Analyses of craniofacial and dental morphology in monozygotic twins discordant for cleft lip and unilateral cleft lip and palate

Carroll-Ann Trotman, BDS, MA; Anthony R. Collett, BDSc, MDSc, PhD; James A. McNamara, Jr., DDS, PhD; Steven R. Cohen, MD

Clefts of the lip and palate are the most common craniofacial deformities. These anomalies have multifactorial inheritance, with both genetics and environment making varying contributions, and they can occur as a feature of various genetically determined syndromes.[1] Treatment involves a multidisciplinary approach[2] and many children require orthodontic intervention in infancy.[3] Of particular importance with regard to orthodontic treatment is an appreciation of the effects of clefting on the craniofacial and dentoalveolar development.

Skeletal relationships in the cleft population may be a result of either the cleft, surgery to repair the cleft, or a combination of both.[4] Available evidence suggests that the source of the reported midface deficiency in cleft patients is, for the most part, iatrogenic, that is, as a consequence of the surgical repair. Recent reports relating to unoperated cleft patients[5,6] found that there is potential for normal maxillary growth in cleft lip and palate patients (specifically unilateral clefts), with anteroposterior maxillary growth being more favorable than in surgically treated patients.

Constriction of the maxillary dental arch often occurs as a consequence of cleft palate surgery;[7,8] however, the associated skeletal transverse dimensions have for the most part been ignored, or the results have been equivocal.[9-13] The literature is also inconclusive with regard to nasal widths of cleft patients[11,13,14] and due to the large within-group ranges for both normal and cleft groups, definitive conclusions cannot be drawn from these studies.

Monozygotic twins provide a useful source of matched controls and tests. Because such twins result from fertilization of one ovum, they are genetically identical (whereas dizygotic twins are no more genetically alike than any other pair of siblings). That monozygotic twins have smaller

Abstract

The Michigan Cleft Twin Sample data was analyzed in order to investigate dental arch and craniofacial morphology. The present study consisted of 12 monozygotic twins discordant for either cleft lip or unilateral cleft lip and palate. Individuals having CL (repaired) alone did not differ from their unaffected counterparts in dental arch and skeletal morphology. Repaired UCLP subjects were characterized by having a shorter and more posteriorly positioned maxilla. Although reduction of dental arch width as a result of scar contraction following surgery was evident, the effects of scar tissue pull did not affect maxillary basal width.

Key Words

Monozygotic twins • Cleft lip and palate • Craniofacial morphology • Cephalometrics

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Figure 1
Lateral cephalometric landmarks used in analysis
N-nasion, junction of nasal and frontal bones
Ba-basion, anterior border of foramen magnum
S-sella, estimated center of the pituitary fossa
Or-orbitale, inferior point on the outline of the orbit
Po-porion, superior border of external auditory meatus
PMP-posterior maxillary point, a construct created by dropping a perpendicular from the inferior point on the pterygomaxillary fissure to a line joining ANS and the posterior nasal spine
ANS-anterior nasal spine
A-point of greatest concavity of the alveolar process of the maxilla
Co-condylion, posterior superior point on the outline of the condyle
Go-gonion, constructed on the outline of the mandible by bisecting the ramus and corpus plane
Gn-gnathion, most anterior inferior point on the symphysis

Figure 2
Frontal cephalometric landmarks used in analysis:
Co-lateral point of condyle
Z-lateral point of zygomatic bone
Em-Ectomaxillare, point on lateral contour of maxilla, that is closest to the median plane
Na-lateral point of nasal aperture

