Received: 14 August 2022 | Revised: 30 August 2023 | Accepted: 23 September 2023

DOI: 10.1111/ocr.12719

RESEARCH ARTICLE

Orthodontics & Craniofacial Research WILEY

Non-progressive mandibular changes in children with Type I and II craniofacial microsomia

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Abstract

Objective: To describe the mandibular growth of craniofacial microsomia (CFM) patients during early childhood to adolescence with attention to symmetry.

Materials and Methods: Altogether 61 CFM patients were studied at the Cleft Palate and Craniofacial Center, Helsinki University Hospital between 1986 and 2006. In this cohort study, we measured and analysed 293 radiographs (posteroanterior, panoramic and lateral); 165 radiographs of 40 patients met the final inclusion criteria. The vertical height of the ramus in anteroposterior and panoramic radiographs, the length of the mandible in anteroposterior radiographs and the maxillary protrusion and mandibular retrognathia in lateral cephalograms were measured in four different age groups.

Results: A statistical difference existed between the groups in the vertical height of the ramus and in the mandibular length. The vertical height of the ramus measured from the panoramic radiograph grew on both sides, and the ratios remained unchanged. In the sagittal dimension, the maxilla and mandible grew forward, but no significant differences emerged between the groups.

Conclusions: Results suggest that mild-type CFM is not progressive in nature. During growth, mandibular asymmetry measured in the horizontal, vertical and sagittal planes did not increase.

KEYWORDS
craniofacial microsomia, symmetry

1 | INTRODUCTION

Craniofacial microsomia (CFM) is a congenital deformity of the head and face, occurring second most commonly after cleft lip and palate.[1,2] The incidence of CFM is reported to be 1/3000–5600.[2–5] There are a variety of terms applied to CFM, including Goldenhar syndrome, first and second pharyngeal arch syndrome, hemifacial microsomia and oculoauriculovertebral dysplasia.[6] The umbrella term, oculo-auriculo-vertebral spectrum (OAVS), includes CFM among other anomalies of the head and neck.

The aetiology of the syndrome is unknown. Two theories are suggested as the cause of the deformity: a local haemorrhage near the first and second branchial arch or a disturbed neuroectodermal migration of neural crest cells during foetal development. Third aetilogical theory involves some kind of interference to Meckel's cartilage during its formation.[7,8] CFM has been associated with various genetic causes, although unfortunately the gene causing the malformations remains usually unknown. Previous publications and one more recent publication have noted that copy number variations (CNVs) and especially 14q22.3 duplications are linked to formation of OAVS and CFM within it.[9–11]

The phenotype of CFM is extremely variable;[12] clinical findings range from mild to severe deformities found in the facial skeleton and soft tissue, the external and internal ear and the cranial nerves.[13] The mandibular malformations range from only involving the condyle to severe conditions where the ramus and the temporomandibular joint are missing completely.[14] The condition can occur unilaterally or more rarely, bilaterally.[14–16] CFM nearly always involves the ear and mandibular malformations, even though the severity of these varies.[17] However, because of the extreme variability of the condition, CFM may also be diagnosed without ear or mandibular involvement.[18] The main reason for facial asymmetry is a partial or fully absent condyle.[19]

There are numerous phenotypic descriptive classifications of CFM. The most known is the Pruzansky classification in which the severity of the lacking condyle is divided to three categories.[12–14] Pruzansky classification was later modified by Kaban et al. by dividing the Pruzansky type II into IIa and IIb.[14,15] OMENS classification includes orbital anomalies, mandibular hypoplasy, ear anomalies, nerve involvement and soft tissue deficiency.[20] Expansion of the OMENS classification is the OMENS(+), which includes extracranial features.[21]

How facial asymmetry continues to develop during growth remains unclear. Some studies suggest that there is a progression of facial asymmetry[22] during growth, and other studies have shown that the affected side of the face grows at the same rate as the non-affected side.[23] The clinical significance of this debate is whether to perform surgical intervention during or after the growth of an individual patient. The aim of this retrospective radiographic study was to describe the mandibular growth of CFM patients during early childhood to adolescence with attention to symmetry.

