Facial and midfacial symmetry in cleft patients: Comparison to non-cleft children and influence of the primary treatment concept

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A B S T R A C T

Purpose: Patients with cleft lip, alveolus and palate (CLAP) may suffer from marked asymmetry with an impact on attractiveness and psychosocial aspects. The aim of this study was to assess symmetry in CLAP patients compared to non-cleft controls of similar age with regard to cleft type and treatment concept.
Materials and methods: In CLAP patients with different cleft forms and in healthy non-cleft subjects (control group) a three-dimensional stereophotogrammetric face scan was performed and an objective 3D asymmetry index (AI) was calculated for the whole face, the midface, the upper lip and the nose.
Results: In total, 305 patients were included: 140 CLAP patients (90 male, 50 female, mean age 9.9 ± 3.6 years) and 165 controls (87 male, 78 female, mean age 8.7 ± 2.1 years). In general, CLAP patients showed significantly higher asymmetry than controls, with the most severe asymmetry found in unilateral complete CLAP. Patients treated according to an actual concept considering reconstruction of all affected muscular systems had a significant lower and more favourable AI than patients not treated according to this concept ($p < 0.05$).
Conclusion: An adequate treatment concept is essential to achieve better results concerning symmetry in CLAP, but symmetry values of healthy non-cleft controls are not reached.

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1. Introduction

Cleft lip, alveolus and palate (CLAP) is one of the most common malformations of the maxillofacial region with an incidence at birth of approximately 1:500 to 1:700 in Central Europe (Mossey et al., 2009). CLAP affects various functions and aspects, e.g. maxillofacial growth, aesthetics, speech and swallowing. Adequate reconstruction is challenging, as it requires meticulous interdisciplinary treatment concept. Of special importance for enabling physiological development is an adequate reconstruction of all affected muscles to connect primary and secondary growth centers of the face (Joos, 1987). Previous studies revealed that a concept especially taking into account the reconstruction of the perioral, midfacial and velopharyngeal muscle rings leads to good results concerning maxillary growth and speech. Thus, the need for secondary corrective surgery is reduced (Joos, 1995; Joos et al., 2006).

Whereas the prevention of maxillary hypoplasia and retrognathia is a main goal in treatment of CLAP patients as far as sagittal and transversal dimensions are concerned, in the frontal view also symmetry is an important aspect (Brattström et al., 2005; Meyer-Marcotty et al., 2011; Semb et al., 2005). Especially unilateral clefting may result in relevant asymmetry of the face, especially in the region of lip and nose (Ayoub et al., 2011b, p. 1, 2011b, p. 2; Freeman et al., 2013; Kluba et al., 2015; Reddy et al., 2013; Semb et al., 2005; Stauber et al., 2008).

The degree of symmetry shows a clear correlation with attractiveness (Edler et al., 2010; Meyer-Marcotty et al., 2010; Ostwald et al., 2015; Scheib et al., 1999). In maxillofacial surgery, achieving symmetry close to normal is an important goal, not only in cleft surgery but also in orthognathic and aesthetic surgery as well as in trauma and tumour treatment. Various two-dimensional (2D) and

three-dimensional (3D) methods of assessing or measuring the degree of facial asymmetry have been reported so far (Berlin et al., 2014; Berssenbrügge et al., 2015, 2014). In recent literature an unequivocal trend to favouring 3D face scan over 2D analysis is obvious (Al-Rudainy et al., 2018; Bagante et al., 2018; Bell et al., 2014; Khambay and Ullah, 2015; Kornreich et al., 2016). This implicates that also in CLAP patients measuring asymmetry three-dimensionally is beneficial, e.g. to compare different treatment strategies and to evaluate facial development (Bell et al., 2014; Sharma et al., 2012; Sitzman et al., 2014). In theory, a treatment concept leading to better midfacial growth and good lip function should be positively correlated with less asymmetry and more favourable results concerning this aesthetically and psycho-socially relevant aspect.

The objectives of this study were (a) to measure asymmetry in patients with different forms of CLAP in comparison to healthy non-cleft subjects of comparable age, and (b) to evaluate the impact of the primary treatment concept on facial symmetry.

2. Material and methods

2.1. Patients and investigations

Patients with all forms of CLAP were included during their routine consultation at the Department of Oral and Maxillofacial Surgery, University Hospital Muenster, Germany, in a prospective manner consecutively. Inclusion criteria were non-syndromic CLAP, a minimum age of 6 years and sufficient compliance for participation in this study. Exclusion criteria were noncompliance, age below 6 years and craniofacial syndromes. The control group consisted of healthy non-cleft subjects (volunteers) from an elementary school. Again, the inclusion criterion was a minimum age of 6 years. Exclusion criteria were maxillofacial malformations or craniofacial syndromes, postoperative state or relevant treatment affecting growth in the head and neck area with the exception of cleft surgery itself, and neurological or other general disorders that could affect facial development.

All patients and healthy controls, or their parents or legal guardians, gave written informed consent for participation in this study. The study and application of the 3D scanning system were approved by the local ethical committee of the University of Muenster (AZ 2009-131-f-S). All data were anonymized, and this study was conducted in according with the Declaration of Helsinki for Good Clinical Practice (GCP).

