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Three-dimensional assessment of facial asymmetry in preschool patients with orofacial clefts after neonatal cheiloplasty

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ABSTRACT

Objectives: To evaluate facial asymmetry changes in pre-school patients with orofacial clefts after neonatal cheiloplasty and to compare facial asymmetry with age-matched healthy controls.
Methods and materials: The sample consisted of patients with unilateral cleft lip (UCL), unilateral cleft lip and palate (UCLP), and bilateral cleft lip and palate (BCLP). The patients were divided in two age groups with a mean age of 3 years (n = 51) and 4.5 years (n = 45), respectively, and 78 age-matched individuals as controls. Three-dimensional (3D) facial scans were analyzed using geometric morphometry and multivariate statistics.
Results: Geometric morphometry showed positive deviations from perfect symmetry on the right side of the forehead in the intervention groups and the controls. The UCL groups showed the greatest asymmetric nasolabial area on the cleft-side labia and the contralateral nasal tip. The UCLP group showed, moreover, asymmetry in buccal region due to typical maxillar hypoplasia, which was accentuated in the older group. The BCLP groups showed slightly similar but greater asymmetry than the control groups, except for the philtrum region.
Conclusions: Asymmetry of each of the cleft groups significantly differed from the controls. Except for the buccal region in the UCLP and BCLP groups, asymmetry did not significantly increase with age.

1. Introduction

Facial symmetry refers to a state of balance, where the size, form, and arrangement of facial tissues and structures on the opposite sides of the median sagittal plane correspond. Thus, the right and left sides in the craniofacial complex, comprising identical structures, must grow and develop equally to reach symmetry [1]. Nonetheless, a mild degree of asymmetry is a common biological characteristic in healthy individuals [2].

The degree of asymmetry considered to be reasonable often varies between 2 and 4 mm [3]. There are no existing objective standards for establishing abnormality [4] and it is often determined by the clinician's perception of balance and the patient's perception of imbalance [5].

The etiology of facial asymmetry for many cases is still unknown but it can be attributed to genetic and environmental factors or a combination of both [6,7]. Hence, the etiology of asymmetry can be grouped into three main categories, (A) congenital, originating prenatally; (B) developmental, arising during growth with inconspicuous etiology; and (C) acquired, resulting from injury or disease [8].

The theoretical basis for congenital asymmetry is that the lower and midface develop from the medial and lateral nasal processes as well as maxillary and mandibular processes, and despite innate synchronization, these structures might indicate failure of development or maturation of such embryonic processes [9]. The changes associated with facial asymmetry comprise facial clefts, hemifacial microssomia, congenital muscular torticollis, unilateral coronal craniosynostosis, positional plagiocephaly and others [8].

As yet, there is no reasonable explanation for the causative mechanism of lateral guidance of the face but it might be related to the imbalanced development of neural crest cells. It has been speculated that neural crest cell migration happens earlier on the right side and tends to be delayed on the left side [9,10]. It could be associated with preferential laterality for some anomalies, such as cleft lip, which occur

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more commonly on the left side.

Facial asymmetry is one of the most common features in cleft lip or cleft lip and palate patients [11]. The UCL nasal deformity is dominated by the asymmetry of the soft tissue in the lip and nose area, as well as in the underlying skeleton [12]. However, there was no statistically significant difference between the amount of facial asymmetry in children with repaired isolated cleft palate and their healthy peers [13].

Treatment of cleft lip and palate patients is focused on the soft tissues of the lip and nose, and the hard tissues of the maxilla and dental abnormalities [14].

Neonatal cheiloplasty performed in the first week of life solves some of the problems connected with cleft lip such as feeding problems, and leads to positive psychosocial outcomes for the whole family, enhanced wound healing and excellent aesthetic results [15]. However our previous results revealed that it is still a cause of minor craniofacial growth impairment. The differences in patients with cleft lip only were least and observable only in the cleft area itself [16].

This study aimed at illustrating and evaluating facial asymmetry in pre-school patients with various orofacial clefts who underwent neonatal cheiloplasty. To find out if there are any developmental trends in asymmetry two age groups of patients were selected. The visualization and 3D analysis of facial asymmetry in healthy children was carried out to detect any similarities in asymmetry with cleft patients.

2. Participants and methods

2.1. Participants

The intervention group consisted of 96 patients with unilateral cleft lip (UCL), unilateral cleft lip and palate (UCLP) and bilateral cleft lip and palate (BCLP). Individuals with associated syndromes were excluded from the study. All the patients were Caucasian and underwent surgery at the Faculty Hospital Motol, Prague, Czech Republic, by the same surgeon. Primary cheiloplasty in all the patients was performed using the modified Tennison's method within the first 10 days of life (exceptionally 14 days). The UCLP and BCLP groups underwent palatoplasty, which was performed at a mean age of 10.3 months using Furlow's technique by the same surgeon. The intervention group was comprised of two separate age groups and both groups contained subgroups with each of the three cleft types. The younger category with a mean age of 3 years (2.5–3.7 yrs) consisted of 51 patients (31 UCL, right-8, left-23; 15 UCLP right-3, left-12; 5 BCLP). The older category with a mean age of 4.5 years (4.0–5.0 yrs) consisted of 45 patients (21 UCL, right-8, left-13; 15 UCLP, right-9, left-6; 6 BCLP).