2 | MATERIALS AND METHODS

This was a cohort study in which the patients' clinical records were collected retrospectively from the patient data archives.

2.1 | Material

Altogether 61 CFM patients were investigated at the Cleft Palate and Craniofacial Centre, Helsinki University Hospital between 1986 and 2006. Patient databases were carefully gone through to recognize all CFM patients to minimize risk of selection bias. Only CFM patients with a unilateral condition were included. The diagnosis was based on clinical and radiological findings. Twelve patients underwent ramus distraction osteogenesis and were excluded from this study. These 12 surgical patients were more severe cases of CFM with smaller ramus ratios. Of the remaining 49 patients, 9 were excluded because of lack of sufficient patient information or the final diagnosis was not CFM. The exclusion and inclusion criteria are depicted in the flow chart in Figure 1.

We measured and analysed 197 radiographs (posteroanterior, panoramic and lateral); 165 radiographs (orthopantomograms (ptg) n = 55; PA cephalograms (pa) n = 55; lateral cephalograms (ceph) n = 55)) of 40 patients met the final inclusion criteria (Figure 1). Orthopantomograms and lateral cephalograms have been previously demonstrated to be reliable in mandibular deformity diagnostics and especially vertical and linear measurements.[24,25] Orthopantomograms, lateral cephalograms and PA-cephalograms have been used in previous studies in analysing and measuring mandibular dimensions.[19,26–28]

