ORTHODONTICS & CRANIOFACIAL RESEARCH

ORIGINAL ARTICLE

Skull thickness in patients with clefts

T Arntsen
I Kjær
L Sonnesen
K Mølsted

Authors' affiliations:
T. Arntsen, I. Kjær, L. Sonnesen, Department of Orthodontics, Institute of Odontology, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark
K. Mølsted, Copenhagen Cleft Lip and Palate Centre, Hellerup, Denmark

Correspondence to:
Inger Kjær
Department of Orthodontics, Institute of Odontology
Faculty of Health Sciences
University of Copenhagen
20 Nørre Allé
DK-2200 Copenhagen
Denmark
E-mail: ik@odont.ku.dk

Dates:
Accepted 5 November 2009

To cite this article:
Arntsen T, Kjær I, Sonnesen L, Mølsted K: Skull thickness in patients with clefts
Orthod Craniofac Res 2010;**13**:75–81

Structured Abstract

Authors – Arntsen T, Kjær I, Sonnesen L, Mølsted K

Objectives – The purpose was to analyze skull thickness in incomplete cleft lip (CL), cleft palate (CP), and combined cleft lip and palate (UCLP).

Setting and Sample Population – Copenhagen School of Dentistry and Copenhagen Cleft Lip and Palate Centre. Patients with cleft lip, cleft palate, and combined cleft lip and palate and normal adult men.

Material and Methods – Four groups of patients comprised the study. One group of patients with CL (24 patients; 7 women, mean age 6; 17 men, mean age 7.1), one group of patients with UCLP (28 patients; 11 women, mean age 6.6; 17 men, mean age 6.7), one group of patients with CP (57 male patients aged 18–33), and one normal adult male control group. The CL and UCLP groups were compared. The CP group was compared with the normal adult male control group.

Results – CL women had a significantly thinner occipital bone compared with CL men (p = 0.027). Women with UCLP had significantly thicker occipital bone than the control women (incomplete CL) (p = 0.014). The study showed gender differences in skull thickness in different cleft types. It also demonstrated that particularly the occipital bone deviated in patients with UCLP, which may explain the considerable deviations in jaw shape and position, previously registered in patients with UCLP.

Key words: bone; cephalometry; clefts; human; skulls

Introduction

The genetic background for cleft lip (CL), cleft palate (CP), and combined cleft lip and palate (UCLP) malformations is considered to be different (1, 2), but still not mapped out in detail. Therefore, it is important to focus on the phenotypic similarities and phenotypic differences between the cleft groups. The craniofacial phenotype in different types of clefts is thoroughly described, and several studies have reported on differences in craniofacial morphology (3–11). These different phenotypic appearances registered on the craniofacial profile radiographs might support the theories on the different genetic backgrounds and/or genetic penetrance.

Also in the cervical spine, morphological differences between the cleft groups have been reported. The prevalence of anomalies was higher in the cleft groups compared to normal. Within the cleft groups, the prevalence of anomalies was significantly higher in the CP group (12–14). The

anomalies in the cervical spine were divided into the following two main groups: posterior arch deficiency with short and/or abnormal arches and fusions between arches and vertebral bodies (12, 14).

Other additions to phenotypic characteristics are differences in the length of the nasal bone in different cleft types (8, 9). In these studies, the nasal bone appeared short only in the CL group. In another study, measurements on axial radiographs of the maxillary area revealed diminished distances only in the UCLP group (10). Measurements of the sella turcica showed deviations, most severe in the UCLP group (10).

Studies on the cranial base in cleft groups have been performed on profile radiographs (3, 7, 15). Dahl (3) studied the cranial base in adult men with CL, UCLP, and CP and compared them with a control group of 102 male dental students collected by Solow (16). Concerning the size of the neurocranium, which includes the cranial base and skull bones, Dahl (3) found in the CL group an overall smaller cranial size, but generally a high degree of conformity between the CL group and the control group. A marked difference between the cleft groups was observed in the occipital bone in the UCLP group (3). In this group, the lower part of the occipital squama was located more cranially, when compared with the CL and CP groups. Also, in the UCLP group, the basilar part of the occipital bone was shorter and the cranial base angle larger compared to the CL and CP groups. The occipital bones were almost similar in the CL and CP groups. This aspect is of interest because in prenatal studies on malformed human fetuses, it has been suggested that the basilar part of the occipital bone and its relation to the notochord share the developmental origin with the vertebral bodies, while the lower part of the squama shares the developmental origin with the vertebral arch (17–19).