The control group consisted of age-matched healthy children attending preschools in Letná, Hrabákova, Kolovraty and Vozová in Prague. The younger subgroup in the control group was comprised of 40 individuals and the older subgroup was comprised of 38 individuals. All the children in the control group had harmonious balanced faces and no craniofacial abnormalities.

2.2. Methods

A facial scan was obtained from each subject using a non-invasive optical scanner Vectra 3D (Canfield Scientific Inc., Fairfield, NJ, USA) and 3dMDface System (3dMD Limited, Brentford, London, UK). Surface models were built automatically using the bundled software. Next, each model was processed in RapidForm 2006 (INUS Technology Inc., Seoul, South Korea). The processing involved manual trimming with removal of the ears, neck and hair, closure of any holes and simplification to roughly 30k triangles. Finally, scans with a unilateral cleft on the right side were reflected about a plane to keep all clefts on the left side.

Before any statistical processing of the surfaces, vertex homology had to be enforced. This was done using CPD-DCA [17], which is an extension of the original DCA that uses an automatic nonrigid registration algorithm. Nine landmarks were placed on each model in standard locations (exoR = right exocanthion; exoL = left exocanthion; enR = right endocanthion; enL = left endocanthion; N = nasion; Pn = pronasale; chR = right cheilion; chL = left cheilion; Pg = pogonion). These landmarks were used for rigid prealignment of the facial surfaces by means of Generalized Procrustes Analysis (GPA). Vertex homology was created by resampling all surfaces based on one arbitrarily chosen surface from the sample called the *base mesh*. Automatic nonrigid registration and projection of the base mesh to each surface was used to transfer the topology of the base mesh to all other meshes. The resulting vertices can be considered homologous across the data set and are subject to the same methods as ordinary landmarks; they are therefore referred to as *quasi-landmarks*. Finally, the surfaces were rigidly aligned to a mean surface using GPA.

Detailed analysis of asymmetry was evaluated using special workflow in Morphome3cs software (www.morhome3cs.com), whose outputs are both color-coded maps and shell distance significance maps. From the *correspondence meshes*, *symmetric meshes* were created as follows. Each correspondence mesh was reflected about an arbitrary plane and resampled to the topology of its non-reflected counterpart with the same method that was used in the construction of correspondence meshes. Rigid alignment of these two surfaces with GPA also produced a mean surface, which was the sought symmetric mesh. Subtracting the symmetric quasi-landmarks from those of the correspondence meshes yielded the individual asymmetry (IA). For visualization, signed IA has been calculated. Sign of IA in each vertex has been determined based on the position of the correspondence vertex relative to the symmetrized vertex, with respect to local surface normal. Positive values were assigned if the correspondence vertex was in front of the symmetrized vertex; negative values if the converse was true.

The color-coded maps are interpreted in the following way: red areas that are in the front of the corresponding mirrored counterpart, suggest that they may be larger than the corresponding paired counterpart (= positive values of asymmetry), while blue areas are smaller and located behind the aligned mirrored counterpart (= negative values of asymmetry) [18]. Shell distance significance maps were used to show where the asymmetry was statistically significant. The corresponding p-values were coded in shades of blue.

In addition, asymmetry of the forehead in patients with left and right side unilateral clefts, which were unlikely to be associated with the oral defect, were separately analyzed for evaluation and illustration.

3. Results

Using scatter plots of principal components analysis, we visualized variability of asymmetry in the cleft and control groups. First, we observed that the cleft groups exhibited a greater variability in the principal components (PCs) scores than the controls. The first 6 PCs have been kept for statistical processing according to the broken-stick method criterion. The most apparent separation of the groups were observed from PCs 3 and 5 (Fig. 1).

Both the parametric and permutation version of Hotelling's T2 tests on PC scores revealed that in each cleft or control group, the degree of asymmetry did not differ significantly between age groups. This could not be confirmed between BCLP groups alone due to the small sample in the three-year-old group. Although there were no statistically significant differences between age groups in overall facial asymmetry, we decided to visualize age groups separately because of the possible presence of local differences.

Further testing was focused on cleft groups in comparison with the controls. The parametric and permutation version of Hotelling's T2 test detected statistically significant differences in all the cases tested; ($p < 0.01$) in the BCLP group, and ($p < 0.001$) in the UCL and the UCLP groups.

After determining the presence of the differences in asymmetry in specific groups of probands using PCA scores, we visualized the differences in asymmetry using color-coded maps and calculated per-