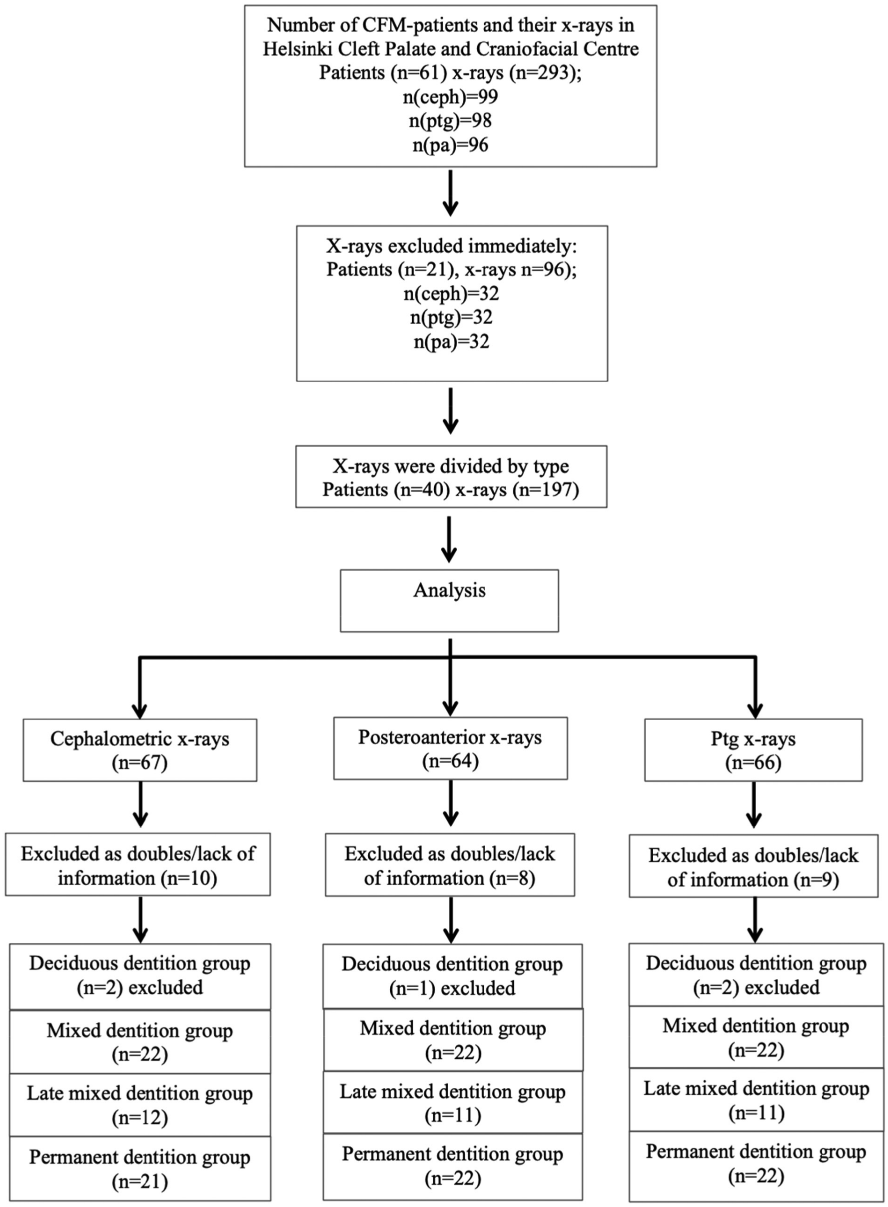
3 | METHODS

We divided the patients into four age groups based on the stage of dental development. Deciduous dentition group comprised patients with full deciduous dentition; this group was subsequently excluded since there were too few radiographs (orthopantomograms (n = 2), PA cephalograms (n = 1) and lateral cephalograms (n = 2)). Mixed dentition group comprised patients with ongoing first stage of eruption of permanent teeth. Late mixed dentition group comprised patients with ongoing second stage of eruption of permanent teeth. Permanent dentition group comprised patients with only permanent dentition. We outlined these groups according to the orthopantomograms. Mixed dentition group included patients who had lost their deciduous mandibular central incisors as seen on the panoramic radiograph due to erupting permanent ones. Late mixed dentition group included patients who had lost their maxillary deciduous canines due to erupting permanent ones and permanent dentition group included patients with only permanent teeth seen on the panoramic radiographs. Mixed dentition group had a mean age of 7.4 (SD ± 1.49), late mixed dentition group had a mean age of 10.9 (SD ± 1.63) and permanent dentition group had a mean age of 17.0 (SD ± 5.23). Twenty-seven radiographs were excluded at this stage so that no doubles of an individual patient were included in any age group (Figure 1).

Vertical height of the ramus was measured in PA cephalograms (Horizontal plane - Gonion) and orthopantomograms (Condylion – Gonion). In PA cephalograms, the length of the mandible was measured from the midline (Menton) to the condyle (Condylion). In lateral cephalograms, maxillary protrusion (Sella – Nasion – A-point) and mandibular retrognathia (Sella - Nasion - B-point) were measured (Figure 3A–C). The traced measurements were digitized, and each group was compared by the Mann–Whitney test.

All 197 radiographs were first analysed manually on a light box with a magnifying glass. One experienced investigator traced the radiographs on 0.003-inch acetate paper with transfer of anatomic landmarks. Cases requiring clarification were additionally evaluated by two senior orthodontists. The radiographic landmarks, planes and their definitions are presented in Figure 3A-C. These landmarks were digitized with a computerized digitizer (X-metrix; Smartsystem,

FIGURE 1 Flow diagram of the study.



Turku, Finland) to evaluate the structural changes in mandibular and maxillary positions. A magnification of 10% was taken into account in the linear measurements.

The groups were compared using the Mann–Whitney test. All tests were two-sided. A *P*-value of ≤0.05 was considered significant. Correction for multiple testing was done using the Benjamini-Hochberg procedure, with the false discovery rate of 0.05. All statistical analyses were done with SPSS version 24.0 (IBM SPSS Statistics, version 24.0 for Mac; SPSS, Inc., an IBM Company).

The study was approved by the institutional review board of Helsinki University Hospital (HUS/917/2021).

4 | RESULTS

Forty patients and their radiographs (n = 197) were categorized by Pruzansky classification. Twenty-eight patients were classified as Pruzansky type I and 12 patients were classified as Pruzansky type II.

4.1 | Sagittal changes

The sagittal changes were evaluated from lateral cephalograms (Figure 3A; Table 1). For each age group, maxillary protrusion and mandibular retrognathia were evaluated by SNA and SNB angle, respectively. Both grew slightly forward to the same extent. A small statistically insignificant decrease occurred between mixed dentition group and late mixed dentition group and a small increase occurred between age late mixed dentition group and permanent dentition group to almost the same angulation as in mixed dentition group in both SNA and SNB angles. A statistically insignificant change in the ANB angle (antero-posterior jaw base relationship) confirmed the finding. The ANB angle increased between mixed

TABLE 1 Radiologic measurements comparing different dental development stages in patients with craniofacial microsomia.