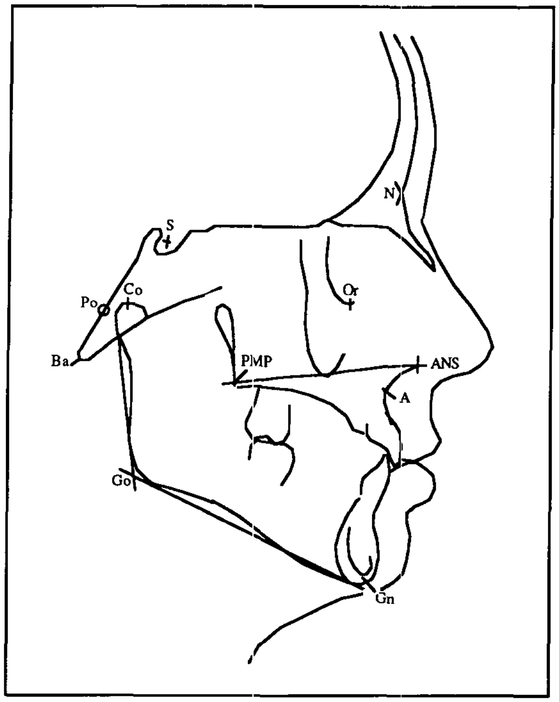

Figure 1

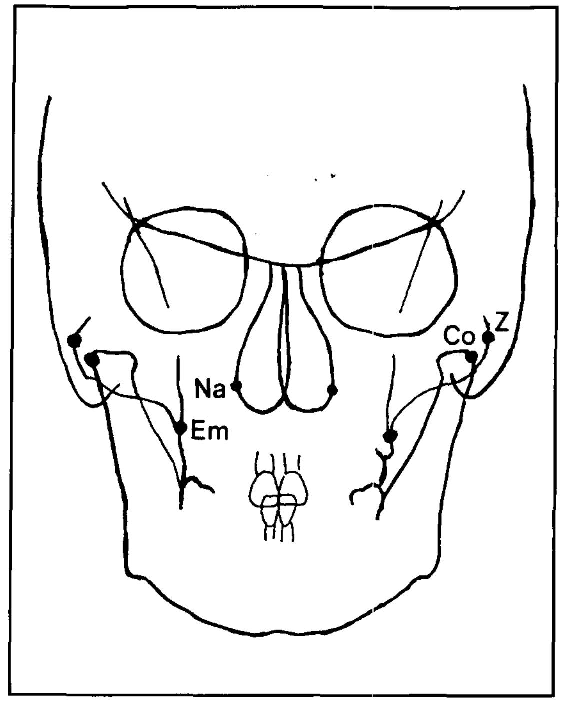

Figure 2

intrapair differences regarding craniofacial and dental morphology than do, for example, dizygotic twins has been confirmed by a number of investigators.[26]

Studies of exclusively monozygotic twins, in which the trait being investigated is present in one but not the other, are often not feasible due to the small numbers available. Only an estimated one in 40,000 births on average results in a twin with a cleft,[15] and the incidence of monozygotic twins discordant for clefts would be appreciably lower than this figure. This low incidence is reflected in previously published reports concerning craniofacial and dental morphology of monozygotic twins discordant for clefts in which, generally either a single pair were considered,[16-18] or two sets.[19] Studies using slightly increased numbers of twins have been published by Blake and Wreakes[20] (four sets) and Ross and Coupe[21] (six sets). None of the above reports evaluated transverse skeletal parameters. Thus, the Michigan set of 20 monozygotic twins discordant for clefts constitutes a still unparalleled data source. In 1971-72, cross-sectional data for pairs of monozygotic and dizygotic twins discordant for cleft lip and/or palate were collected by the Center for Human Growth and Development at The University of Michigan. Investigators Hunter[22-25] and co-workers documented and published a number of craniofacial and dental findings based on the Michigan Cleft Twin Sample.

Factors studied by Hunter included the effects of clefting on crown-root length, tooth eruption and craniofacial morphology. The effects of clefting (lip and/or palate) on crown root length and eruption times were minimal. Of particular interest are the findings relating to craniofacial morphology. Morphological differences were assessed using lateral cephalometric radiographs. Hunter[24] reported that while the presence of cleft lip (CL) has no apparent effect on the maxilla, clefts that involve the palate (unilateral cleft lip and palate, UCLP; cleft palate, CP; bilateral cleft lip and palate, BCLP) are associated with maxillary deficiency in both anteroposterior size and position. In addition to lateral cephalometric radiographs, the subjects in the Michigan cleft twin study also had postero-anterior (PA) and/or occipito-mental (OM) radiographs taken, and these have not been previously evaluated. Also, a number of parameters relating to the dental casts have not yet been documented in the literature.