Also, a characteristic finding in the UCLP group was a broader spheno-occipital synchondrosis and a shorter distance from the superior part of the synchondrosis to the sella point in the UCLP group compared to children with a minor incomplete CL, described by Mølsted et al. (7). These findings might be associated with a malformation or a possible delay in maturity in the early development of the cartilaginous basilar part of the occipital bone in children with major clefts. A later study also showed differences in the cranial base in different cleft groups (15).

The hypothesis of the present study is that differences might occur in the thickness of the bones in the skull. According to previous findings, it is presumed that differences may occur specifically in the occipital squama. The purpose of this study was to compare the skull thickness in two groups of children, the CP and UCLP groups. The aim of this comparison was to clarify whether the UCLP group had deviations in the occipital squama, which could be associated with previously described deviations in the basilar part of the occipital bone. The purpose was also to analyze skull thickness in the two groups of adult men, the CP group, and the control group.

Material

Four groups of patients were described. The CL and UCLP group comprising children were compared, and the CP men and normal men comprising adults were compared. General inclusion criteria for CL and UCLP groups were 1) Danish Caucasians; 2) no accompanying physical anomalies; 3) no mental disturbances or retardation; and 4) no history of orthodontic treatment before registration.

Cleft lip group

The cleft lip group (CL) consisted of 24 patients, 7 women all 6 years old and 17 men aged 5–9 (mean 7.1 year). The patients had incomplete cleft lip and an apparently unaffected alveolar process. The profile radiographs were selected by Mølsted (7) from roentgen material at the Copenhagen Cleft Lip and Palate Center. No hand radiographs were available as the children were within the juvenile growth period. As the craniofacial morphology of this type of cleft is assumed to be close to normal, this group represented the child control group.

Unilateral cleft lip and palate group

The unilateral combined cleft lip and palate group (UCLP) consisted of 28 patients, 11 women aged 6–8 (mean 6.6 year) and 17 men aged 5–9 (mean 6.7 year). All patients had a unilateral complete cleft of the lip and palate. The profile radiographs in the UCLP group were selected by Mølsted (7) from roentgen material at

the Copenhagen Cleft Lip and Palate Center. No hand radiographs were available as the children were within the juvenile growth period. The lip was closed at 2 months of age with the use of the Tennison procedure. At the same time, the anterior part of the hard palate was closed by a vomer flap. The rest of the palate was closed at 2 years of age using a Wardill push-back procedure. Ten patients had a small Simonart's band.

Cleft palate group

The cleft palate group (CP) consisted of 57 adult male patients aged 18–33 (mean age unknown). The profile radiographs in the CP group were collected by Dahl (3) during the years 1959–1962 using the following inclusion criteria: 1) a cleft of the secondary palate; and 2) male patients aged 18–33 years, born between 1928 and 1942. Forty-one of the patients have had the defect repaired surgically, while 16 were unoperated.

Normal men

The adult control group comprised profile radiographs (not taken for orthodontic purposes) from 20 men, all dental students aged 20–30 (mean age unknown), selected from material registered by Solow (16) between 1965 and 1975 at the Department of Orthodontics, University of Copenhagen, Denmark. These were healthy Danish Caucasians with no prior history of orthodontic treatment or craniofacial anomalies. They had at least 24 permanent teeth present, neutral occlusion, and normal vertical and sagittal jaw relationship diagnosed according to Björk (20). The control group was age-matched and gender-matched to the CL group, which comprised male patients only.

Methods

The profile radiographs from the adult groups were taken in a cephalostat with a film-to-focus distance of 180 cm and a film-to-median plane distance of 10 cm. No correction was made for the constant linear enlargement of 5.6 percent (20). The same cephalometric setup was used for the children with cleft lip/cleft lip and palate. A digital slide caliper was used for measuring the thickness.