	Mixed dentition group		Late mixed dentition group		Mixed dentition group-late mixed dentition group		Permanent dentition group		Mixed dentition group – Permanent dentition group		Late mixed dentition group-Permanent dentition group	
	Mean	SD	Mean	SD	Mean	*P*-value	Mean	SD	Mean	*P*-value	Mean	*P*-value
Sagittal measurements												
Cephalometric x-ray												
SNA	82.1	7.9	81.8	7.2	−0.4	0.71	82.9	7.0	0.8	0.79	1.1	1.00
SNB	77.3	7.0	76.5	6.1	−0.8	0.76	78.9	6.7	1.6	0.59	2.3	0.49
ANB	4.8	2.8	5.2	2.4	0.4	0.76	4.3	2.7	−0.6	0.53	−1.0	0.33
Ar-Go-Me affected	134.3	7.1	133.5	7.3	−0.9	0.66	133.6	9.2	−0.7	0.94	0.1	0.90
Ar-Go-Me non-affected	129.0	8.3	129.4	10.8	0.3	0.93	126.1	10.7	−2.9	0.22	−3.3	0.37
Horizontal planes and measurements												
Posteroanterior x-ray												
Horizontal plane/gonial plane	4.8	4.0	5.5	3.2	0.6	0.40	5.8	4.5	1.0	0.45	0.3	0.96
Vertical planes and measurement												
Posteroanterior x-ray												
Horizontal plane-Go affected (mm)	76.6	8.4	84.0	11.7	7.4	0.03	88.2	11.7	11.6	<0.0001*	4.2	0.36
Horizontal plane-Go non affected (mm)	80.9	7.3	88.4	8.0	7.5	0.01*	93.0	11.0	12.2	<0.0001*	4.6	0.04
Midsagittal/Menton	4.0	3.0	5.1	2.9	1.1	0.19	4.2	3.3	0.2	0.83	−0.9	0.25
Condyle-Menton affected (mm)	81.2	8.0	85.5	13.7	4.3	0.90	90.8	15.6	9.6	0.01*	5.3	0.05
Condyle-Menton non-affected (mm)	88.5	8.1	91.3	12.0	2.8	0.51	101.7	8.9	13.1	<0.0001*	10.4	0.03
Ptg x-rays												
Ramus height (affected) (mm)	43.9	10.0	49.2	10.5	5.3	0.16	48.2	14.0	4.3	0.16	−1.0	0.90
Ramus height (non-affected) (mm)	51.7	7.2	58.1	9.8	6.3	0.04	58.2	9.8	6.5	0.04	0.1	1.00
Cephalometric x-ray												
Maxilla/Mandibula°	30.0	5.4	29.1	7.3	−1.0	0.85	30.9	7.2	0.9	0.64	1.8	0.49

*P-values after correction for multiple testing remaining statistically significant using the Benjamini-Hochberg procedure with false discovery rate of 0.05.

dentition group and late mixed dentition group and decreased again between late mixed and permanent dentition groups to almost the same angulation as in mixed dentition group, but these changes were not statistically significant (Table 1).

The gonial angle (Ar-Go-Me) on the affected side slightly decreased between mixed and late mixed dentition groups and thereafter remained the same. On the unaffected side, the gonial angle remained the same between mixed dentition group and late mixed dentition group and showed a slight decrease between late mixed and permanent dentition group. These slight changes in the gonial angle were not statistically significant on either side (Table 1).

4.2 | Horizontal changes

The angle between the gonial plane (plane between GoR-GoL) and the horizontal plane measured from PA cephalograms indicated horizontal symmetry of the mandible (Figure 3B). The asymmetry of the mandible in the horizontal plane in the gonial region increased during growth since the angle between the gonial plane and the horizontal plane grew slightly, but the change was not statistically significant (Table 1).

4.3 | Vertical changes

The ramus height ratios were measured on orthopantomograms and PA cephalograms by dividing the affected height of the ramus by the unaffected ramus height. The radiographic landmarks, planes, angles, and their definitions are depicted in Figure 3B,C.