The aim, therefore, of the present study was to re-evaluate the Michigan cleft twin data which comprised monozygotic twins discordant for CL and UCLP, together with records on a pair of monozygotic twins discordant for UCLP which was previously assembled by Ross[21] at The Hospital for Sick Children, Toronto. These records will be used to assess lateral and transverse craniofacial relationships.

Materials and methods

Dental and medical records, including radiographs and dental casts, of 12 pairs of monozygotic twins discordant for CL (7 pairs) and UCLP

Table 1
Ages at cleft lip and palate repairs

Cleft Type	Age/lip repair (mo=months)	Age/ palate repair (mo=months)
CL	4 mo	-
CL	4 mo	-
CL	4 mo	-
CL	1 week	-
CL	2 mo	-
CL	10 mo	-
CL	5 mo	-
UCLP	2 mo	24 mo
UCLP	2 mo	12 mo
UCLP	3 mo	18 mo
UCLP	3 mo	20 mo
UCLP	4 mo	Staged repair soft palate at 15 mo hard palate at 18 mo

Table 2
Transverse skeletal and dental dimensions. The intratwin differences (NC-C) were evaluated using Students t -test (paired, two-tailed; *p<0.05). For dental dimensions relating to UCLP refer to case studies.

Transverse width (mm)	Non-Cleft (NC) mean (S.E.) n=12	CL (NC-C) mean (S.E.) n=7	UCLP (NC-C) mean (S.E.) n=5
Bicondylar (Co-Co)	112.0 (4.0)	-0.2 (0.7)	0.0 (0.8)
Bimaxillary (Em-Em)	64.0 (2.0)	-0.6 (0.5)	0.4 (0.7)
Bizygomatic (Z-Z)	118.0 (2.0)	-0.6 (0.8)	1.0 (0.7)
Nasal (Na-Na)	26.0 (1.0)	-0.3 (0.7)	-2.0 (0.6)
Intermolar (6-6)	53.0 (2.0)	-0.6 (0.5)	-
Intercanine (3-3)	35.0 (1.0)	0.1 (0.3)	-

(5 pairs) were assembled. The source of the data was the previously collected twin records of The Center for Human Growth and Development, University of Michigan, and The Hospital for Sick Children, Toronto. The mean age of the twin pairs, both CL and UCLP groups, was 121 months (range 68 to 180 months, S.E.=21, n=12). That of the CL group was 109 months (range 68 to 164 months, S.E.=13, n=7), and the UCLP group 137 months (range 82 to 180 months, S.E.=21, n=5). The ages at lip and palate repair are given in Table 1.

Monozygotic status had been previously determined as outlined by Hunter.[24] For each twin pair the diagnosis and surgical procedures were documented, and the lateral and postero-anterior (PA) or occipito-mental (OM) radiographs were assessed (depending on availability) as described below. Lateral cephalometric radiographic landmarks were digitized (Figure 1) and analysis performed. In addition, where dental casts were available prior to maxillary orthodontic treatment transverse dental arch dimensions were recorded.

For each of the PA and OM radiographs the bicondylar width, bizygomatic width, bimaxillary width and nasal cavity width were determined (Figure 2). The intercanine and intermolar widths (using buccal gingival margins) of the dental arches were measured using a set of electronic digital calipers accurate to 0.03 mm. The intratwin differences for these parameters were calculated as the non-cleft dimension minus the cleft dimension (NC-C) for each monozygotic pair. For each set of radiographs and models measurements were taken by two independent operators (AC and CT) and the interobserver reliability was negligible.

Dimensional and angular differences, together with means and standard errors (S.E.), between non-cleft (NC) and cleft (C) twins were assessed by means of a two-tailed paired *t*-test. The null hypothesis was rejected at probability levels of less than 0.05. Cases in which orthodontic treatment had been undertaken in the maxillary arch were eliminated from the dental cast analysis. As a result, there were insufficient study model data for the UCLP twin pairs, and these data are reported as case studies.

