doi:10.25143/prom-rsu_2011-29_dts

Rīgas Stradiņa universitāte

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Craniofacial Morphology in the Parents of Children with Cleft Lip, Cleft Lip and Palate and Isolated Cleft Palate

Summary of Promotion Work
Speciality – Orthodontics

Riga, 2011

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(Speciality – orthodontics)

Summary of promotion work

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RIGA - 2011

Promotion work was carried out at:

Riga Stradins University Institute of Stomatology

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Defence of promotion work will be held 23rd of November 2011, 5.00 pm at the meeting of Promotion council of Stomatological disciplines of Riga Stradins University at RSU Hippocrates lecture room in Riga, Dzirciema street 16.

The promotion work is available at RSU library

Secretary of Promotion council:

Dr. habil. med., professor **Ingrida Cema**

INTRODUCTION

Congenital anomalies are of great concern to individuals considering having a child, and there is much research concerning the evaluation of congenital anomalies and associated risk indicators and the prevalence of such anomalies. Orofacial cleft (OFC) is one of the most frequently encountered congenital malformations (Lindral et al., 2008; Melnick 1992; Mooney et al., 2002; Raghavan et al., 1994) that occurs among all ethnic groups, with an incidence that varies according to race and nationality (Lindral et al., 2008; Melnick 1992; Mooney et al., 2002; Raghavan et al., 1994).

The OFC anomaly develops during the initial period of foetal intrauterine development, and is associated with aesthetic and functional impairments from the first day of life, indirectly affecting a child's physical and mental development. In complicated cases, the cleft affects the lip, alveolar arch and the palate. Newborns with this anomaly have greatly changed facial features and impaired dentofacial structure functions including breathing, swallowing and mimics; later in life chewing and speech are affected. In order to provide adequate rehabilitation for a child with OFC, complex treatment is required including surgical, speech therapeutical, otorhinolaryngological and psychological treatments.

In Latvia, 25-30 children are born with OFC each year, and at present there are 600 children under 18 years of age in the active accounting of the Riga Cleft Lip and Palate Centre.

The craniofacial form of individuals with OFC is distinct from that of unaffected individuals (Mooney et al., 2002; Suzuki et al., 1988; Wyszynski, 2002). However, several craniofacial studies have revealed that it is distinctive not only for individuals with OFC but for their parents as well, who are characterized by distinct craniofacial features (Al Emran et al., 1999; Chatzistavrou et al., 2004; McIntyre et al., 2002; 2003; Perkiomaki et al., 2003;

Yoon et al., 2002; 2004). In addition, it has been reported that the craniofacial morphology of the parents of children with OFC differs from that of unaffected people, and that morphological features differ between parents of children with cleft lip with or without cleft alveolus or cleft lip and palate (CL±P) and parents of children with isolete cleft palate (CP). However, the results of these studies are inconsistent (Al Emran et al., 1999; Chatzistavrou et al., 2004; McIntyre et al., 2002; 2003; Perkiomaki et al., 2003; Yoon et al., 2002; 2004). There are no clearly defined morphological differences, but a parent's craniofacial morphology is considered a predisposing factor for the development of OFC in children (Al Emran et al., 1999; Chatzistavrou et al., 2004; McIntyre et al., 2002; 2003; Perkiomaki et al., 2003; Yoon et al., 2002; 2004).

Several studies report at least one increased facial width measurement in parents (McIntyre et al., 2003; Nakasima et al., 1983; 1984; Prochazkova et al., 1995; Raghavan et al., 1994; Suzuki et al., 1999; Yoon et al., 2004), and this is consistent with Trasler's embryonic face-shape hypothesis and available evidence from unrepaired cleft cases (Trasler, 1968; Weinberg et al., 2006). Trasler *(Trasler)* established the embryonic face-shape hypothesis during an experimental study on mice and discovered that the craniofacial form of the embryo could be a predisposing factor for the development of OFC (Trasler, 1968; Weinberg et al., 2006). This finding was indirectly supported by the observation that certain race populations with relatively wider faces have a very high incidence of clefting (Chung et al., 1985; Tolarova et al., 1998; Vanderas 1987) and this could be a predisposing factor in the development of OFC (Siegel et al., 1986; Vergato et al., 1997).

Conflicting results from previous studies can be explained by methodological differences, ethnic and geographic variability in craniofacial morphology, the incidence of OFC, and the ratio of cleft type in the population (McIntyre et al., 2003). Therefore, it is important to assess the differences in one population.

The identification of craniofacial features in parents of children with OFC may assist in the identification of genes involved in the aetiopathogenesis of OFC. Non-syndromic orofacial cleft could be identified using markers of developmental disturbances. If there are craniofacial differences between parents of children with OFC and a control group, genetic counselling could be offered to individuals with predisposing risk factors who are considering having a child.

AIM OF THE PROMOTION WORK

The identification of specific morphological craniofacial features in the parents of children with orofacial clefts.