Cephalometric analyses

The measurements of the thickness of the skull were defined according to Axelsson et al. (21). The thickness of the frontal bone, the parietal bone, and the occipital bone was measured. On Fig. 1, the cephalometric fix points and the lines necessary for measuring the skull thickness including the actual locations on the skull for measuring thickness are defined and marked on a profile radiograph.

Method error

The reliability of the variables describing the thickness of the frontal, parietal, and occipital bones was assessed by remeasurement of 20 lateral radiographs selected at random from the previously recorded

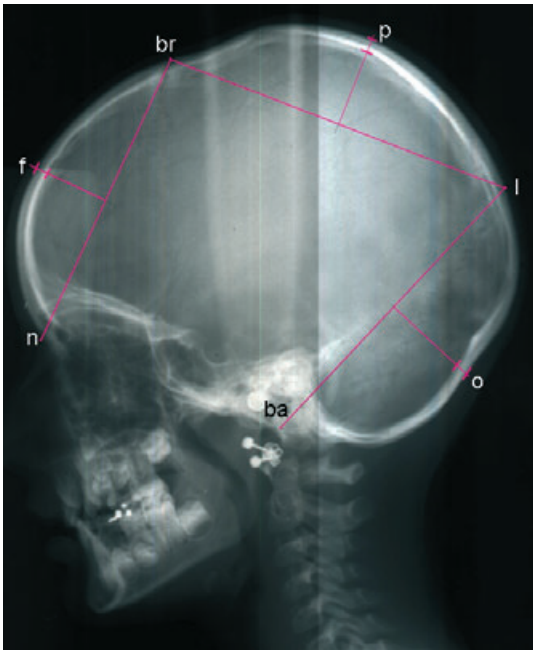

Fig. 1. Profile radiograph of a 7-year-old girl with UCLP. On the radiograph is marked the location of the cephalometric fix points and lines necessary for measuring skull thickness: Basion (ba): the most posterior–inferior point on the clivus. Bregma (br): the intersection between the sagittal and coronal sutures on the surface of the cranial vault. Frontale (f): the point on the surface of the frontal bone determined by a perpendicular to the nasion-bregma line and passing through its midpoint. Lambda (l): the intersection between the lambdoid and sagittal sutures on the surfaces of the cranial vault. Nasion (n): the most anterior point on the fronto-nasal suture. Reference points according to Björk (28). The thickness of the frontal, parietal, and occipital bones were defined as the distances from the points where the perpendicular bisectors of the cords nasion-bregma, bregma-lambda, and lambda-basion intersected the inner and outer contours of the respective bones (the points f, p and o). This definition is according to Axelsson et al. (21).

radiographs in the unilateral cleft lip and group. The radiographs were measured again after 2 weeks, and the differences between the two sets of recordings were calculated. No significant differences between the two sets of recordings were found, assessed by paired *t*-test. The method errors ranged from 0.03 to 0.47 mm (22), and the reliability coefficients from 0.80 to 1.00 (23).

Statistical methods

The normality of the distribution was assessed by parameters of skewness and kurtosis and by the Shapiro–Wilks *W*-test. The thickness of the frontal, the parietal, and occipital bones was, except for the frontal bone in the cleft palate group, normally distributed in all groups. Differences in the means of thickness of the frontal, parietal, and occipital bones between the groups and between genders were assessed by unpaired *t*-tests. The CP and normal groups were not compared with the CL and UCLP groups because of age differences. The results of the test were considered to be significant at *p*-values below 0.05. The statistical analyses were performed using SPSS 13.00 (Inc., Chicago, Illinois, USA).

Results

Gender differences

In the CL group, the women had a significantly thinner occipital bone compared to the men ($p = 0.027$). In the UCLP group, no significant differences in thickness were observed between the genders. The results are summarized in Table 1.

Differences in skull thickness

CL compared with UCLP

When the CL and UCLP groups were compared, the women in the UCLP group had significantly thicker occipital bone than the women in the CL group ($p = 0.014$) (Table 2). Comparison of skull thickness in other regions did not show significant differences.

Cleft palate men compared with normal men

When the CP and the adult control groups were compared, no differences in skull thickness were found (Table 3).