Besides the usual clinical examination and routine check-up by a maxillofacial surgeon, an orthodontist and a speech pathologist, a 3D-scan of the full face in a frontal view with the head in normal position (see Fig. 1A) and in a reclined head position (retroflexion) to provide a basal view of the nose (for better view of the nostrils, see Fig. 1B) was performed in all participants. Participants were asked to maintain a neutral facial expression with closed lips and teeth in loose contact.

2.2. 3D scanning system

Our 3D scanning system is based on the fringe projection technique using only visible light without any type of ionizing radiation. It has been developed at the Faculty for Dentistry and Oral Medicine, Department of Prosthetic Dentistry and Biomaterials, at the University of Muenster. Technical details and data acquisition were described in previous publications (Berssenbrügge et al., 2015; Bischoff et al., 2007; Ostwald et al., 2015; Wermker et al., 2014). The system enables a 3D facial scan yielding approximately 200,000 3D points (full density point cloud) including skin colour (true colour rgb model) within 1.5 seconds. Accuracy of the measured 3D coordinates is approximately 0.6 mm lateral (X- and Y-axis) and 0.2 mm axial (Z-axis) within a maximum field of 600 mm × 450 mm.

2.3. Calculation of the 3D asymmetry index

For objective measurement of asymmetry, a three-dimensional asymmetry index (AI) was calculated on the basis of the optically acquired data. The procedure is described in (Berssenbrügge et al., 2015). First the original 3D dataset ("original cloud") is mirrored automatically at the median–sagittal plane to generate a "mirrored cloud." Afterwards, the original and mirrored cloud are matched. Registration is performed automatically using the ICP (iterated
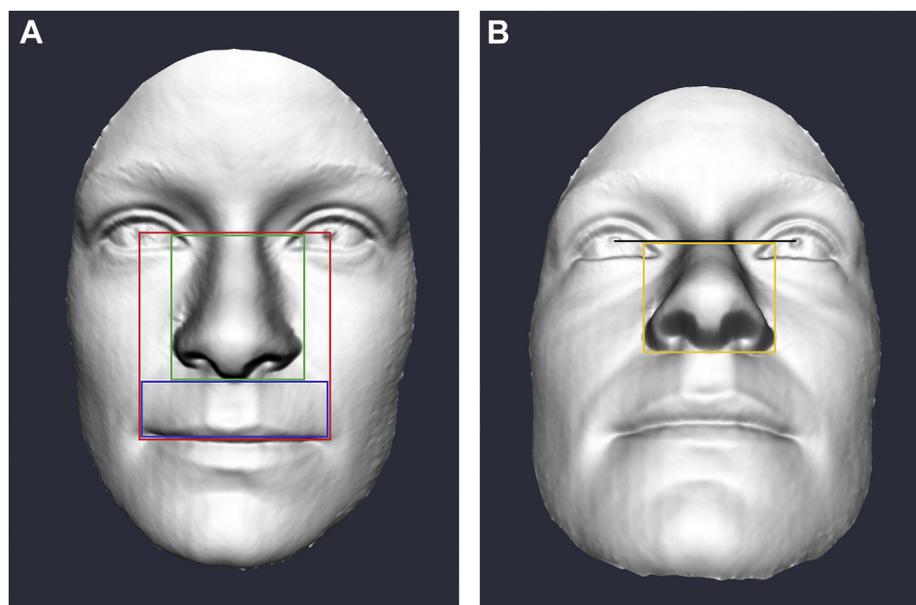

Fig. 1. (A) Assessed regions in the frontal view. Without box: whole face (AI face); red box: midface (AI midface); green box: node in the frontal view (AI nose frontal); blue box: upper lip (AI upper lip). AI = asymmetry index. (B) Basal view with the head in a reclined position (retroflexion). Black line: bipupillar line; yellow box: nose in the basal view (AI nose basal).

closest point) algorithm (Besl and McKay, 1992), which matches both clouds with the lowest achievable distance from each other. Mirroring and matching processes are repeated several times. The AI is calculated from the mean of all distances between original and mirrored-matched clouds (d) and the frontal face diagonal of the bounding box of the face (D) to compensate for differences between smaller and larger faces, using the following formula: $AI = \frac{d}{D} \times 1000$. In a perfectly symmetric face, the AI would be 0. A greater value of the AI indicates a more asymmetric face. This AI is easy to calculate and enables an objective assessment of facial asymmetry.

For visualization of asymmetries, a pseudocolour image can be generated, showing the asymmetric regions of the face in warmer colours (Wermker et al., 2014). In previous studies, we found a significant correlation between this AI and subjectively rated facial symmetry and attractiveness (Berssenbrügge et al., 2015; Ostwald et al., 2015).