OBJECTIVES OF THE PROMOTION WORK

1. To identify informative markers of craniofacial measurements for the parents of children with orofacial clefts.
2. Lateral and posterioanterioal (PA) cefalometry were used to:
    1) compare the craniofacial morphology of parents of children with isolated cleft palate (CP) and a control group with no family history of orofacial clefts;
    2) compare the craniofacial morphology of parents of children with cleft lip with or without cleft alveolus or cleft lip and palate (CL±P) and a control group with no family history of orofacial clefts;
    3) determine the craniofacial features characteristic of parents of children with orofacial clefts;

4) assess the craniofacial symmetry of parents of children with orofacial clefts.

3. To establish the relationship between distinct craniofacial features in the parents of children with orofacial clefts and the cleft type of their children.

TOPICALITY OF PROMOTION WORK

The foundation for the concept of an expanded orofacial cleft phenotype is based on the wide variety of subclinical morphological variations manifested more frequently in the unaffected relatives of cleft individuals than in unaffected controls (McInture et al., 2004; Weinberg et al., 2006). The evidence suggests that these associated traits may represent cleft microforms (for example, muscle orbicularis oris defect) or result from a more generalized developmental disturbance (Martin et al., 1993; Weinberg et al., 2006).

There is no common phenotypic feature in parents or relatives of children with orofacial cleft, but the search for such features in terms of craniofacial morphology and other biological systems is ongoing. The existence of such traits could be used as a risk indicator for genetic predisposition to orofacial clefts.

NOVELTY OF PROMOTION WORK

A scientifically systematized study concerning the craniofacial morphology of parents of children with orofacial clefts in Latvia.

HYPOTHESIS OF PROMOTION WORK

Non-syndromic orofacial cleft phenotype is a combination of distinct craniofacial features that uniquely segregate in affected families and are present in affected and unaffected family members to varying degrees. There are

craniofacial features that predispose an individual to orofacial clefting and these markers differ between parents of children with cleft lip with or without cleft alveolus and cleft lip and palate (CL±P) and parents of children with isolated cleft palate (CP).

MATERIAL AND METHODS

Study groups

The subjects in this prospective study were the parents of children with non-syndromic CL±P or CP born in Latvia. Families were registered in the Riga Cleft Lip and Palate Centre of the Institute of Stomatology, Riga Stradins University, the only referral unit for cleft children in Latvia. The children were subjected to surgery in the Cleft Lip and Palate Centre between 2006 and 2008, and their families voluntarily agreed to participate in this study. Concomitantly, a genetic study concerning the parents of children with OFC was carried out in Department of Medical Biology and Genetics at the Riga Stradins University. Within the framework of a gene mapping study, parental analysis was carried out to select biological parents. The data were collected in accordance with the regulations issued by the Central Medical Ethics Committee of Latvia.

The exclusion criteria for experimental participants were: orofacial cleft or any associated congenital disease, orofacial cleft in the family (except children), orofacial trauma, ortognatic surgery and extreme edentulousness (subjects included in this study had at least three pairs of antagonist teeth).

The exclusion criteria for the control group were: orofacial cleft or any associated congenital disease, orofacial cleft in the family, orofacial trauma, ortognatic surgery and extreme edentulousness (subjects included in this study had at least three pairs of antagonist teeth). No specific skeletal or occlusal traits were excluded so that the comparison group would represent the normal variability in craniofacial morphology in the general population.

Table 1

Study and control groups

Participants	CL±P		CP		Control groups	
	F	M	F	M	F	M
Individuals in the lateral cephalometry study	38	38	19	19	40	42
Individuals in the PA cephalometry study	37	37	17	17	40	42
Age when the cephalograms were taken	32	32	30	31	24	25
Age when the child was born	26	27	26	27	_	_

F – female
M- male

Cephalometric measurements

Lateral (fig. 1) and PA (fig. 3) cephalometiric radiographs were obtained from each study subject and used to analyse linear and angular measurements. There were 196 lateral and 190 PA cephalograms produced. All digital cephalograms were taken in the RSU Stomatology Institute using Kodak Trophy 6.0. The analysis was carried out using the Dolphin Imaging version 10.5 programme. The magnification of x-rays was 5.6%, which was not corrected. Craniofacial measurements of the study and control groups were verified using double digitization of all radiographs and these were carried out by the same investigator (the author of this study, Ieva Mauliņa).

Cephalometric measurements in the lateral cephalograms

The craniofacial landmarks and measurements in the lateral cephalograms are presented and described in fig. 2 and tables 2, 3 and 4.

