

Original article

Regional facial asymmetries in unilateral orofacial clefts

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Summary

Objectives: Assess facial asymmetry in subjects with unilateral cleft lip (UCL), unilateral cleft lip and alveolus (UCLA), and unilateral cleft lip, alveolus, and palate (UCLP), and to evaluate which area of the face is most asymmetrical.

Methods: Standardized three-dimensional facial images of 58 patients (9 UCL, 21 UCLA, and 28 UCLP; age range: 8.6–12.3 years) and 121 controls (age range 9–12 years) were mirrored and distance maps were created. Absolute mean asymmetry values were calculated for the whole face, cheek, nose, lips, and chin. One-way analysis of variance, Kruskal–Wallis, and *t*-test were used to assess the differences between clefts and controls for the whole face and separate areas.

Results: Clefts and controls differ significantly for the whole face as well as in all areas. Asymmetry is distributed differently over the face for all groups. In UCLA, the nose was significantly more asymmetric compared with chin and cheek ($P = 0.038$ and 0.024 , respectively). For UCL, significant differences in asymmetry between nose and chin and chin and cheek were present ($P = 0.038$ and 0.046 , respectively). In the control group, the chin was the most asymmetric area compared to lip and nose ($P = 0.002$ and $P = 0.001$, respectively) followed by the nose ($P = 0.004$). In UCLP, the nose, followed by the lips, was the most asymmetric area compared to chin, cheek ($P < 0.001$ and $P = 0.016$, respectively).

Limitations: Despite division into regional areas, the method may still exclude or underrate smaller local areas in the face, which are better visualized in a facial colour coded distance map than quantified by distance numbers. The UCL subsample is small.

Conclusion: Each type of cleft has its own distinct asymmetry pattern. Children with unilateral clefts show more facial asymmetry than children without clefts.

Introduction

Perfect symmetry in the human face does not exist. Very often a slight asymmetry in the face is appreciated more than a perfectly symmetric face, but abnormal proportions in faces, especially close to the facial midline, are perceived as less attractive (1, 2). Cleft lip and palate (CLP) patients differ from the noncleft population, because they have a congenital defect in the face, which expresses

itself in the hard as well as in the soft tissues of the face. Patients with a unilateral defect like unilateral cleft lip and palate (UCLP) may express this as an asymmetry of the face (2–5).

In the past, studies to assess (a)symmetry mainly used landmark comparisons based on the studies of Farkas and Cheung (6) but they may have underestimated the spatial three-dimensional (3D) composition of the face. Nowadays, 3D evaluation techniques are available to assess cleft care outcome more objectively. 3D stereophotogrammetry

is an especially preferred method for soft tissue analysis (7, 8). 3D visualization may also help to clarify changes over time and to explain treatment objectives and possibilities to the patient (9).

Therefore, the aim of this study was to assess and compare facial asymmetry in patients with various types of clefts [unilateral cleft lip (UCL), unilateral cleft lip and alveolus (UCLA), and unilateral cleft lip, alveolus and palate (UCLP)] with a large pre-adolescent control group to evaluate which area of the face is the most asymmetrical and if asymmetry is distributed differently in cleft groups and controls before alveolar bone graft and orthodontics.

Patients and methods

Patients

This research was conducted in accordance with the Helsinki Declaration with regard to research in human subjects. Approval from the Institutional Review Board was obtained. Cleft palate patients of the Cleft Palate Craniofacial Unit of Radboud University Medical Center, Nijmegen, The Netherlands, with the following inclusion criteria: 1. diagnosis of complete nonsyndromic (ascertained by a clinical geneticist) unilateral cleft lip (UCL), unilateral cleft lip and alveolus (UCLA), or unilateral cleft lip, alveolus and palate (UCLAP); 2. Caucasian; 3. 3D stereophotogrammetric images of the face taken at approximately 10 years of age and; 4. All treatment performed in one and the same CLP team were included in the study.