2.4. Measured anatomical regions

The previously defined AI was measured for the following five facial areas: (1) the whole face (AI face), which encompasses the entire scanned face from ear to ear (ears are excluded) and from the forehead to the chin; (2) the midface (AI midface), which is defined by two horizontal planes through the bipupillar line and the corners of the mouth and two vertical planes, perpendicular to the horizontal planes, through both pupils; (3) the upper lip (AI upper lip): this area is defined by two horizontal planes through the corners of the mouth and the subnasal point and two vertical planes perpendicular to the latter two through the corners of the mouth; (4) the nose in frontal view (AI nose frontal), where the lower border is the above mentioned horizontal plane through the subnasal point and upper border of which is defined by the bipupillar plane; two vertical planes perpendicular to the horizontal one through the most lateral and caudal point of the alar wing of the nose define the lateral borders on each side; and (5) the nose in a basal view (AI nose basal), this scan was performed with the head in a retroflexed (reclined) position and renders anatomical structures of the nostrils that are not captured in the frontal view. Fig. 1A, B illustrate the measured regions.

2.5. Statistical analysis

Data were tested for normality by a Kolmogorov–Smirnov test. To assess significance of differences between different groups of patients (e.g. according to gender, type of cleft or performed primary operative treatment concept), a Chi-square test and Fisher exact test were applied for categorical variables, for metric parameters Kruskal–Wallis H test or Mann–Whitney U test were used as non-parametric tests for non–normally distributed data, and analysis of variance (ANOVA) with post hoc Tamhane T2 test and t test were used for normally distributed variables. A minimum size of 10 subjects per group was assumed to perform analytic statistics; otherwise only descriptive data are presented (group bCL [bilateral cleft lip]: n = 2). All tests were two-sided and the level of significance was set to 5% (p < 0.05). All statistical analyses were performed by a statistician using the Statistical Package for Social Sciences (SPSS), version 22.0 for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Study population

The study population comprised 305 subjects (177 male, 128 female): 140 patients with CLAP (90 male, 50 female) and 165

healthy controls (87 male, 78 female). Mean age of both groups was similar, with a mean age of 9.9 years (SD 3.6 years) in cleft patients and 8.7 years (SD 2.1 years) in controls (p > 0.05). In 78 patients, clefting was unilateral (unilateral cleft lip [uCL], unilateral cleft lip and alveolus [uCLA] and unilateral cleft lip, alveolus and palate [uCLAP]), 15 participants suffered from a bilateral cleft type (bilateral cleft lip [bCL], bilateral cleft lip and alveolus [bCLA] and bilateral cleft lip, alveolus and palate [bCLAP]) and 47 patients had a cleft palate only (CP). A detailed overview concerning cleft type and gender is given in Table 1.

With regard to the primary treatment concept, 98 (70.0%) cleft patients had been treated completely at our cleft and craniofacial malformations center (MS + group, current Muenster Centre protocol). These patients all received primary closure of lip and/or alveolus and/or palate within their first year of life according to a previously described concept (Anastassov and Joos, 2001). Lip closure was performed at the age of 3–4 months according to Delaire/Joos, including closure of the nasal floor and alveolus. Closure of hard and soft palate was done in one operation at the age of 7–9 months. The primary goal and mainstay of all operations was the anatomical correct reconstruction of all affected muscle rings (perioral, midfacial and velopharyngeal muscles) to connect primary and secondary growth centers of the midface, leading to normalized physiology and function with good results concerning growth and speech (Joos, 1995; Joos et al., 2006). All operations were performed by the same craniofacial team. In 42 (30%) CLAP patients, these primary operations were performed with a different technique according to an older concept by a different team (MS– group): primary lip closure was performed using the Millards technique at the age of 5–8 months (Millard, 1966), and single-step closure of hard and soft palate was done according to Campbell and Widmaier at the age of 12–16 months (Widmaier, 1959). In 11 of these 42 patients, the primary cleft surgery was performed at other German hospitals, but detailed reports of the operations were obtained to enable correct classification of the performed treatment.

3.2. Symmetry and cleft type

The healthy controls showed the lowest AI values in all facial subregions and for the entire face, i.e. the highest symmetry, compared to cleft. All measured asymmetry values with respect to the cleft type are presented in detail in Table 2. As expected, unilateral cleft types showed more unfavorable (i.e. higher) AI for almost all measurements. The following differences between groups reached statistical significance (p < 0.05): (a) for the whole face between controls and uCL (p < 0.001), uCLA (p = 0.001), uCLAP (p < 0.001) and CP (p = 0.002) and in cleft patients between uCLAP and CP (p = 0,003); (b) for the midface between the control group and all tested cleft groups (p < 0.01) and in the cleft population

Table 1
Study population by cleft type and gender.

	Gender		Total n (%)
	Male n (%)	Female n (%)	
Controls	87 (52.7)	78 (47.3)	165 (100.0)
uCL	21 (70.0)	9 (30.0)	30 (100.0)
bCL	1 (50.0)	1 (50.0)	2 (100.0)
uCLA	7 (63.6)	4 (36.4)	11 (100.0)
bCLA	-	-	-
uCLAP	30 (81.1)	7 (18.9)	37 (100.0)
bCLAP	8 (61.5)	5 (38.5)	13 (100.0)
CP	23 (48.9)	24 (51.1)	47 (100.0)
Total	177 (58.0)	128 (42.0)	305 (100.0)

uCL = unilateral cleft lip; bCL = bilateral cleft lip; uCLA = unilateral cleft lip and alveolus; bCLA = bilateral cleft lip and alveolus; uCLAP = unilateral cleft lip, alveolus and palate; bCLAP = bilateral cleft lip, alveolus and palate; CP = cleft palate.