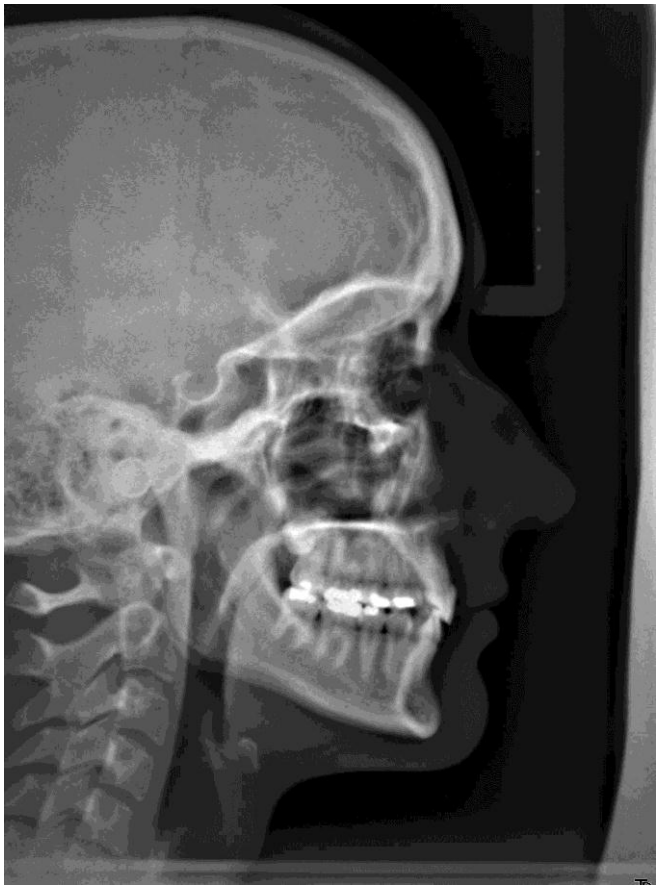

Figure 1. Lateral cephalogram

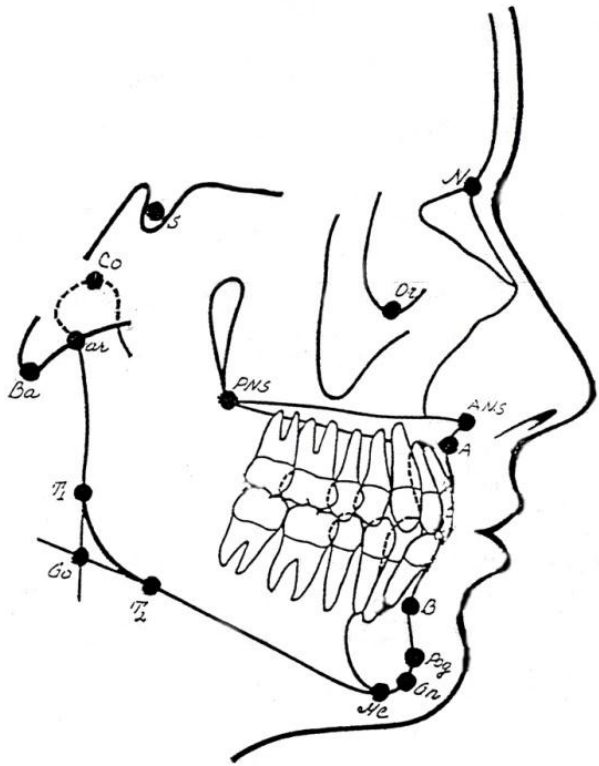

Figure 2. Craniofacial landmarks in the lateral cephalogram

Table 2

Lateral cephalogram landmarks

Craniofacial landmark	Explantion of landmark	Location of the craniofacial landmark
A	A	The deepest point in the concavity of the anterior maxilla
ANS	Anterior nasal spine	The anterior limit of the floor of the nose
B	B	The deepest point in the concavity of the anterior mandible
Cond	Condylus	The most posterio-superior point of the mandibular condyle
Gn	Gnation	The most anterio-inferior point of the mandibular symphysis
Go	Gonion	A mid-plane point at the gonial angle of the mandible located by bisecting the posterior and inferior borders of the mandible
Me	Mention	The mandibular frontal point farthest from the condyle
N	Nasion	Junction of the frontal and nasal bones at the naso-frontal suture
Or	Orbitale	The most inferior point on the infra-orbital margin
Pg	Pogonion	The most anterior point of the mandibular symphysis
PNS	Posterior nasal spine	The posterior limit of the floor of the nose
Po	Porion	The most superior point of the external auditory meatus
S	Sella	The midpoint of the sella turcica
Po-Or		Frankfurt horizontal

Table 3

Linear craniofacial measurements in the lateral cephalograms

Linear measurement	Anatomical formation
S-N	Anterior cranial base
S-Ba	Posterior cranial base
Ar-Go	Mandibular ramus length
Go-Gn	Mandibular corpus length
N-Me (AFH)	Anterior face height
N-ANS (UAFH)	Upper anterior face height
ANS-Me (LAFH)	Lower anterior face height
S-Go (PFH)	Posterior face height
PNS-ANS	Palatal plane length
PNS-A	Palatal length

Table 4

Angular craniofacial measurements in the lateral cephalograms

Angular measurement	Explanation of the measurement
Po-Or/ N-A	Maxillar position in the sagittal plane
SNA	Maxillar position against the anterior cranial base
Po-Or/ N-Pog	Mandibular position in the sagittal plane
SNB	Mandibular position against the anterior cranial base
ANB	Maxillar and mandibular angle in the sagittal plane
N-S-Ar	Saddle angle or cranial base angle
S-Ar-Go	Articular angle
Ar- Go- Me	Gonial angle
N-S-Ar + S-Ar-Go + Ar- Go-Me	Saddle + articular + gonial angle = the sum of the angles (Jaraback)
S-N/ Go-Me	The angle formed by the mandibular plane and anterior cranial base
Po-Or/ Go-Me	Mandibular plane position against the Frankfurt horizontal
S-N/ ANS- PNS	The angle formed by the maxillar plane and anterior cranial base
ANS- PNS/ Go- Me (MMPA)	The angle formed by the maxillar and mandibular plane
FH- SN	The angle formed by Frankfurt horizontal and anterior cranial base

Cephalometric measurements in the PA cephalograms

The craniofacial landmarks and measurements in the PA cephalograms are presented and described in fig. 3 and table 5. The craniofacial measu_rements of symmetry were carried out using the landmarks from the right and left sides of the midline.