The ratios describe the relation between the affected side and the unaffected side of the mandible during growth. The ramus ratios measured from the orthopantomograms and PA cephalograms remained almost the same during growth (Figure 2A,B; Table 1).

Vertical height of the ramus measured from the PA cephalogram (horizontal plane-Go [mm]) on the affected side of the mandible increased during growth, and this was significant between mixed dentition group and late mixed dentition group (mean increase 7.4 mm) and mixed dentition group and permanent dentition group (mean increase 11.6 mm. On the unaffected side of the mandible, the vertical height of ramus increased also during growth, and the increase was significant between every dental age group (mean increase between mixed dentition group and late mixed dentition group was 7.4 mm, between late mixed dentition group and permanent dentition group was 4.6 mm and between mixed and permanent dentition group was 12.2 mm) (Table 1). After correction for multiple testing the increase between the mixed and permanent dentition group on the affected side and the increase between mixed and late mixed and mixed and permanent dentition groups on the unaffected side remained under the false discovery rate and thus remained significant.

The length of the lower jaw measured from the condyle to the menton (mm) in PA cephalograms increased on both the affected side and the non-affected side during growth, and the increase was significant on both sides between late mixed dentition group and permanent dentition group (mean increase on the affected side 5.3 mm and on the unaffected side 10.4 mm) and between mixed dentition group and permanent dentition group (mean increase on the affected side 9.6 mm and on the unaffected side 13.1 mm) (Table 1). The increase between the late mixed and permanent dentition groups did not remain significant after multiple testing.

The angle between the menton and the midsagittal line on the PA cephalogram stayed almost the same during growth, with a minor increase during the growth spurt between mixed dentition and late mixed dentition groups and a minor decrease after the growth spurt between late mixed dentition group and permanent dentition group, but these changes were statistically non-significant (Table 1).

Ramus height (Condylion-Gonion) measured from the orthopantomogram increased on the affected side during growth (mean

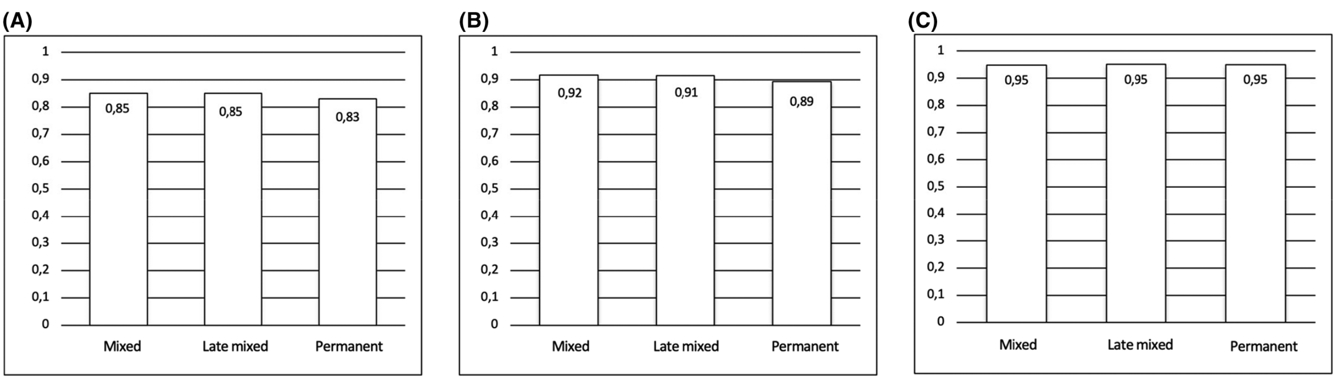


FIGURE 2 (A) Ramus ratio (mean affected ramus height/mean non-affected ramus height) measured from the orthopantomogram in different age groups. Mixed dentition group (mean age 7.4, SD ± 1.49), late mixed dentition group (mean age 10.9, SD ± 1.63) and permanent dentition group (mean age 17.0, SD ± 5.23). (B) Condyle-Me ratio (mean affected codyle-menton height/mean non-affected condyle-menton height) measured from the PA cephalogram in different age groups. Mixed dentition group (mean age 7.4, SD ± 1.49), late mixed dentition group (mean age 10.9, SD ± 1.63) and permanent dentition group (mean age 17.0, SD ± 5.23). (C) Horizontal plane-Go ratio (horizontal plane-gonion height affected/horizontal plane-gonion height non-affected) measured from the PA cephalogram. Mixed dentition group (mean age 7.4, SD ± 1.49), late mixed dentition group (mean age 10.9, SD ± 1.63) and permanent dentition group (mean age 17.0, SD ± 5.23).