Table 1. **Mean and SD values for the thickness of the frontal, parietal, and occipital bones, and significant levels between the genders in the CL and the UCLP groups**

		Women			Men			
Variables	Group	N	Mean	SD	N	Mean	SD	*p*-value
Frontal	CL	7	4.80	1.15	17	5.46	1.00	NS
	UCLP	11	5.50	1.09	17	5.44	1.06	NS
Parietal	CL	7	5.55	0.61	17	6.10	1.05	NS
	UCLP	11	6.09	1.02	17	6.00	1.11	NS
Occipital	CL	7	3.54	0.82	17	5.00	1.53	*
	UCLP	11	5.79	2.04	17	4.54	1.20	NS

*$p < 0.05$.
SD: Standard deviation.
NS: Not significant.

Discussion

The present study showed differences within and between the groups investigated. Within the CL group, the women had a statistically significant thinner occipital bone compared with the men. In the study by Axelsson et al. (21), differences were also found between genders in normal children (thinner in women), but squama thickness did not differ significantly between men and women. An interesting finding by Axelsson et al. (21) was that the squama occipital bone was thinner in normal women in the 21-year-old group compared with the 18-year-old group. This aspect should be considered in future studies, although it does not influence the results of the present study in which the occipital bone in particular deviated in patients with UCLP (mean age women 6.6, men 6.7).

In accordance with other studies (3, 7, 15), the present study revealed that the occipital bones in the UCLP group differed from those in the CL and CP groups. The present study showed that the occipital bone was markedly thicker in women with combined UCLP compared to the women with CL. Similar differences were not registered when men in these two groups were compared. Clearly, thickness measurements would be greatly affected by differences in proximity to the protuberance in clefts as well as in normal controls. It could be discussed whether the method used in the present study (21) should be combined in future studies with measurements of the thinnest areas in the bones of the skull. In the comparison between the CP male group and the male controls, no difference was found in the

Table 2. **Mean and SD values for the thickness of the frontal, parietal, and occipital bones, and significant levels between the CL and UCLP groups in women and men**

	Women						Men					
		CL		UCLP				CL		UCLP		
Variable	N	Mean	SD	Mean	SD	*p*-value	N	Mean	SD	Mean	SD	*p*-value
Frontal	7	4.80	1.15	5.50	1.09	NS	17	5.46	1.00	5.44	1.06	NS
Parietal	7	5.55	0.61	6.09	1.02	NS	17	6.10	1.05	6.00	1.11	NS
Occipital	7	3.54	0.82	5.79	2.04	*	17	5.00	1.53	4.54	1.20	NS

*$p < 0.05$.
SD: Standard deviation.
NS: Not significant.

Table 3. **Mean and SD values for the thickness of the frontal, parietal, and occipital bones, and significant levels between the CP group and the control group**

	CP			Control group			
Variable	N	Mean	SD	N	Mean	SD	*p*-value
Frontal bone	57	6.98	1.25	20	7.28	1.33	NS
Parietal bone	57	8.60	1.46	20	8.70	1.11	NS
Occipital bone	57	6.61	2.18	20	6.91	1.40	NS

SD: Standard deviation.
NS: Not significant.

thickness of the skull. It was not possible to extend the control group as it consisted of healthy subjects with no medical or odontological indications for radiology. Therefore, profile radiographs of a normal group without deviations in occlusion are difficult to obtain in Denmark because of Danish legislation implemented by the national ethical committee.

Nielsen et al. (10) studied the shape of the sella turcica in patients with cleft lip and patients with combined cleft lip and palate. They showed deviations in the sella turcica shape in half of the subjects in the cleft groups and found that the patients with UCLP had more severely deviating sella turcica morphology compared with the CL group. Also in the present study, the UCLP women deviated significantly in the occipital area from the CL women. The explanation for these major deviations in cleft lip and palate is not known, but might be found in the embryonic development of the sella turcica and the occipital squama. The vertebral column, the sella turcica, and the occipital squama covering the cerebellum are all structures bordering the cerebellar field and developed under direct control by the notochord (18, 19, 24). The sella turcica and the lower part of the occipital squama (cartilage-formed) thus have a common developmental origin, which might explain the association between the different osseous components within the field (18).