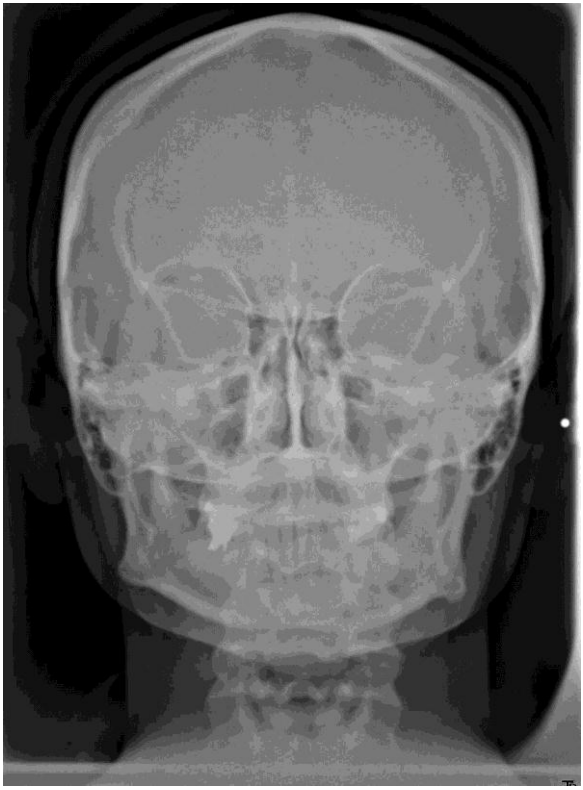

Figure 2. Posterioanterior cefalogram

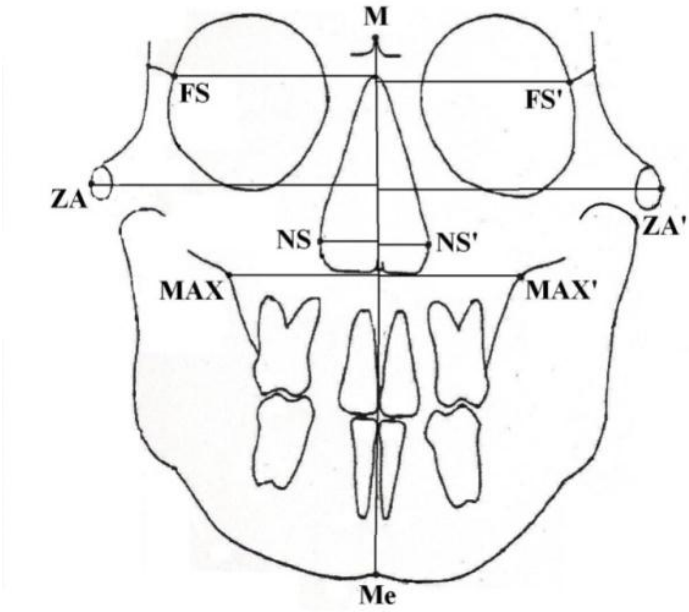

Figure 3. Craniofacial landmark PA cephalogram

Table 5

Craniofacial landmarks and measurements in the PA cephalogram

Cephalometric landmarks and measurements	Anatomical formation
FS; FS’	A point located on the lateral border of the orbital margin, at the inner aspect of the fronto-zygomatic suture
M	The most superior point of the outline of the nasal orifice
N; N’	The most lateral point on the outline of the nasal orifice in the region of the pyriform aperture
ZA; ZA’	The lateral aspect of the zygomatic arch

Max; Max’	A point located at the depth of concavity of the maxillary contour, at the junction of the maxilla and the zygomatic buttress
Me	The most inferior point on the border of the mandible at the symphysis
M - Me	Midline (ML)
FS - FS’	Biorbital width
N - N’	Nasal width
ZA - ZA’	Facial width
Max - Max’	Maxillar width

‘cephalometric landmark in the left side

STATISTICAL ANALYSIS

The following descriptive and analytical methods were used for statistical analysis: Dahlberg’s formula was used to calculate the methodological error between duplicate measurements.

$$ME = \sqrt{\frac{\Sigma(X-X_1)^2}{2n}}$$

where X and X1 are the first and second measurement and n denotes the sample size (number of measurements).

ANOVA was used for statistical analysis. For the comparison of mean values among groups, BONFERRONI analysis was used. Right and left side symmetries were compared using a t-test. Statistical significance was considered when $p<0.05$.