Fifty-eight patients born between 1998 and 2004 (age range: 8.6–12.3) were selected. Nine of them presented with UCL (6 girls and 3 boys), 21 had UCLA (4 girls and 17 boys), and 28 had UCLP (13 girls and 15 boys). All patients were treated according to the standardized protocols used at the Unit. Lip closure (Millard cheiloplasty) was done at age 6–8 months together with a primary nose correction (McComb); soft palate closure was performed at the age of 12–14 months. All surgical procedures were performed by two surgeons. At the time of the 3D-stereophotogrammetric image, the included patients with an alveolar cleft did not have their bone grafting procedure yet, neither hard palate closure.

The control group consisted of 121 patients (age range: 9–12 years), 82 girls, and 39 boys, taken from the patient files of the Department of Orthodontics, Radboud University Medical Center, Nijmegen, The Netherlands. Inclusion criteria were 1. maximum overjet of 6 mm, and 2. Caucasian. Exclusion criteria were 1. congenital malformation, 2. forced bite with lateral displacement of the mandible, 3. juvenile idiopathic arthritis (JIA), 4. impacted canines, and 5. negative overjet.

3D stereophotogrammetry

Three-dimensional images of patients and controls were taken with the same stereophotogrammetrical camera set-up (3dMD face™ System, 3dMD LLC, Atlanta, Georgia, USA) under standardized conditions. Patients were positioned in natural head position and were asked to keep their eyes open and to relax their facial musculature. All images were taken by an experienced photographer. The setting of the system was calibrated every morning.

Processing of the image was performed as described in detail by Verhoeven *et al.* (10). Confounding regions (neck, ears, and hair) in the images were removed in 3dMDpatient v3.1.0.3 computer software (3dMD patient™ Software Platform, 3dMD LLC). The adjusted 3D photograph was imported into Maxilim® software (Medicim NV, Mechelen, Belgium). In Maxilim®, a 3D-mirrored image was created and surface registration of the original and mirrored 3D photograph was done to create a distance map. The distance map illustrates the distance between corresponding points on both 3D images of the full face,

and therefore represents the difference between the surface of the original 3D image and its mirrored image (Figure 1). The numeric measurements ($\pm 20\ 000$) from the distance map were imported into Matlab® software [7.4.0 (R2007a) Mathworks, Natick, Massachusetts, USA] to calculate the absolute mean and the 95th percentiles of the asymmetry. This absolute mean is the absolute mean difference of the distance between the original and mirrored image expressed in millimetres. This mean represents a direct measurement of facial asymmetry, the larger a facial asymmetry, the greater the mean absolute distance.

Measurements

Based on the 3D images (1) mean absolute asymmetry, and (2) asymmetry in specific regions of the face were assessed (Figure 2). The areas were nose, lips, cheeks, and chin and they were defined according to defined planes. A 3D reference plane was constructed according to Plooiij *et al.* (7) using the following planes:

1. The Horizontal (x) 3D Cephalometric Reference Plane is automatically computed as a plane 6.6 degrees below the Canton—Superaurale line, along the horizontal direction of the natural head position and through the Pupil Reconstructed Point translated 77.2 mm more posteriorly.
2. The Pupil Constructed Point is positioned on the crossing of the midline of the nose and the bipupillar line.
3. Vertical plane: The Vertical (y) 3D Cephalometric Reference Plane is computed as a plane perpendicular to the Horizontal (x) 3D Cephalometric Reference Plane and along the horizontal direction of the natural head position.

Then the following planes were defined to divide the face into five areas, using the following landmarks: left and right Exocanthion, left and right Endocanthion, left and right Cheilion, Subnasale, labiale inferius, and mid pupillar point (Table 1):

1. Upper cheek plane: from left to right exocanthion over mid pupillar
2. Right border nose: A plane through landmarks endocanthion right and cheilion right; Left border nose: A plane through landmarks endocanthion left and cheilion left and perpendicular to vertical plane
3. Subnasal plane: the plane through subnasale and parallel to horizontal plane
4. Lower lip plane: A plane through labiale Inferius and parallel to horizontal plane
5. Median plane: The median (z) 3D Cephalometric reference plane is computed as a plane perpendicular to the horizontal (x) and the vertical (y) 3D Cephalometric Reference Planes

The following areas were defined (Figure 2):

1. Nose area was defined by upper cheek plane, left and right border nose, and subnasal plane.
2. Cheeks were defined by either left or right border nose, upper cheek plane, and lower lip plane.
3. Lips were defined by right and left border nose and subnasal and lower lip planes.
4. The chin area was the area below the lower lip plane.