increase 4.3 mm), but the change was not statistically significant. On the unaffected side, the ramus height increased during growth and the increase was significant between mixed dentition and late mixed dentition groups (mean increase 6.3 mm) and between mixed dentition group and permanent dentition group (mean increase 6.5 mm) (Table 1) but did not remain significant when adjusted for multiple testing.

The angle between the maxilla and mandible, a measurement that reflects divergence between jaws, measured from the lateral cephalograms, remained the same during growth (Figure 3A; Table 1).

The ramus height ratios between the different age groups were very close to each other, and no change was seen during growth. This suggests that growth on the affected and unaffected sides occurs at the same relative proportion (Figure 2A-C).

5 | DISCUSSION

We show that asymmetry in CFM does not have a progressive nature. This is, to our knowledge, the first follow-up study of this size that uses measurements of radiographs from all three dimensions. We focused on describing the mandibular growth of non-operatively treated CFM patients from early childhood to adolescence, paying special attention to symmetry of the mandible. Patients were divided by the stage of eruption of permanent teeth.[29,30] Patients were classified as Pruzansky types I or II, and an earlier study has shown that there is no delay in dental development in CFM patients of Pruzansky types I and II.[31]

In the anteroposterior or sagittal dimension in normally growing individuals, the ANB angle decreases with age. This is because the SNA angle and SNB angle both increases, but SNB increases slightly more. The main reason for this ANB angle decrease is the forward growth of the mandible.[29] In the present study, we observed that the SNA and SNB angles of CFM patients both increased slightly, and the SNB angle increased slightly more. The ANB angle of CFM patients remained the same throughout the growth, even though this finding was not statistically significant. This still indicates that the mandibula and maxilla of CFM patients grew and the mandibular retrusion did not increase. The retrusion and the asymmetry of the mandible of CFM patients are produced by the more affected side of the mandible being smaller from the beginning of growth than the unaffected side. CFM patients start with shorter ramus heights on both sides than a healthy control group.[32] There were five measurements that differed between the dentition groups with statistical significance; however, these differences were clinically irrelevant.

Vertically, the ramus height increases on both sides as seen on the panoramic and posteroanterior radiographs, even though the growth is not statistically significant. Since our patient material was heterogenic and the radiographs were taken at different ages, the ramus height ratios measured from the panoramic radiograph and the two ramus height ratios (affected/non-affected) measured from the posteroanterior radiograph describe the growth and the asymmetry more clearly than individual measurements of the affected and non-affected sides of the mandible. Our study shows that the ramus height ratios stay the same during growth, which indicates that both sides of the mandible grow at a similar pace, and thus, the asymmetry does not progress. This finding parallels with findings in earlier reports.[23,32,33]

Most of the previous CFM studies have used measurements from only posteroanterior cephalograms or only lateral cephalograms. Posteroanterior cephalograms were used by Kearns et al.[22] who documented in their study that the facial asymmetry in patients with CFM is progressive, and the progression correlates with the severity of the mandibular deformity. On the other hand, lateral cephalograms were used by Ongkosuwito et al.[13] that patients with CFM showed retrusion of both the maxilla and mandible, with the mandible being more affected, compared with a Dutch reference group. One study had a sample of three-dimensional images from 6 CFM patients and showed that the ramus was always smaller on the affected side and grew at a slower rate in 5 of the 6 patients.[34] However, this sample was small, even though they utilized three-dimensional imagery. Ideally, mandibular growth should be examined with 3D scans or models since it is a complex phenomenon occurring in all three dimensions.[25] Computed tomography images were used by Kim et al.[35] to compare the growth of the CFM mandible with a normal control group. They had 28 CT images at hand, but the patients had a large age range (mean age 14.8 ± 7.1 years) and consisted of two different racial populations (French and Korean), with the control group comprising a Korean adult population only.