RESULTS

Random error

Each measurement was calculated twice. Random error varied from 0.2 to 1.0 mm for different measurements and a random error for linear and angular measurements greater than 1.5 was considered significant (Solow 1966). No significant random errors were recorded.

Mean values and standard deviations for the craniofacial measurements were established. The mean values were compared between male and female study groups, and between the study and control groups.

Results of lateral cephalometry

Comparing craniofacial measurements from the lateral cephalograms of the study group and the control group revealed statistically significant differences in some measurements.

The mean values, standard deviations and comparison of craniofacial measurements of the lateral cephalograms among fathers of children with CL±P, fathers of children with CP and the male control group are presented in table 6. No statistically significant differences were found among these groups.

Table 6

Comparison of craniofacial measurements in the lateral cephalograms among CL±P fathers, CP fathers and the control group of males

Measurements	Fathers (CL±P) n = 38		Fathers (CP) n = 19		Control group n = 42		p value
	Mean	SD	Mean	SD	Mean	SD	
S - N (mm)	72.2	3.3	73.1	2.7	72.1	3.2	ns
S - Ba (mm)	45.1	3.2	45.5	3.1	46.5	3.3	ns
Po – Or / N – A (^{0})	87.4	4.0	88.2	3.4	87.9	3.8	ns
SNA (^{0})	82.9	4.5	82.9	3.9	82.7	4.1	ns
Mandibular ramus length	53.0	5.2	53.6	6.1	53.3	5.4	ns
Mandibular corpus length	80.4	5.3	81.6	4.9	81.3	5.0	ns
Po – Or/ N - Pog (^{0})	86.6	4.0	87.6	3.4	87.4	3.1	ns
SNB (^{0})	81.1	4.4	81.0	4.0	80.7	3.5	ns
ANB (^{0})	1.8	2.5	1.9	2.4	1.9	2.3	ns
Saddle angle (^{0})	121.4	5.3	120.2	5.1	122.2	5.5	ns
Articular angle (^{0})	143.5	6.6	146.6	7.7	143.0	7.1	ns
Gonial angle (^{0})	125.7	7.0	123.0	8.5	124.1	8.0	ns
The sum of angles (Jaraback) (^{0})	390.6	5.6	389.6	9.1	389.4	6.2	ns
S – N/ Go – Me (^{0})	30.6	5.6	29.6	9.1	29.4	6.2	ns
Po – Or/ Go – Me (^{0})	26.1	5.0	24.1	8.2	24.1	5.4	ns
S – N/ ANS – PNS (^{0})	5.6	3.8	5.7	3.1	5.9	3.3	ns
ANS – PNS/ Go – Me (^{0})	25.0	5.3	23.8	9.3	28.0	22.0	ns
AFH (mm)	119.7	5.8	118.3	6.6	119.7	6.1	ns
UAFH (mm)	52.7	3.4	52.0	2.7	53.3	3.8	ns
LAFH (mm)	69.3	5.2	68.7	6.7	68.4	4.8	ns
PFH (mm)	85.0	5.8	84.1	6.6	86.0	5.8	ns
PNS – ANS (mm)	50.5	2.6	50.6	3.5	49.9	3.2	ns
PNS – A (mm)	47.8	2.5	47.3	3.5	47.8	3.3	ns
FH – SN (^{0})	4.5	3.1	5.3	2.9	4.7	3.0	ns

SD – standard deviation
ns – not statistically significantly different

The mean values, standard deviations and comparison of craniofacial measurements of the lateral cephalograms among mothers of children with CL±P, mothers of children with CP and the female control group are presented in table 7. Statistically significant differences were evident between mothers of children with CP and mothers of children with CL±P. The mothers of children with CP had a longer palatal plane length - PNS-ANS ($p<0.01$) and palatal length - PNS-A ($p<0.05$).

Table 7

Comparison of craniofacial measurements in the lateral cephalograms among CL±P mothers, CP mothers and the control group of females