Statistical analysis

For patients and controls (full face and separate areas), the absolute mean and the 95th percentile of the asymmetry were calculated. To assess which areas were the most asymmetrical areas within the face in the control group and the cleft groups, all different areas in the face were compared with each other using a *t*-test.

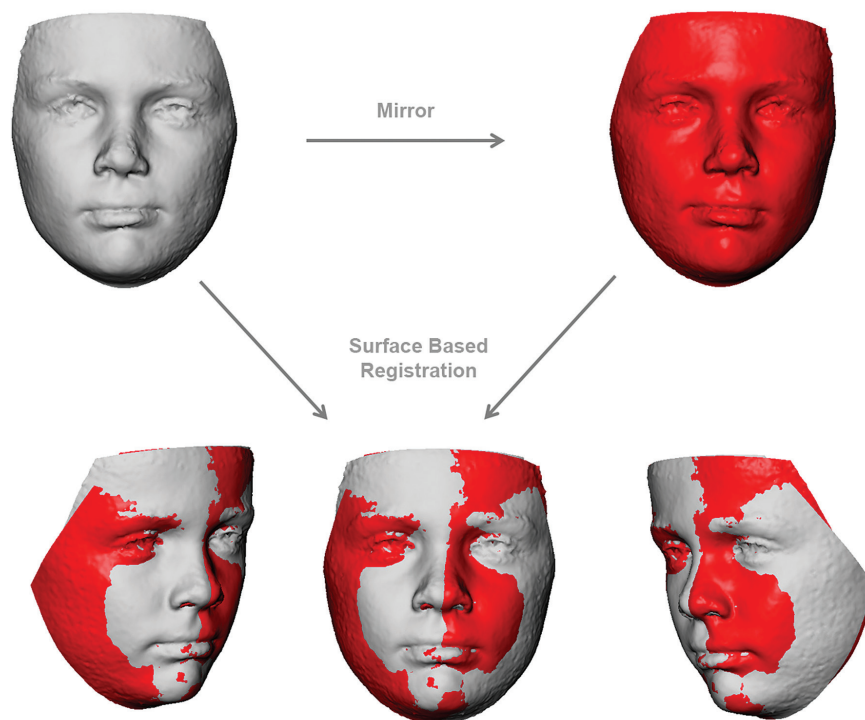


Figure 1. Registration of original and mirrored data of an unilateral cleft lip, alveolus and palate patient.

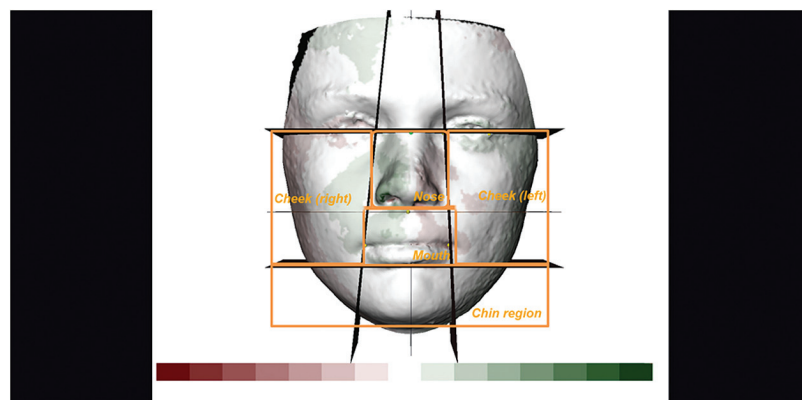


Figure 2. Picture of a face showing distance map and areas selected for comparison: nose, lips, cheeks, and chin.

Table 1. Definition of the facial landmarks on the 3D photographs used to divide the face into five areas.