The progressive nature of facial asymmetry in CFM remains a controversial topic. This radiographic follow-up study using radiographs from all three dimensions shows that the asymmetry of CFM does not progress with time and growth. The clinical significance of this controversy is whether early correction of the asymmetry is justified. Early intervention is favoured by the progressive asymmetry hypothesis.[15,22] In cleft patients, surgical procedures are suggested to cause growth-restricting scar tissue.[36] Surgical treatments like distraction osteogenesis have provided many excellent short-term results, but the tendency for reappearance of the asymmetry over time has clearly been shown.[27,37]

Even though CFM is the second most common craniofacial malformation our cohort is relatively small. This may be due to the extremely variable phenotype of the condition. Many CFM patients do not need to seek care since their malformation type is mild and it does not affect their facial symmetry. This may also be the reason a substantial portion of CFM patients remain undiagnosed and patients who seek treatment are the more severe types. In addition, the treatment of CFM patients in Fin is not fully concentrated in one craniofacial center, causing treatment of mild cases scattered around the country. This study included patients with only mild deformities classified as Pruzansky types I and II, and the more severe cases were excluded since they were surgically treated with distraction osteogenesis. The patients with severe CFM malformations may need early surgical treatment even if the condition does not progress over time, e.g. with severe sleep apnea, eating difficulties and aesthetic or psychological problems.