Measurements	Mothers (CL±P) n = 38		Mothers (CP) n = 19		Control group n = 40		p value
	Mean	SD	Mean	SD	Mean	SD	
S - N (mm)	69.0	3.1	68.3	3.7	68.5	2.8	ns
S - Ba (mm)	42.7	3.0	41.6	2.3	42.5	2.9	ns
Po – Or/ N - A (^{0})	87.8	3.6	88.9	2.3	87.4	3.6	ns
SNA (^{0})	82.1	4.6	82.8	3.5	81.5	3.9	ns
Mandibular ramus length	47.6	4.9	46.2	3.5	47.4	5.3	ns
Mandibular corpus length	74.1	5.5	74.0	6.0	75.0	4.3	ns
Po – Or/ N - Pog (^{0})	85.8	4.7	86.2	3.7	85.7	3.0	ns
SNB (^{0})	78.9	4.8	79.1	4.2	78.4	3.5	ns
ANB (^{0})	3.2	2.6	3.7	3.0	3.1	2.0	ns
Saddle angle (^{0})	122.8	5.0	123.6	5.6	123.4	3.6	ns
Articular angle (^{0})	142.4	8.4	141.2	6.9	143.5	7.3	ns
Gonial angle (^{0})	126.8	6.2	128.2	7.9	125.0	7.6	ns
The sum of angles (Jaraback) (^{0})	392.0	6.6	393.0	5.9	391.9	6.3	ns
S – N/ Go – Me (^{0})	31.2	7.7	32.8	5.9	31.6	6.3	ns
Po – Or/ Go – Me (^{0})	26.3	5.9	26.6	6.1	25.7	6.0	ns
S – N/ ANS – PNS (^{0})	6.8	3.2	6.8	3.8	6.9	3.5	ns
ANS – PNS/ Go – Me (^{0})	25.3	5.3	25.9	7.0	24.6	5.6	ns
AFH (mm)	110.7	5.5	108.3	6.3	110.8	6.1	ns
UAFH (mm)	49.7	3.5	49.2	3.6	50.4	3.3	ns
LAFH (mm)	63.4	3.7	62.1	5.8	62.8	5.0	ns
PFH (mm)	76.2	4.5	73.7	4.0	76.7	5.2	ns
PNS – ANS (mm)	46.4”	3.7	49.2”	2.6	48.0	2.7	0.007**
PNS – A (mm)	44.2”	3.8	46.5”	2.5	45.8	2.8	0.038*
FH – SN (^{0})	5.9	2.5	6.0	2.3	5.9	2.4	ns

SD – standard deviation
ns – not statistically significantly different
″ the values with statistically significant differences
*p<0.05; **p<0.01

RESULTS OF LATERAL CEPHALOMETRY

The mean values, standard deviations and comparison of craniofacial measurements of the PA cephalograms among fathers of children with CL±P, fathers of children with CP and the male control group are presented in table 8.

Some statistically significant differences were evident among these groups.

Significant differences were identified in facial width (ZA-ZA'; $p<0.05$) and biorbital width (FS-FS'; $p<0.01$), in measurements from the midline to the right side zygomatic arch (ZA-ML; $p<0.01$) and in measurements from the midline to the right and left side orbital margin (FS-ML; $p<0.05$; FS'- ML; $p<0.01$) between fathers of children with CP and males from the control group. All significantly different mean values were less for fathers of children with CP than for control males.

Table 8

Comparison of craniofacial measurements (mm) among CL±P fathers, CP fathers and the control group of males

Measurements	CL±P fathers (n=37)		CP fathers (n=17)		Control group (n=42)		p value
	Mean	SD	Mean	SD	Mean	SD	
Max'-ML (left)	31.1	1.9	30.8	1.9	31.4	1.8	ns
Max-ML (right)	30.6	1.7	30.6	2	30.3	1.8	ns
ZA'- ML (left)	67.3	2.2	66.5	3	68.4	2	ns
ZA- ML (right)	66	2.4	65″	3	66.2″	2.6	0.012**
FS'- ML (left)	46.5	2.1	45.4″	1.5	47.1″	1.8	0.006**
FS- ML (right)	46.4	2.6	45.1″	1.7	46.8″	2	0.028*
N - N' Nasal width	30.7	2.7	30.2	2.3	30.5	2.5	ns
Max - Max' Maxillar width	61.7	3.2	61.6	3.5	61.8	2.7	ns
ZA- ZA' (facial width)	133.3	3.9	131.4″	5.7	134.7″	4	0.031*
FS- FS' (biorbital width)	92.9	4.4	90.5″	2.6	93.9″	3.5	0.007**

ML- midline
ns – not statistically significant difference
″ the values with statistically significant differences
*p<0.05; **p<0.01

The mean values, standard deviations and comparison of craniofacial measurements of the PA cephalograms among mothers of children with CL±P, mothers of children with CP and the female control group are presented in table 9. No statistically significant differences among these groups were identified.

Table 9

Comparison of craniofacial measurements (mm) among CL±P mothers, CP mothers and the control group of females

Measurements	CL±P mothers (n=37)		CP mothers (n=17)		Control group (n=40)		p value
	Mean	SD	Mean	SD	Mean	SD	
Max'-ML (left)	29.7	2	30	2.5	29.5	1.6	ns
Max-ML (right)	29.3	2	29.2	1.8	28.7	1.6	ns
ZA'- ML (left)	63.2	2.1	62.3	2	63.2	2.2	ns
ZA- ML (right)	62.1	2.1	61.1	2.1	61.3	2.2	ns
FS'- ML (left)	44.8	1.9	44.8	2.1	44.8	2	ns
FS- ML (right)	44.9	1.8	44.6	2.1	44.3	1.6	ns
N - N' Nasal width	28.4	2.9	28.7	2.9	28.5	2.7	ns
Max - Max' Maxillar width	59	3.6	59.1	4.1	58.1	2.6	ns
ZA- ZA' (facial width)	125.4	3.2	123.3	3.7	124.5	4.1	ns
FS- FS' (biorbital width)	89.8	3.2	89.4	3.9	89.1	3.2	ns

ns – not statistically significant diference

Results of the symmetry

Comparison of symmetry of the right and left sides of the CL±P mothers and fathers, CP mothers and fathers and the control group are presented in tables 10 and 11. Asymmetry of zygomatic width was evident in all study groups compared to control individuals (ZA- ML, ML- ZA'; $p<0.01$). Left side dominance was evident in each of these measurements. Left side dominance was detected in the maxillary region in the mothers of CP children and in both control groups (MX- ML, ML- MX'; $p<0.01$), but not in the CL±P mothers and fathers or CP fathers.