Results

Absolute dimensions and angles for the 12 non-affected individuals are given in Tables 2 and 3. Analysis of transverse skeletal dimensions revealed that regardless of the cleft type, or age of the twins, there was no difference between the cleft and non-cleft individuals (Table 2). Although the variation in age of the overall sample was large, the intratwin differences were consistently small. In considering the bimaxillary width, for example, within the UCLP group bimaxillary widths differed by up to 14 mm, whereas the maximal intratwin difference was 2 mm. No significant intratwin differences were found for dental arch dimensions between the non-cleft and CL monozygotic twin pairs. The transverse dimensions relating to UCLP twins are discussed below

Table 3
Lateral cephalometric analysis. The intratwin differences (NC-C) were evaluated using Students t-test (paired, two-tailed; *p<0.05).

Variable	Non-Cleft (NC) mean (S.E.) n=12	CL (NC-C) mean (S.E.) n=7	UCLP (NC-C) mean (S.E.) n=5
N-S (mm)	74.9 (1.6)	-0.4 (0.4)	2.6 (0.3)*
S-Ba (mm)	45.8 (1.2)	1.6 (0.8)	0.4 (0.5)
S-N-Ba (deg)	130.2 (1.8)	-2.0 (1.3)	2.2 (1.1)
N-ANS (mm)	50.2 (1.8)	1.3 (1.2)	-0.2 (0.7)
Po-Or-SN (deg)	3.9 (1.0)	-1.9 (1.0)	-0.4 (1.0)
Po-Or-ANS (deg)	0.7 (1.1)	3.8 (2.5)	-1.4 (1.8)
ANS-PMP (mm)	47.2 (1.6)	0.4 (1.4)	2.3 (0.5)*
S-PMP (mm)	47.3 (1.6)	0.4 (1.4)	2.3 (0.5)*
Ba-PMP (mm)	47.1 (1.1)	0.7 (0.4)	4.5 (1.1)*
SNA (deg)	81.1 (1.1)	0.7 (1.9)	2.5 (1.3)
N Perp-A (mm)	3.4 (0.8)	1.3 (1.4)	-2.9 (1.7)
Co-Gn (mm)	111.8 (3.2)	0.0 (1.4)	1.4 (2.0)
Go-Gn (mm)	74.7 (2.3)	1.3 (0.9)	1.5 (1.3)
Co-Go (mm)	52.8 (2.0)	-0.9 (0.9)	-0.2 (1.2)
Co-Go-Gn (deg)	122.7 (1.4)	-0.8 (0.7)	-1.2 (1.2)

as case studies.

As evident in Table 3, the presence of CL alone had no apparent effect on lateral skeletal dimensions. Individuals exhibiting UCLP were characterized by having a shorter anterior cranial base (S-N), a more posteriorly positioned maxilla (Ba-PMP), and a decreased maxillary length (ANS-PMP). In addition, the vertical maxillary distance (S-PMP) was less in the UCLP twins. The position of Point A (relative to both sella-nasion and the nasion perpendicular) was not significantly different to that of their unaffected twin.

Case A

A pair of monozygotic male twins discordant for unilateral cleft lip and palate were assessed at age 7 years 6 months. The affected twin had a left unilateral complete cleft. At 4 months of age surgical lip repair was undertaken using the Millard technique, followed by repair of the soft palate at 15 months. Second stage hard palate repair was performed at 18 months. A Z-plasty to the nasal tip and lip was completed at 2 years 5 months, and then a pharyngeal flap procedure at 5 years 6 months. Further lip and nasal surgery was carried out at 6 years 11 months.

Transverse skeletal and dental measurements are given in Table 4. Inspection of the data reveals that although considerable contraction of the maxillary arch had occurred, there was no decrease in skeletal transverse dimensions.

Case B

The second case report concerns a pair of male monozygotic twins discordant for unilateral cleft lip and palate at age 13 years 3 months. In this case the affected twin presented with an incomplete cleft of the right lip and a complete cleft of the hard and soft palate. Cheiloplasty to the right lip was performed at 2 months, a palate repair employing bilateral relaxing incisions undertaken at 2 years of age, and finally an adenoidectomy and bilateral myringotomies at approximately 7 years 8 months.

The records show that although substantial maxillary dental arch contraction was evident for the cleft twin, transverse skeletal dimensions were the same for the unaffected twin (Table 4).

Discussion

The present finding of no alteration in skeletal and transverse dental arch dimensions in repaired cleft lip subjects is in agreement with most previous reports.[8] Of note is the small intratwin differences for the skeletal and dental dimensions. Thus it would appear that in monozygotic twins, hereditary factors dictate remarkably similar facial morphology between twins, being consistent with other reports concerning craniofacial morphology in monozygotic twins.[21,26] The intratwin differences did not appear to be age dependent.