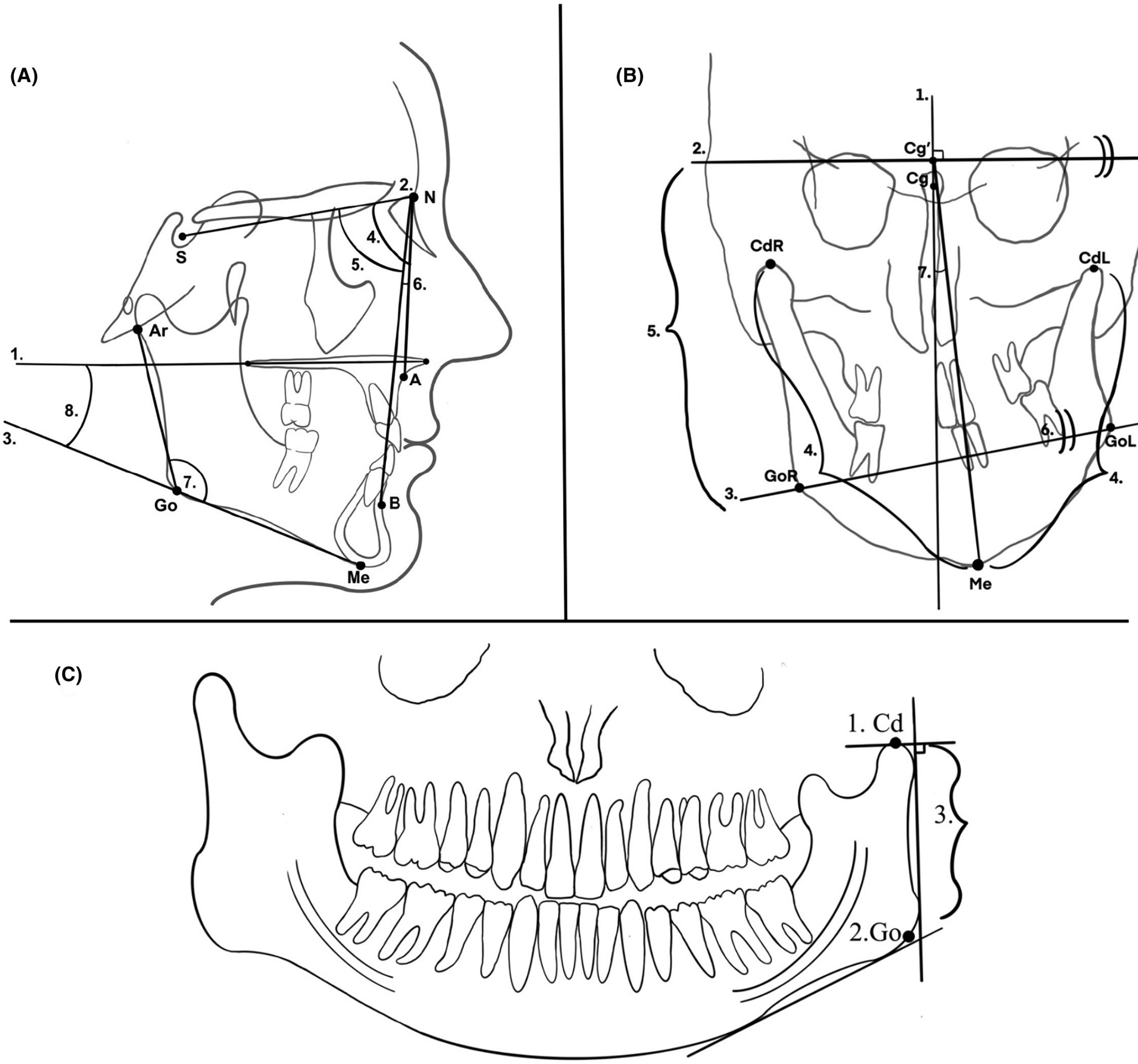


FIGURE 3 (A) Cephalometric points, planes and angles used. S; sella, N; nasion, B; B-point, A; Go; gonion, Me; menton, Ar; articulare. Planes: 1. Palatal Plane, 2. Sella-Nasion, 3. Mandibular plane. Angles: 4. SNA, 5. SNB, 6. ANB, 7. Gonial angle (AR-Go-Me), 8. Maxillar plane/ Mandibular plane. (B) Points and angles used in PA cephalograms. Cg; crista galli, Cg'; crista galli cut point, Go; gonion, Me; menton, Cd; condylion, ANS. Planes: 1. Midsagittal plane, 2. Horizontal plane, 3. Gonial Plane. Distance: 4. Cd-Me (R and L), 5. Horizontal plane-Go (R and L). Angles: 6. Horizontal plane/Gonial plane, 7. Midsagittal plane/Me. (C) Measurements used in orthopantomograms. 1. Cd; Condylion, 2. Gonion, 3. Ramus height.

Our cohort comprises patients who have not been surgically treated. This enables us to examine and demonstrate undisturbed growth of CFM patients, and this is unique in such a rare condition. The limitations of our study include the retrospective design, the heterogenic patient material and the lack of a control group for all three radiographic images. Selection bias is a known weakness in retrospective study design; however, in our study, risk of this is minimal due to clearly defined population and accessible and reliable patient data.

CFM is a complex malformation occurring in all three dimensions and ideally should be assessed in that way. Data captured from a cone beam computed tomography system would be the ideal approach, but large radiation doses used with young children would not be ethically approved. Today, modern technology and 3D photography would enable us to create a more precise approach to this problem, but since this cohort was gathered from 1986 to 2006, only two-dimensional records were available. Since radiographs are two-dimensional, small errors occurring during patient preparation and positioning can have various effects on the produced radiograph and should be assessed with caution.

In conclusion, we have shown that in mild cases CFM does not have a progressive nature, thus, operative treatment can be postponed until skeletal maturity is reached if no other medical conditions require early intervention. Even though there have been some large multicenter studies published in recent years,[38,39] due to the rarity and the heterogeneity of the condition, future studies should be performed collaboratively between craniofacial centers and documentation of patients and their growth preferably using 3D photography should be done in a uniform fashion to enable true longitudinal studies.

ACKNOWLEDGEMENTS

We wish to express our warmest gratitude to Kirsti Hurmerinta, who gave her time and experience to this research.

FUNDING INFORMATION

We received the HUCH research grant.

CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest to report.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

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How to cite this article: Kaprio L, Grann A, Leikola J, Saarikko A, Kurimo J, Kiukkonen A. Non-progressive mandibular changes in children with Type I and II craniofacial microsomia. *Orthod Craniofac Res*. 2023;00:1-9. doi:10.1111/ocr.12719