Landmarks	Definition
Exocanthion	Point at the outer commissure of the eye fissure
Endocanthion	Point at the inner commissure of the eye fissure
Cheilion	Point located at each labial commissure
Subnasale	Midpoint on the nasolabial soft tissue contour between the columella crest and the upper lip
Labiale inferius	Midpoint of the vermillion line of the lower lip
Mid pupillar point	Point positioned on the crossing of the midline of the nose and the bipupilar line

One-way analysis of variance was used to compare the whole face and the separate areas to assess if there were significant differences between the different areas of the face of the different cleft

groups. A Kruskal–Wallis test was used to compare the control group with cleft groups for the whole face and the separate areas. Differences between boys and girls in the control group, UCLA, and UCLP groups were assessed by using a Mann–Whitney test.

To calculate the inter-rater reliability, 25 randomly selected images were analysed again for asymmetry and mirroring by two observers. Inter-rater reliability of the calculation of the mean absolute asymmetry was assessed by computing duplicate measurement errors (DME), correlation coefficients, and the differences between the means. Also, paired *t*-tests were run to assess if there were systematic errors between two observers.

Results

Reliability

Correlation coefficients of the assessment of the mean absolute asymmetry were good. The inter-rater DME was 0.05 mm, the correlation

coefficient was 99.1 per cent, and the difference of the means between the observations was 0.008 mm (95% CI: -0.01891 ...0.03495).

Asymmetry assessment of patients with cleft versus controls

Descriptive statistics for the absolute mean distances (in millimetres) between the original image and the mirrored image are presented in Table 2.

Differences between the cleft groups and the control group are mentioned in Table 3. There were significant differences between the UCLP group and the controls in all areas ($P = 0.012$ for chin and $P < 0.001$ for all other areas). Significant differences were also found between the UCLA group and the control group for the whole face, nose and lip ($P < 0.001$). No significant differences were found between the UCL group and the controls.

Table 2. Descriptive statistics for the absolute mean distances (in mm) between the original image and the mirrored image of the controls and three different cleft groups. UCL, unilateral cleft lip; UCLA, unilateral cleft lip and alveolus; UCLP, unilateral cleft lip, alveolus, and palate.

Group	Facial area	Mean	SD	Std. error mean
Controls ($n = 121$)	Whole face	0.483	0.148	0.013
	Nose	0.419	0.212	0.019
	Lip	0.447	0.215	0.020
	Chin	0.540	0.364	0.033
	Cheek	0.482	0.203	0.018
UCLP ($n = 28$)	Whole face	0.741	0.310	0.058
	Nose	1.130	0.538	0.102
	Lip	0.937	0.467	0.088
	Chin	0.689	0.330	0.062
	Cheek	0.689	0.330	0.062
UCLA ($n = 21$)	Whole face	0.723	0.422	0.092
	Nose	1.105	0.614	0.134
	Lip	0.826	0.440	0.096
	Chin	0.724	0.494	0.108
	Cheek	0.719	0.569	0.124
UCL ($n = 9$)	Whole face	0.640	0.310	0.103
	Nose	0.785	0.507	0.169
	Lip	0.653	0.372	0.124
	Chin	0.466	0.193	0.064
	Cheek	0.650	0.368	0.123

Differences between the cleft groups themselves are depicted in Table 4. There were no statistical differences between the cleft groups for any of the areas of the face neither for the whole face.

Asymmetry assessment within the groups

Descriptive statistics (Table 2) show that the nose was the most asymmetric area in all CLP groups, followed by the lips and the chin the most asymmetric area in the controls. There were significant differences between several areas within the face in all groups when comparing them with each other (Table 5).

In the control group, the asymmetry difference within the face was significant between chin and lip, chin and nose, and nose and cheek ($P = 0.002$, $P = 0.001$ and $P = 0.004$, respectively).

For the UCLP group, the nose was significantly more asymmetric than all other areas of the face (chin $P < 0.001$; lip $P = 0.044$; cheek $P = 0.016$). Furthermore, the lip area was more asymmetric than the chin area ($P < 0.001$).