Asymmetry in the orbital region was only detected in the female control group (FS- ML, ML- FS'; $p<0.05$), where left side dominance was apparent.

No other measurements were significantly different.

Table 10

Comparison of symmetry of right and left side of CL±P fathers, CP fathers and control males (mm)

Measurements of the symmetry		Fathers (CL±P) n = 37		Fathers (CP) n = 17		Control group n = 42	
Right	**Left**	**Right (mm)**	**Left (mm)**	**Right (mm)**	**Left (mm)**	**Right (mm)**	**Left (mm)**
FS – ML	**ML - FS'**	46.4	46.5	45.1	45.1	46.8	47.1
p value		ns		ns		ns	
ZA - ML	**ML - ZA'**	66	67.3	65	66.5	66.2	68.4
p value		0.0028**		0.0065**		ns	
Max - ML	**ML - Max'**	30.6	31.1	30.6	30.8	30.3	31.4
p value		ns		ns		0.0044**	

**p<0.01
ns – no significant diference

Table 11

Comparison of symmetry of the right and left side of CL±P mothers, CP mothers and control females (mm)

Measurements of the symmetry		Mothers (CL±P) n = 37		Mothers (CP) n = 17		Control group n = 40	
Right	**Left**	**Right (mm)**	**Left (mm)**	**Right (mm)**	**Left (mm)**	**Right (mm)**	**Left (mm)**
FS –ML	**ML -FS'**	44.9	44.8	44.6	44.8	44.3	44.8
p value		ns		ns		0.02**	
ZA –ML	**ML- ZA'**	62.1	63.2	61.1	62.3	61.3	63.2
p value		0.0137**		0.0129**		ns	
Max - ML	**ML - Max'**	29.3	29.7	29.2	30	28.7	29.5
p value		ns		0.0132**		0.009**	

**p<0.01
ns – no significant difference

DISCUSSION

The aetiology of orofacial clefts is considered polygenetic and multifactorial, with influences from genetic and environmental sources. The genetic influence could be minimal in some cases, but in other cases could be heavily weighted to one parent or approximately equal with regards to the parents where each possesses the same degree of predisposing factors (Ward et al., 1994). The parents of cleft children in this study had no history of cleft in previous generations, so it is possible that environmental factors have an important role in the aetiology of cleft in these families.

Children do not always have the same facial features as their parents, but often have inherited characteristics of a first or second stage relative (Ward et al., 1994). This would indicate that the expression of characteristics of genetic origin may not be observed in their parents (Ward et al., 1994).

Studies concerning the craniofacial morphology of noncleft parents of children with OFC have invariably reported differences that distinguish them from the general population. These findings encourage further investigations concerning the questions of heritability and genetic susceptibility to clefting.

Such studies require a large study group. One limiting factor concerning the size of the study groups in this study was the comparative rarity of this anomaly in Latvia, and parents' refusal to participate in the study. It was often difficult to involve both biological parents in this study as some live outside Latvia, the socioeconomic situation had a bearing in some cases, and some parents were dead. Parents of children with syndromic clefting were excluded. The number of parent pairs decreased owing to edentulousness – parents with fewer than three antagonist pairs of teeth were excluded. The parental analysis revealed that six fathers were not the biological parents of the children in question.

A series of lateral and PA cephalograms that could have been used as a control group in this study were not available. Furthermore, involving ionizing radiation (although low dose) and financial considerations would have been unethical in terms of taking a random population sample. After approval from the Central Medical Ethics Committee of Latvia, volunteers from RSU Institute of Stomatology (doctors, assistants, students) and soldiers from the Latvian Army participated in this study. The control group was a suitable comparison group, representative of the population, and was ethnically, epidemiologically and morphogenetically matched to the parental group. However, the majority of the control group were not parents. Healthy children in family is not a guarantee that next baby will be healthy as well – exist small percent of possibility to born child with a congenital anomaly.

The choice of measurements was based on easily identified and reliably reproduced landmarks, in an attempt to establish the main facial parameters of the Latvian population. Measurements were verified by double digitization of all radiographs. Dahlberg's formula was used to calculate the methodological error between duplicate measurements and is often used in dental studies. In cases where more than two groups were compared, ANOVA and Bonferroni correction were used to control the overall type I error rate.

The most frequently reported features of unaffected parents of children with OFC are wider interorbital, nasal cavity and upper facial dimensions, narrower cranial vaults, longer cranial bases, longer and more protrusive mandibles and shorter upper faces compared with controls (McIntyre et al.,2003; Nakasima et al., 1983; 1984; Prochazkova et al., 1995; Raghavan et al., 1994; Suzuki et al., 1999; Yoon et al.,2004). These features were verified by producing lateral and PA cepahalograms for all participants.

