syndromic patients. Similarly, the anterior nasal spine of the maxilla is not always visible, making it difficult to obtain a correct measurement of the inclination of the maxilla relative to the SN reference line [7]. Moreover, the patients in this study displayed large individual variations in symptoms and severity both between and within groups, making precise comparison of outcomes between individuals difficult. Development of new surgical strategies, such as counterclockwise distraction osteogenesis [22], may improve outcomes for these patients.

The overall goal with surgical correction of facial anomalies is to improve function, breathing and aesthetics. Patients with Crouzon display a good surgical outcome in general. Patients with Apert syndrome are more difficult to treat because of the anatomical shape of the head and jaws [7]. These patients usually present an abnormal craniofacial morphology that is much more severe than that observed with Crouzon syndrome. Furthermore, additional malformations and cleft palate are more common in children with Apert syndrome [22]. A previous study involving cephalometric analysis of five patients with severe Crouzon syndrome revealed reasonable stability in the A-point and sagittal and vertical positions of the jaw at 2.5-years post-surgery [7].

Some of the clinical features of Saethre-Chotzen syndrome include facial asymmetry, depressed nasal bridge, and deformities of the maxilla, sometimes accompanied by a narrow and/or cleft palate [23,24]. Maxillary hypoplasia is a less common manifestation of Saethre-Chotzen syndrome [25], and this was corroborated by our findings, in which Saethre-Chotzen patients demonstrated mean SNA, SNB, and NSL/NL angles comparable with the control group pre-surgery. Post-surgery results showed a higher mean SNA value and lower SNB and NSL/NL values, although all values remained similar to that of the control group. The mean ML/NL value exclusively deviated from the control value both pre- and post-surgery, indicating a vertical open bite.

This study has some limitations. First, although the patient cohort underwent surgery over an extended time period, the sample size remains relatively small due to the limited incidence of CFS within the overall population. The limited number of cases may also explain the general lack of statistical significance in the changes observed between pre- and post-surgery. Second, we exclusively evaluated skeletal characteristics in this study and not overall appearance or patient satisfaction. We acknowledge the value of patient experience and expectations in allowing a full assessment of surgical outcomes. Furthermore, large anterior movements of the maxillo-mandibular complex pose a risk for skeletal relapse, reinforcing the need for long-term follow-up studies.

In conclusion, we found that orthognathic surgery performed on CFS patients improved skeletal characteristics in all patient groups. Notably, the most difficult patients to rehabilitate were those with Treacher Collins syndrome due to the complexities of the associated anatomical structures.

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