Table 2
Values of the three-dimensional asymmetry index (AI) in different groups according to cleft type.

		Asymmetry index (AI)				
		Face	Midface	Upper lip	Nose frontal	Nose basal
Controls	mean	2.309	2.974	4.522	5.241	7.083
	SD	0.670	0.797	1.851	1.459	1.985
uCL	mean	3.271	6.352	10.181	10.302	15.999
	SD	0.843	1.962	2.460	2.886	3.892
bCL	mean	3.894	8.570	6.530	8.670	12.485
	SD	2.007	0.735	0.269	2.758	3.231
uCLA	mean	3.166	6.206	10.364	9.936	15.877
	SD	0.428	1.412	2.608	1.817	7.486
uCLAP	mean	3.725	7.283	11.454	12.342	19.189
	SD	1.189	2.369	3.988	3.992	8.152
bCLAP	mean	3.636	5.992	8.112	9.081	12.643
	SD	1.305	2.290	3.841	3.882	5.668
CP	mean	2.817	4.476	5.543	6.953	10.437
	SD	0.753	1.586	2.676	2.781	4.455

For significance of differences, see text.
uCL = unilateral cleft lip; bCL = bilateral cleft lip; uCLA = unilateral cleft lip and alveolus; uCLAP = unilateral cleft lip, alveolus and palate; bCLAP = bilateral cleft lip, alveolus and palate; CP = cleft palate; mean = arithmetic mean; SD = standard deviation.

between CP and uCL ($p = 0.001$), uCLA ($p = 0.049$) and uCLAP ($p < 0.001$); for the upper lip region between controls and uCL, uCLA and uCLAP (all $p < 0.001$) and in the cleft subjects between CP and also uCL, uCLA and uCLAP (all $p < 0.002$); for the frontal view of the nose between controls and all unilateral clefts (uCL, uCLA and uCLAP, all $p < 0.001$) and CP ($p = 0.003$) and in cleft patients between CP and uCL ($p < 0.001$), uCLA ($p = 0.005$) and uCLAP ($p < 0.001$); and for the basal view of the nose between the control group and uCL, uCLAP and CP (all $p < 0.001$) and in the cleft cohort between CP and uCL and uCLAP (both $p < 0.001$).

When comparing controls, unilateral clefts (uCL, uCLA and uCLAP), bilateral cleft types (bCL, bCLA and bCLAP) and cleft palate (CP) asymmetry values, the highest symmetry was generally observed in healthy controls, closely followed by patients with CP and bilateral cleft and finally patients with unilateral cleft type. The boxplot diagrams demonstrate this for the AI of the midface (Fig. 2) and the nose (frontal view) (Fig. 3). Asymmetry was significantly different between controls and all types of unilateral cleft for all measured AI values (all $p < 0.001$), between controls and bilateral clefts again for all measurements (p-values between <0.001 and
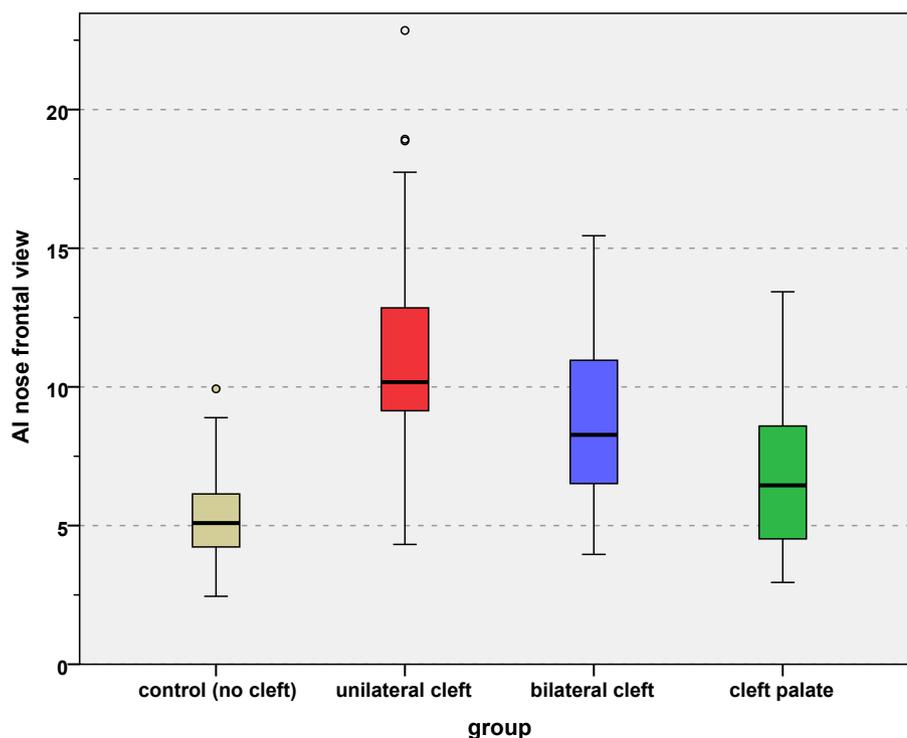