The nose was significantly more asymmetric in the face of UCLA patients compared to chin and cheek ($P = 0.038$ and 0.024 , respectively).

For the UCL group, differences between nose and chin and chin and cheek were statistically significant ($P = 0.038$ and 0.046 , respectively).

There were significant sex differences for amount of asymmetry in the different areas of the face of UCLP patients. In the UCLP groups, boys were more asymmetric than girls in the chin ($P = 0.037$) and lip area ($P = 0.007$). There were no gender significant differences in the UCLA group and controls.

Discussion

In this study, 3D stereophotogrammetry was used to compare facial asymmetry of patients with a unilateral cleft deformity with a large control group. The whole face and different areas of the face of cleft patients were compared with controls. Furthermore, different areas within the face were compared with other areas to assess which one is the most asymmetrical. The latter assessment was done to see whether there were distinct patterns of asymmetry for different types of unilateral clefts.

Asymmetry has been reported in several studies starting with the studies of Ras *et al.* (11, 12) who used stereophotogrammetry for the assessment of asymmetry over time in CLP patients and non-cleft

Table 3. Results of the Kruskal–Wallis test comparing the control group with the cleft groups for the whole face and the separate areas in the face. UCL, unilateral cleft lip; UCLA, unilateral cleft lip and alveolus; UCLP, unilateral cleft lip, alveolus, and palate.

Area	Variable	Comparison	Mean control group	Mean cleft group	P value
Face	Control ($n = 121$)	UCLP ($n = 28$)	0.483	0.741	<0.001
		UCLA ($n = 21$)		0.723	0.000
		UCL ($n = 9$)		0.637	0.571
Nose	Control	UCLP	0.419	1.130	<0.001
		UCLA		1.105	<0.001
		UCL		0.785	0.052
Lip	Control	UCLP	0.447	0.937	<0.001
		UCLA		0.826	<0.001
		UCL		0.653	0.277
Chin	Control	UCLP	0.540	0.689	0.012
		UCLA		0.724	0.178
		UCL		0.466	1.000
Cheek	Control	UCLP	0.482	0.689	<0.001
		UCLA		0.719	0.188
		UCL		0.650	0.386

Table 4. Results of the one-way analysis of variance comparing whole face and different areas in the face for the three different cleft groups. UCL, unilateral cleft lip; UCLA, unilateral cleft lip and alveolus; UCLP, unilateral cleft lip, alveolus, and palate.

Area	Group	Comparison	Mean difference	P value	Confidence interval	
					Lower	Upper
Face	UCLP	UCLA	0.018	0.983	-0.223	0.264
		UCL	0.104	0.735	-0.223	0.431
	UCLA	UCLP	-0.018	0.983	-0.264	0.223
		UCL	0.086	0.815	-0.254	0.426
	UCL	UCLP	-0.104	0.725	-0.431	0.223
		UCLA	-0.086	0.815	-0.426	0.254
Chin	UCLP	UCLA	-0.035	0.947	-0.302	0.232
		UCL	0.223	0.292	-0.132	0.578
	UCLA	UCLP	0.035	0.947	-0.232	0.302
		UCL	0.258	0.220	-0.111	0.627
	UCL	UCLP	-0.223	0.292	-0.578	0.132
		UCLA	-0.258	0.220	-0.627	0.111
Lip	UCLP	UCLA	0.111	0.664	-0.198	0.420
		UCL	0.284	0.226	-0.126	0.695
	UCLA	UCLP	-0.111	0.664	-0.420	0.198
		UCL	0.173	0.594	-0.253	0.560
	UCL	UCLP	-0.284	0.226	-0.695	0.126
		UCLA	-0.173	0.594	-0.560	0.253
Nose	UCLP	UCLA	0.024	0.988	-0.367	0.412
		UCL	0.344	0.255	-0.175	0.864
	UCLA	UCLP	-0.024	0.988	-0.412	0.367
		UCL	0.320	0.334	-0.220	0.860
	UCL	UCLP	-0.344	0.255	-0.864	0.175
		UCLA	-0.320	0.334	-0.860	0.220
Cheek	UCLP	UCLA	0.135	0.677	-0.250	0.519
		UCL	0.204	0.604	-0.306	0.713
	UCLA	UCLP	-0.135	0.677	-0.519	0.250
		UCL	0.069	0.947	-0.461	0.600
	UCL	UCLP	-0.204	0.604	-0.713	0.306
		UCLA	-0.069	0.947	-0.600	0.461