With regard to repaired UCLP cases, there was no apparent alteration in transverse skeletal morphology, disagreeing with an earlier report concerning CP patients by Farkas and Lindsay.[14] The results of Wepner and Hollmann[13] indicating that bizygomatic and bimaxillary widths were increased in young (10 to 14 years) cleft patients but normalize by adulthood were not supported by our results, which suggest that this age group do not differ from non-cleft individuals in transverse skeletal morphology.

In addition, transverse skeletal parameters for discordant UCLP twins were not related to dental arch dimensions. Although contraction of the dental arch was evident in the two UCLP cases (no previous orthodontic treatment) presumably as a result of surgical repair of the palate, the transverse skeletal dimensions were virtually identical to the non-affected twin. The pattern of maxillary dental arch contraction observed here is similar to that noted by Dixon,[27] in which the greatest contraction was in the canine region.

The findings that the maxilla was more posteriorly positioned, and shorter anteroposteriorly, in UCLP patients is consistent with earlier reports using these data.[22,24] With regard to maxillary length, Ross[28] reported the same in UCLP patients, and proposed that there may be some intrinsic growth deficiency in the midfacial skeleton. An explanation for the relative retropositioning of the maxilla with growth has been proposed by Ross,[7] who introduced the concept of maxillary ankylosis to describe the situation whereby as a result of surgery a continuum of scar tissue joins the maxilla, the palatine bone, and the pterygoid plates of the sphenoid thus inhibiting separation of these bones, and ultimately forward maxillary movement. That intratwin differences for SNA and Nasion perpendicular to Point A were not significant most likely arises from Point A being under dental influence, rather than constituting a strictly skeletal landmark.

A shorter anterior cranial base length in UCLP twins compared to their non-cleft counterparts is consistent with a study by Aduss,[29] but at variance with the results of Cronin and Hunter[22]. The reason for the difference between our finding and that of Cronin and Hunter is unknown, but may relate to the fact that our data sample is a subset of the original Michigan Twin Sample previously described by these authors.

Conclusions

In conclusion, while cleft lip repair is not associated with any difference in craniofacial and dental arch morphology compared to matched non-cleft twins, UCLP affected twins display a relatively retropositioned and short maxilla following surgical repair. Although surgery to repair the palatal defect gives rise to constriction of the maxillary dental arch, this effect is confined to dentoalveolar structures; transverse skeletal development being unaltered.

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Table 4
Transverse sleletal and dental dimensions, and intratwin differences (NC-C) for two pairs of twins discordant for UCLP.

Transverse width (mm)	Case A Non-Cleft (NC)	Case A (NC-C)	Case B Non-Cleft (NC)	Case B (NC-C)
Bicondylar (Co-Co)	109.0	-1.0	138.0	1.0
Bimaxillary (Em-Em)	61.0	1.0	72.0	1.0
Bizygomatic (Z-Z)	123.0	2.0	124.0	3.0
Nasal (Na-Na)	29.0	1.0	31.0	1.0
Intermolar (6-6)	53.4	4.2	60.6	5.4
Intercanine (3-3)	31.9	8.2	38.3	7.2

Author Address

Dr. Carroll-Ann Trotman
Department of Orthodontics and
Pediatric Dentistry
School of Dentistry
University of Michigan,
Ann Arbor, MI 48109-1078

C-A. Trotman is an Assistant Professor in the Department of Orthodontics and Pediatric Dentistry at the University of Michigan, Ann Arbor, Michigan.

A.R. Collett is a Visiting Research Fellow at the Department of Orthodontics and Pediatric Dentistry, University of Michigan, Ann Arbor, Michigan.

J.A. McNamara, Jr. is a Professor in the Department of Orthodontics and Pediatric Dentistry, and a Research Scientist at the Center for Human Growth and Development, University of Michigan, Ann Arbor, Michigan.

S.R. Cohen is an Assistant Professor in the Section of Plastic Surgery, and Director of the Craniofacial Anomalies Program at the University of Michigan, Ann Arbor, Michigan.

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