Fig. 2. Measured asymmetry of the nose in the frontal view (AI nose frontal) with regard to cleft type. AI = asymmetry index.
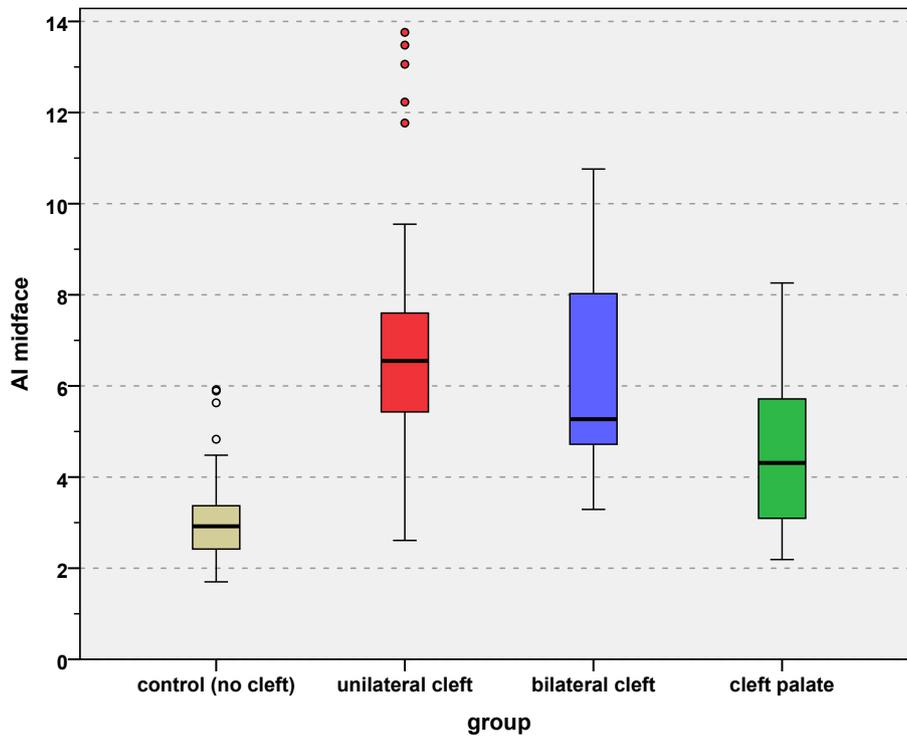
Fig. 3. Measured asymmetry of the midface (AI midface) with regard to cleft type. AI = asymmetry index.

0.016), between the control and the CP groups for all values ($p < 0.01$) except for the upper lip ($p = 0.098$), between uni- and bilateral clefts for the basal view of the nose ($p = 0.03$), and between CP and unilateral clefts for all symmetry values (all $p < 0.001$). Differences between CP and all bilateral cleft types together were not statistically significant (all $p > 0.05$).

3.3. Symmetry and primary treatment concept

The comparison of patients treated according to the current Muenster concept (MS + group) with patients not treated according to this concept (MS− group) showed lower (more favourable) asymmetry values for patients in the MS + group (Table 3). Except for the symmetry index of the upper lip, all other AIs were

statistically significant lower in MS + compared to MS− ($p < 0.05$, t-test). The significant lower AI in MS + patients is demonstrated in Fig. 4 (whole face), Fig. 5 (midface) and Fig. 6 (nose frontal view).

A comparison of controls, MS+ and MS− groups (ANOVA) showed that the differences between controls and both cleft groups were statistically highly significant for all measured symmetry values (all $p < 0.001$).

4. Discussion

In the recent literature, several researchers have underlined the importance of an objective assessment of symmetry and aesthetics in patients with cleft lip, alveolus and palate (Freeman et al., 2013; Gkantidis et al., 2013; Ranganathan et al., 2015; Schwenzer-

Table 3
Values of the three-dimensional asymmetry index (AI) in different groups according to the primary treatment concept.