controls. Most studies concern comparisons before and after treatment, very often without a control group, or with a control group of a different age range (12–14). Various image acquisition techniques have been described to assess changes and asymmetry in the face (8). In comparison to the widely applied landmark-based registration or a combination of landmark-based registration and shape analysis based on a few nasolabial facial curves (5, 15), the use of surface based registration gives a better insight into all morphological differences within a face and between faces (2, 10, 16). As the face is a 3D structure, distance maps give an impression of volume differences in areas that may be more difficult to detect from two-dimensional measurements or when measuring distances perpendicular to a symmetry axis in a 3D image (10, 17). Furthermore, it does not exclude facial regions where landmarks are not identified or difficult to identify. We found that in controls the most asymmetric area of the face is the chin. This was different in CLP patients. In the UCLA and UCLP group, the most asymmetric areas were nose and lips. However, when areas within the face were compared, there were differences in distribution with the nose being the most asymmetric area in the UCLP group followed by the lips. In the UCLA group, asymmetry was mostly visible in the nasal area. This is in accordance with the findings of other researchers (5, 18) who showed more lip dysmorphology due to a wider nostril base in UCLP patients than UCL patients. Bell *et al.* (5) also compared the lips to the upper area of the face to signify that asymmetry mostly concentrated on the nose for UCLP as well as UCL patients. In our study, we analysed the

same groups but we also included a UCLA group. This type of cleft is quite often disregarded in the literature as most published studies deal with UCLP. It is difficult to make a direct comparison with the results of Bell *et al.* (5) as the CLP treatment protocol in our study is different. In our centre, we employed a delayed hard palate closure protocol. So, in contrast to Bell's group, hard palate closure had not yet been performed in the patients in our study.

Bugaighis *et al.* (3) included UCLP and UCLA in their study and described that both groups differed from the controls in the nasolabial area. In their study, the UCLA group showed the same differences but to a lesser extent than the UCLP group. Some areas were similar to controls, especially in the lip area. This is similar to our findings. The drawback of Bugaighis' study was that five different surgeons using different techniques did the surgeries, whereas in our study similar techniques were used on all patients. Ayoub *et al.* (18) proved that UCL patients start to resemble controls more in the nose base and lip area at a later age (8–10 years). This was seen with our UCLA patients in the same age range also. With respect to sex differences, we found that boys were more asymmetric in the chin and lip area than girls in the UCLP and to a lesser extent for UCLA patients. None of the other studies with patients in the same age range (8–12 years) examined sex differences, except Ras *et al.* (11) who found opposite results. Like other studies we did not find differences between boys and girls in the control group. This may be due to the fact that control faces show only minor asymmetry, which makes gender differences not measurable.

Table 5. Results of the *t* test comparing mean absolute distance values of the different areas of the face for the control group and the three different cleft groups. UCL, unilateral cleft lip; UCLA, unilateral cleft lip and alveolus; UCLP, unilateral cleft lip, alveolus, and palate.

	Mean absolute distance compared areas	P value	95% Confidence interval of the difference	
			Lower	Upper
Controls	chin–lip	0.002	0.034	0.151
	chin–nose	0.001	0.048	0.193
	chin–cheek	0.079	–0.007	0.121
	lip–nose	0.258	–0.021	0.077
	lip–cheek	0.096	–0.077	0.006
	nose–cheek	0.004	–0.106	–0.021
UCLP	chin–lip	0.000	–0.374	–0.123
	chin–nose	0.000	–0.640	–0.241
	chin–cheek	0.156	–0.396	0.067
	lip–nose	0.044	–0.379	–0.006
	lip–cheek	0.428	–0.130	0.297
	nose–cheek	0.016	0.056	0.496
UCLA	chin–lip	0.117	–0.233	0.028
	chin–nose	0.038	–0.739	–0.024
	chin–cheek	0.961	–0.200	0.211
	lip–nose	0.082	–0.597	0.039
	lip–cheek	0.261	–0.086	0.301
	nose–cheek	0.024	0.057	0.716
UCL	chin–lip	0.076	–0.398	0.024
	chin–nose	0.038	–0.616	–0.023
	chin–cheek	0.046	–0.363	–0.005
	lip–nose	0.272	–0.391	0.126
	lip–cheek	0.966	–0.150	0.156
	nose–cheek	0.221	–0.100	0.370