The present study reveals an association between malformation in the basilar part of the occipital bone and the cartilaginous part of the occipital squama. A relevant discussion of the anomalies in the occipital bone and of the possible interrelation of these anomalies with the cartilaginous cervical spine cannot be performed before a more detailed classification of the spine malformation has been made.

The tentorium cerebelli attach to the protuberantia occipitalis interna located at the border region between the cartilaginous formed and the desmally formed part of the occipital squama. The region for measuring thickness in the occipital bone in this study is localized caudally to the protuberantia occipitalis interna. Because of the embryological origin, it can be questioned whether this occipital area belongs to the cranial base or the skull structure (24). A local factor, which could also influence the thickness of the occipital squama, is the attachment of the neck musculature at the occipital squama.

Zúñiga et al. (25) compared the curvature of the cervical spine in children with cleft lip and palate with children without clefts. They found that the cleft children had significantly increased extension of the head and also a forward position of the cervical spine. The increased thickness of the occipital squama might be connected with altered function of the neck muscles and changes in the cervical spine, but this is not known.

The present study has revealed significant deviations in the occipital squama in patients with UCLP compared to patients with CL. Previous studies have described significant differences between the basilar part of the occipital bone in patients with UCLP and patients with CL (15). These significant occipital changes in patients with UCLP may explain the considerable deviations in jaw shape and position, characteristic of patients with UCLP. Previous studies have indicated that skull thickness is associated with severe skeletal malocclusions (26, 27).

The finding in the present study of a malformed occipital bone in patients with UCLP is valuable for a pathogenetic understanding of the fetal pathological processes leading to complete clefts. The finding is also valuable for diagnostics as the occipital bone is clearly visible on a profile radiograph. Improved diagnostics influences treatment planning and is necessary in the evaluation of surgical and orthodontic treatment of clefts.

The present study showed that the occipital squama in the UCLP group differed significantly from that of the CL group. As similar differences were found in previous studies on the basilar part of the occipital bone, the present study suggests that the occipital bone is an important key bone for understanding craniofacial abnormalities in clefts.

Conclusion

The study showed gender differences in skull thickness in different cleft types. It also demonstrated that particularly the occipital bone deviated in patients with UCLP, which may explain the considerable deviations in jaw shape and position, previously registered in patients with UCLP.

Clinical relevance

Patients with cleft lip, cleft palate, and cleft lip and palate are genetically different. Also, dentitions and craniofacial skeletons are different. Focus has previously been given to differences in for instance the profile, the nasal bone, the sella turcica, the cranial base angle, and the cervical vertebrae. The present study focuses on skull thickness in different cleft types. It was demonstrated on profile radiographs that particularly the occipital bone was significantly thicker in female patients with UCLP compared with other clefts. It is recommended to register skull thickness and especially squama thickness as part of the phenotypic description of a patient with cleft.

Acknowledgements: The Danish Medical Research Council and the IMK Foundation are acknowledged for funding. Maria Kvetny is acknowledged for manuscript preparation and linguistic support.