AI		Controls (n = 165)	MS+ (n = 98)	MS− (n = 42)	Significance (p-value)
Face	mean	2.309	2.908	4.124	(<0.001)***
	SD	0.670	0.609	1.254	
Midface	mean	2.974	5.446	7.144	(<0.001)***
	SD	0.797	1.941	2.468	
Upper lip	mean	4.522	8.556	9.137	(0.428)
	SD	1.851	3.710	4.517	
Nose frontal	mean	5.241	8.959	10.931	(0.005)**
	SD	1.459	3.522	4.141	
Nose basal	mean	7.083	13.787	16.510	(0.029)*
	SD	1.985	6.102	7.965	

MS + = primary treatment according to the current Muenster concept (Muenster group); MS− = primary treatment not according to the current Muenster concept (non-Muenster group); mean = arithmetic mean; SD = standard deviation.
Significance = significance of difference between MS+ and MS− (t-test).
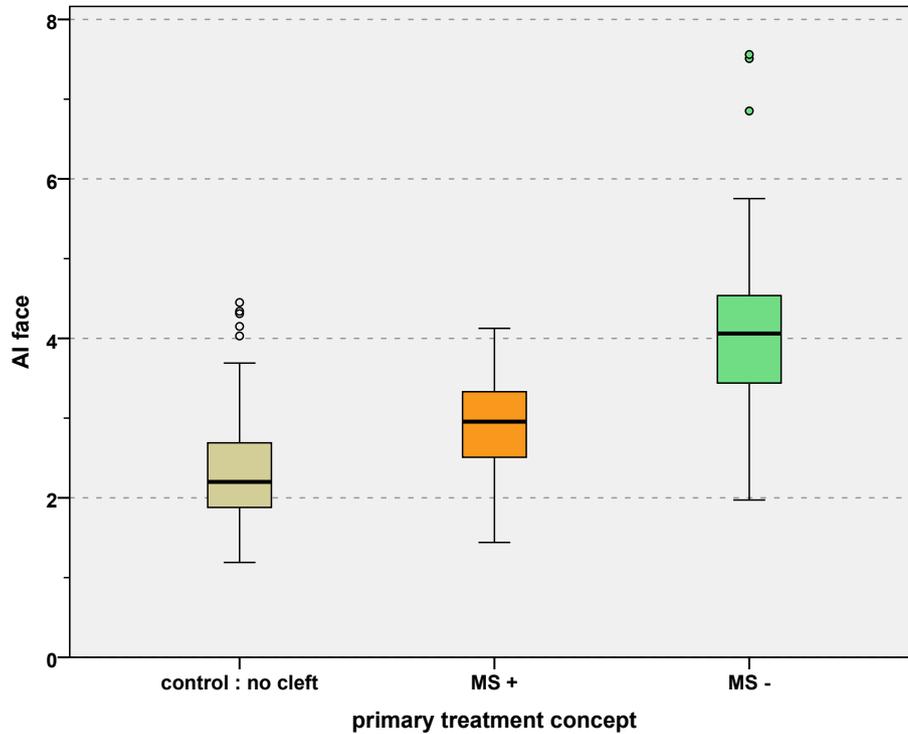*p < 0.05; **p < 0.01; ***p < 0.001.

Fig. 4. Measured asymmetry of whole face (AI face) with regard to the primary treatment concept. AI = asymmetry index; MS+ = cleft patient treated according to the current Muenster concept; MS− = patients not treated to the actual Muenster concept.