The differences found in this study between controls, UCLP and UCLA patients were also found by others (3, 4, 19). Bugaighis *et al.* (3), however, also found significant differences between UCLA and UCLP patients outside the midfacial area, where UCLA patients resembled controls more than they resembled UCLP patients. We did not find this difference. This may be due to the point measurements and Procrustes approach they used, while we used the mean difference between the two surfaces as a measure for asymmetry. No study mentioned a distinctive asymmetry pattern for each unilateral cleft type, except Bell *et al.* (5) who did so for UCL and UCLP. Differences have always been compared to other cleft types and control groups, however, a distinctive asymmetry pattern within a cleft type may influence the overall visual subjective assessment of a face as Meyer-Marcotty *et al.* (2) did describe in their study comparing aesthetics of UCLP and Class III patients. Larger CLP groups will be needed to pinpoint this difference and create means.

The time of assessment in this study was chosen to be prior to alveolar bone grafting and orthodontic treatment for all cleft patients in order to avoid the influence of orthodontic treatment or the alveolar bone graft on the assessment of symmetry differences between the CLP group and controls. That means that the CLP patients in this study had only undergone primary lip closure and, when a palatal cleft was present, soft palate closure. Earlier studies have shown that this treatment protocol produced a favourable treatment outcome (20). Nevertheless, we found significant differences in facial asymmetry of the whole face between controls and patients with a unilateral cleft defect that involved the hard tissues (UCLP and UCLA, see Table 3). These findings may suggest that the anatomical defect of the facial skeleton plays a major role in the asymmetry of the face. Treatment of the anatomical defect may improve asymmetry. Since palatal closure and alveolar bone graft procedure had not been done

in the UCLA and UCLP group, it remains to be investigated whether these procedures do have an effect on asymmetry and facial appearance and demonstrate if differences between UCLP and UCLA and between UCLP, UCLA, and controls remain similar.

Limitations

The subsamples of UCL were too small for meaningful statistical comparisons. The wide confidence intervals show that differences are difficult to assess and it can only be speculated that our UCL patients resemble controls more than patients with UCLP and UCLA. As not much has been published about UCL only it would be interesting to see the results of studies with a higher number of patients in this group.

We used an overall mean score to assess the differences between cleft groups and controls. This may level out the asymmetry scores, because it does not show how asymmetry is distributed over a face, and higher asymmetry scores are levelled out by lower ones to create the mean (16, 21). Therefore, we also divided the face in specific regions to better specify asymmetry. It may, however, still exclude or underrate smaller local areas in the face, which are better visualized in a facial colour coded distance map compared to a table full of calculations.

Three-dimensional measurements may give an impression of general maxillofacial growth in CLP patients. It may also help to quantify overall treatment outcome. Stereophotogrammetry could be a useful non-invasive technique to assess these changes. However, a generally accepted analysis method for CLP still needs to be developed (8). This will be of value for evaluating treatment results and growth for larger patient groups and will probably help to explain treatment objectives and possibilities to the patient. Success of treatment is not only quantified by asymmetry scores, but also by

patient's wellbeing. A study comparing asymmetry scores and treatment outcome with quality of life assessments will be necessary.

Conclusion

Preadolescent children with UCLP show significantly more facial asymmetry than children without clefts, especially in the nasolabial area. Each type of unilateral cleft has its own distinct asymmetry pattern, which can be quantified with stereophotogrammetry. The nose is the most asymmetric in UCLA and UCLP patients whereas the chin is the most asymmetrical area in controls.

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