References

1. Fogh-Andersen P. *Inheritance of Harelip and Cleft Palate.* Copenhagen: Nyt Nordisk Forlag; 1942.
2. Jezewski PA, Vieira AR, Nishimura C, Ludwig B, Johnson M, O'Brien SE et al. Complete sequencing shows a role for MSX1 in non-syndromic cleft lip and palate. *J Med Genet* 2003;40:399–407.
3. Dahl E. Craniofacial morphology in congenital clefts of the lip and palate. An x-ray cephalometric study of young adult males. *Acta Odontol Scand* 1970;28:11–165.
4. Dahl E, Kreiborg S, Jensen BL, Fogh-Andersen P. Comparison of craniofacial morphology in infants with incomplete cleft lip and infants with isolated cleft palate. *Cleft Palate J* 1982;19:258–66.
5. Friede H, Figueroa AA, Naegele ML, Gould HJ, Kay CN, Aduss H. Craniofacial growth data for cleft lip patients infancy to 6 years of age: potential applications. *Am J Orthod Dentofacial Orthop* 1986;90:388–409.
6. Mølsted K. *Kraniofacial morfologi hos børn med inkomplet unilateral læbe- og ganespalte.* Master dissertation, Copenhagen: Royal Dental College; 1987.
7. Mølsted K, Kjær I, Dahl E. Spheno-occipital synchondrosis in three-month-old children with clefts of the lip and palate: a radiographic study. *Cleft Palate Craniofac J* 1993;30:569–73.
8. Hansen L, Skovgaard LT, Nolting D, Hansen BF, Kjaer I. Human prenatal nasal bone lengths: normal standards and length values in fetuses with cleft lip and cleft palate. *Cleft Palate Craniofac J* 2005;42:165–70.
9. Nielsen BW, Mølsted K, Kjær I. Cross-sectional study of the length of the nasal bone in cleft lip and palate subjects. *Cleft Palate Craniofac J* 2005;42:417–22.
10. Nielsen BW, Mølsted K, Kjær I. Maxillary and sella turcica morphology in newborns with cleft lip and palate. *Cleft Palate Craniofac J* 2005;42:610–7.
11. Lidral AC, Moreno LM. Progress toward discerning the genetics of cleft lip. *Curr Opin Pediatr* 2005;17:731–9.
12. Sandham A. Cervical vertebral anomalies in cleft lip and palate. *Cleft Palate Craniofac J* 1986;23:206–14.
13. Horswell BB. The incidence and relationship of cervical spine anomalies in patients with cleft lip and/or palate. *J Oral Maxillofac Surg* 1991;49:693–7.
14. Uğar DA, Semb G. The prevalence of anomalies of the upper cervical vertebrae in subjects with cleft lip, cleft palate, or both. *Cleft Palate Craniofac J* 2001;38:498–503.
15. Mølsted K, Kjær I, Dahl E. Cranial base in newborns with complete cleft lip and palate: radiographic study. *Cleft Palate Craniofac J* 1995;32:199–205.

16. Solow B. The pattern of craniofacial associations. *Acta Odontol Scand* 1966;24:21–41.
17. Kjær I, Keeling JW, Græm N. Cranial base and vertebral column in human anencephalic fetuses. *J Craniofac Genet Dev Biol* 1994;14:235–44.
18. Kjær I, Keeling JW, Hansen BF. *The Prenatal Human Cranium – Normal and Pathologic Development*. Copenhagen: Munksgaard; 1999.
19. Lomholt JF, Nolting D, Hansen BF, Stoltze K, Kjær I. The pre-natal development and osseous growth of the human cerebellar field. *Orthod Craniofac Res* 2003;6:143–54.
20. Björk A. Kæbernes relation til det øvrige kranium. In: Ahlgren J, editor. *Nordisk Lärobok i Ortodonti*. Stockholm: Sveriges Tandläkarförbunds Förlagsförening; 1975. pp. 69–110.
21. Axelsson S, Kjær I, Bjørnland T, Storhaug K. Longitudinal cephalometric standards for the neurocranium in Norwegians from 6 to 21 years of age. *Eur J Orthod* 2003;25:185–98.
22. Dahlberg G. *Statistical Methods for Medical and Biological Students*. New York: Interscience Publications; 1940.
23. Houston WJB. The analysis of errors in orthodontic measurements. *Am J Orthod* 1983;83:382.
24. Kjær I. Orthodontics and foetal pathology: a personal view on craniofacial patterning. *Eur J Orthod* 2009; doi: 10.1093/ejo/cjp059. (Epub ahead of print).
25. Zúñiga C, Miralles R, Carvajal R, Ravera MJ, Contreras P, Cavada G. Comparative study between children with and without cleft lip and cleft palate, part 1: cephalometric analysis. *Cleft Palate Craniofac J* 2000;37:281–85.
26. Jacobsen PE, Kjær I, Sonnesen L. Skull thickness in patients with skeletal deep bite. *Orthod Craniofac Res* 2008;11:119–23.
27. Arntsen T, Kjær I, Sonnesen L. Skull thickness in patients with skeletal Class II and Class III malocclusion. *Orthod Craniofac Res* 2008;11:229–34.
28. Björk A. Cranial base development. *Am J Orthod* 1955;41:198–225.