Fig. 5. Measured asymmetry of midface (AI midface) with regard to the primary treatment concept. AI = asymmetry index; MS+ = cleft patient treated according to the current Muenster concept; MS− = patients not treated to the actual Muenster concept.
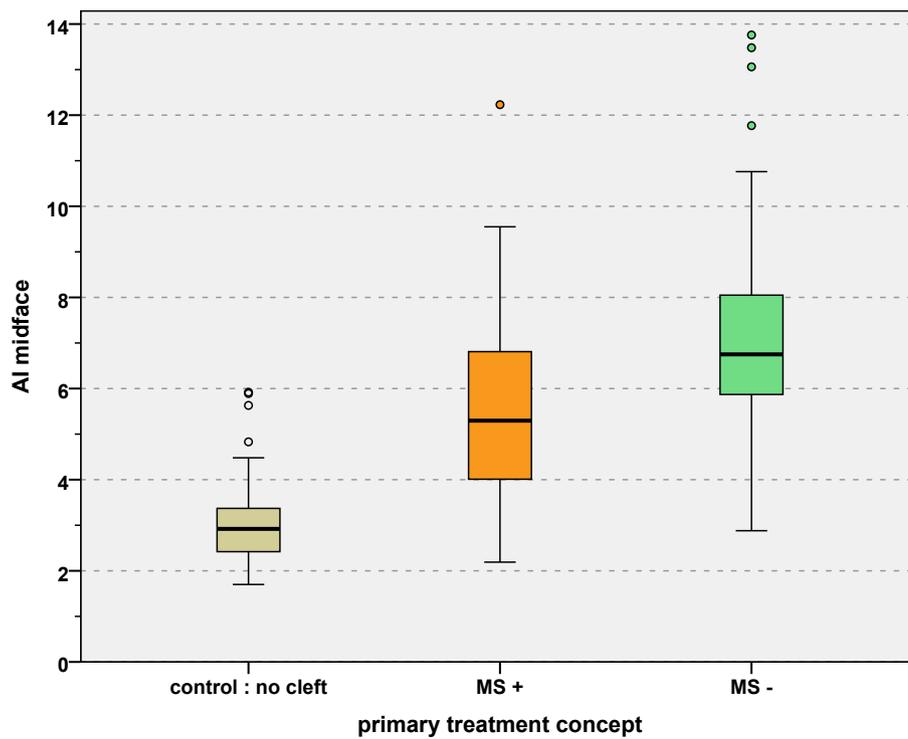
Zimmerer et al., 2008; Sharma et al., 2012; Sitzman et al., 2014). Three-dimensional techniques provide the opportunity to evaluate these aspects without loss of information. In the analysis of symmetry in CLAP, there is now a clear tendency to prefer 3D analysis to 2D evaluation (Al-Omari et al., 2005; Al-Rudainy et al., 2018; Bagante et al., 2018; Bell et al., 2014). Our study demonstrates the capability of the applied measuring technique and the calculated asymmetry index (AI) to objectively assess facial symmetry for the
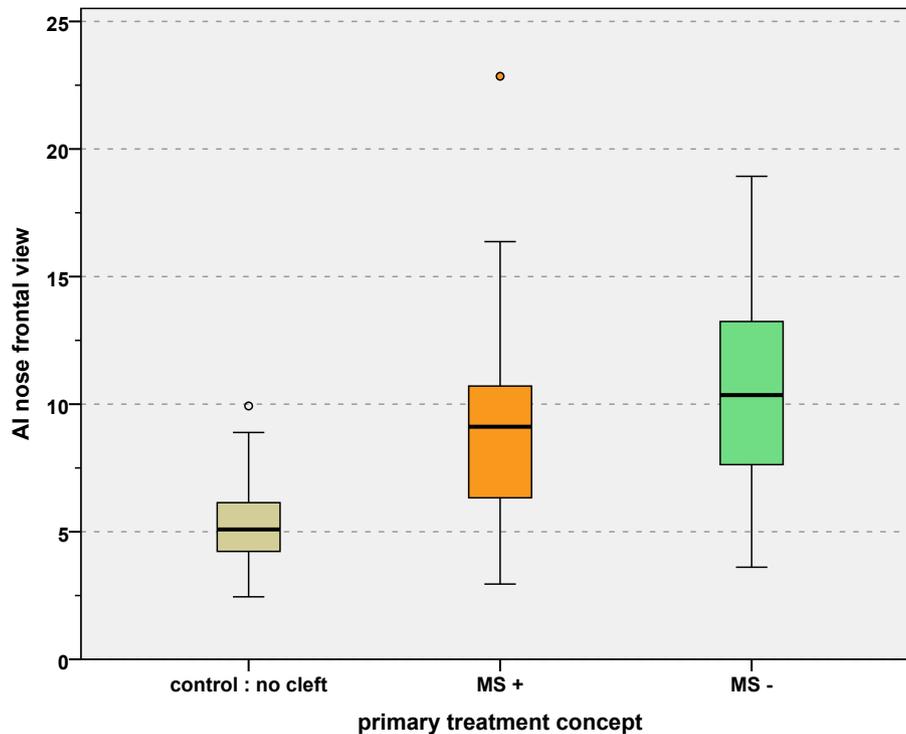
Fig. 6. Measured asymmetry of the nose in the frontal view (AI nose frontal) with regard to the primary treatment concept. AI = asymmetry index; MS+ = cleft patient treated according to the current Muenster concept; MS− = patients not treated to the actual Muenster concept.

whole face and relevant subregions in cleft patients. The significant correlation between this AI and rated attractiveness was demonstrated previously by our research group (Ostwald et al., 2015). The relationship between objectively measured symmetry and subjectively assessed attractiveness is consensus (Edler et al., 2010; Meyer-Marcotty et al., 2011; Scheib et al., 1999). In this context, it is advantageous if the technique used allows reliable symmetry analyses of sub-regions of the face. This applies in particular to the nasolabial area in cleft patients, as this region shows the largest asymmetry in CLAP. Furthermore, this is the region where most cleft patients themselves recognize impairments (Semb et al., 2005; Sitzman et al., 2014). In the presented study, we considered this fact by analyzing the sub-regions "upper lip" and "nose" separately as well as together ("midface"). Using our face scanning system and the proposed 3D asymmetry index (AI), this study provides for the first time objective and reliable data on the symmetry of different sub-regions of the face in cleft patients and healthy controls of similar age.

Looking at measured symmetry in the cleft groups in comparison to healthy controls, the results are as expected. In general, the faces in cleft patients showed more asymmetry (higher AI). The most severe asymmetry was seen in the nasal region, followed by the upper lip and the midface (which includes nose and upper lip). The nasal asymmetry is dedicated to the typical cleft-related nasal deformity, and the results are in line with those of other researchers and are well known (Gassling et al., 2015; Kluba et al., 2015; Krimmel et al., 2006; Othman et al., 2014; Reddy et al., 2013). Especially the asymmetry of the nostrils can be demonstrated clearly in the basal view of the nose (AI nose basal). Within the cleft group, unilateral cleft types (uCL, uCLA and uCLAP) showed more asymmetry than bilateral forms, and the lowest AI values were measured in the isolated cleft palate. Concerning nasal symmetry (in both the frontal and basal views) and labial symmetry (AI upper lip), uCLAP clearly and significantly suffered from the most

asymmetry, i.e. had the highest AI values. The distinct differences that led to upper lip impairments in cleft involving the lip (e.g. differing horizontal and vertical dimensions between operated cleft side and non-cleft side, different upper lip vermillion length, alterations of Cupid's bow) and that explain the resulting differences of symmetry values were described previously and are in line with our findings (Ayoub et al., 2011a; Kluba et al., 2015; Oh et al., 2011). Fig. 7 illustrates typical asymmetries in a uCLAP patient (Fig. 7A) in contrast to a CLP patient (Fig. 7B) using false-colour imaging.