Several studies report at least one increased facial width measurement in parents of children with OFC, so it is assumed that increased facial widths may cause OFC (McIntyre et al.,2003; Nakasima et al., 1983; 1984; Prochazkova et

al., 1995; Raghavan et al., 1994; Suzuki et al., 1999; Yoon et al.,2004). One of the most investigated craniofacial parameters is the width of the nasal cavity (N – N') but results are contradictory (Al Emran et al.,1999; McIntyre et al., 2002, 2004; Nakasima et al., 1983, 1984; Raghavan et al., 1994; Suzuki et al., 1999; Yoon et al., 2003, 2004). The increased nasal width of parents of children with clefts has been reported by several authors (Al Emran et al., 1999; McIntyre et al., 2003; Nakasima et al., 1983; Raghavan et al., 1994; Suzuki et al., 1999; Yoon et al., 2004). It has been suggested that increased width of midfacial structures may prevent palatal shelf contact (Al Emran et al., 1999; McIntyre et al., 2003; Raghavan et al., 1994; Suzuki et al., 1999; Yoon et al., 2003), and several authors have reported a significant reduction in nasal width in the CL±P noncleft twin group (Chatzistavrou et al., 2004; Johnston et al., 1989). The explanation for this finding was that smaller nasal cavity width could represent an inherited reduced size of the frontonasal processes due to a deficiency or failure of contact with the maxillary processes, and thus the development of a cleft of the primary palate (Chatzistavrou et al., 2004; Johnston et al., 1989; Liu et al., 1992). No differences in the nasal width between groups were evident in this study. The results with respect to nasal width were comparable with those observed in an anthropometric study carried out in Latvia (Nagle et al., 2006) and the Czech population (Prochazkova et al., 1995).

One measurement differed between all study groups and the control groups in this study: the zygomatic width asymmetry (ZA – ZA') was more marked ($p<0.01$). Left side dominance was evident in all these measurements. One explanation concerning the left side dominance could be that unilateral cleft lip with or without cleft alveolus or cleft lip and palate more often manifests on the left side (67%) than on the right (33%) in Latvia (Akota et al., 2000).

Craniofacial morphology of parents with children with OFC has been the objective of research for a relatively long time. However, there are no clearly defined morphological features that differ between parents with children with OFC and control groups. In this study, statistically significant differences between the CP fathers group and the male control group were demonstrated for facial and biorbital widths, and statistically significant differences between the study groups and the control groups were evident in terms of symmetry measurements. However, the clinical relevance of these findings has yet to be established, necessitating further investigations into specific traits.

SUMMARY

- Differences in the craniofacial morphology between parents of children with orofacial cleft (OFC) and control groups have been established in several craniofacial studies, but the results are inconsistent.
- There are reports that the craniofacial morphology of parents of children with OFC is distinctive from that of unaffected individuals, and that morphological features differ between parents of children with cleft lip with or without cleft alveolus or cleft lip and palate (CL±P) and parents of children with isolated cleft palate (CP). However, the results of these studies are again inconsistent.
- The aim of the present study was to identify specific morphological craniofacial features in the parents of children with CL±P and the parents of children with CP in Latvia.
- Lateral and posteroanterior (PA) cephalograms were obtained from both noncleft biological parents of children with non-syndromic OFC and from the control groups. A cephalometric analysis was used for craniofacial measurements.

- The study confirmed differences among parents of children with CL±P, parents of children with CP and the control group in these measurements.
- The differences among study groups and the control groups were small and often no larger than differences in the control group, and this is consistent with other studies.
- These results could be of value in predicting clefting and should be taken into account when considering the pathogenesis of CP and CL±P.
- The results of the study are insufficient to be of diagnostic value in terms of predicting predisposing risks for orofacial clefting. Further research concerning craniofacial morphology is required in association with genetic research.

CONCLUSION

1. Analysis of cephalometric craniofacial parameters in this study confirms distinctive differences among the parents of children with cleft lip with or without alveolus or cleft lip and palate, the parents of children with isolate cleft palate, and control groups.
2. One common feature differed between the study groups and the control groups: asymmetry of zygomatic width was evident in all study groups with left side dominance (ZA- ML, ML- ZA'; $p<0.01$).
3. Several measurements differed between fathers of children with CP and males from the control group. Statistically significant differences were identified in facial width (ZA-ZA'; $p<0.05$) and biorbital width (FS-FS'; $p<0.01$), in measurement from the midline to the right side zygomatic arch (ZA-ML; $p<0.01$) and in measurements from the midline to the right and left side orbital margin (FS-ML; $p<0.05$; FS'-

ML; $p<0.01$). All significantly different mean values were less for fathers of children with CP than for control males.

4. Statistically significant differences were evident between the mothers of children with CP and the mothers of children with CL±P. The mothers of children with CP had a longer palatal plane length - PNS-ANS ($p<0.01$) and palatal length - PNS-A ($p<0.05$).
5. Asymmetry was detected in the study groups and the control groups. There was left side dominance in maxillary region of mothers of CP children and in both control groups (MX- ML, ML- MX'; $p<0.01$). Asymmetry in the orbital region was only demonstrated in the female control group (FS- ML, ML- FS'; $p<0.05$) and exhibited left side dominance.

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