An interesting and important finding of this study is the fact that symmetry values significantly depend on the primary treatment concept. We could clearly demonstrate that a functionally orientated concept that especially takes muscular reconstruction into account leads to more harmonious facial growth, resulting in less asymmetry. The influence of this treatment concept on facial growth in terms of sagittal parameters and maxillary development (less retrognathia, less hypoplasia and reduced need for orthognathic surgery) was demonstrated many years ago (Anastassov and Joos, 2001; Joos, 1995). In this study, we can augment this with favorable results concerning facial symmetry. Adequate connection between primary and secondary growth centers of the face therefore supports better facial development in all three dimensions. On the other hand, it has to be mentioned that even the group with the better treatment concept (MS + group) did not reach the symmetry values of normal non-cleft patients (control group). This means that the typical cleft-associated asymmetry, especially in the midfacial regions of the upper lip and the nose, was not corrected completely. There still remains a significant difference between healthy controls and the MS + group.

With more than 300 participants our study, it is, as far as we know, one of the largest ones evaluating three-dimensionally and objectively facial symmetry in cleft patients and non-cleft controls. A similar study design was used by another group for comparison of cleft and non-cleft children of younger age than in our study (pre-
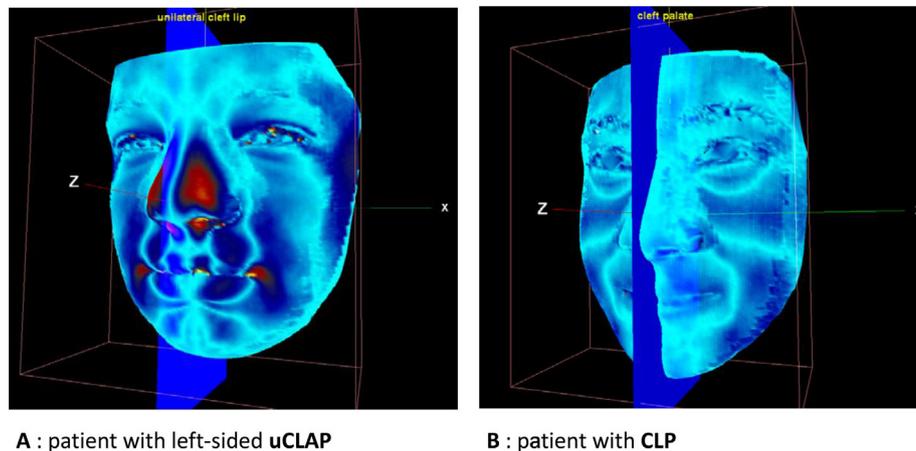
A : patient with left-sided **uCLAP**   B : patient with **CLP**

Fig. 7. Illustration of asymmetry using false-colour imaging. Warmer colours indicate higher asymmetry values. The patient with unilateral cleft lip and palate (uCLAP) (A) shows significantly more asymmetry at the nose (alar and nostrils) and upper lip compared to a patient with cleft palate (CLP) (B).

school patients) in a recently published paper (Moslerová et al., 2018). The authors examined 96 cleft patients and 78 healthy controls of matched age and described even greater asymmetry in bilateral clefts, but on the whole their results were similar.

5. Conclusion

Our study provides basic data for facial, midfacial and nasal symmetry measured three-dimensionally in a non-cleft group and in patients with cleft lip, alveolus and palate. As expected, patients with unilateral cleft showed significant more asymmetry than patients with bilateral clefts or cleft palate only. Independently of the cleft type, the symmetry values of the non-cleft controls were not reached. The primary treatment concept with physiological reconstruction of all affected muscles and structures influences later symmetry results and leads to more favourable results.

Role of funding sources

Conflicts of interest

There were no financial and personal relationships with other people or organizations that could inappropriately influence (bias) our work. All authors declare that there is no conflict of interest.

Authors' contributions

NBB performed data acquisition, data analysis and interpretation and drafted the manuscript. JK made substantial contributions to the study design and leaded the clinical/surgical treatment of the cleft patients. DD substantially contributed together with PB to development of the face scan system and to design of the asymmetry index and gave final approval to the manuscript. PB substantially contributed together with DD to development of the face scan system and to design of the asymmetry index and helped in data acquisition and statistical analysis. CR contributed to study design, to data analysis and to interpretation of the results. KW developed the conception and design of the study, helped to analyze the data and contributed to draft the manuscript.

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