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Cleft Skeletal Asymmetry: Asymmetry Index, Classification and Application

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Abstract

Objective: To quantitatively measure the extent of 3D asymmetry of the facial skeleton in patients with unilateral cleft lip and palate (UCLP) using an asymmetry index (AI) approach, and to illustrate the applicability of the index in guiding and measuring treatment outcome.

Method: Two groups of subjects between the ages of 15 and 20 who had archived CBCT scan were included in this study. Twenty-five patients with complete UCLP were compared with 50 age-matched noncleft subjects. The CBCT scans were segmented and landmarked for 3D anthropometric analysis. An AI was calculated as a quantitative measure of the extent of facial skeletal asymmetry.

Results: For the control group, the AI ranged from 0.72 $\pm$ 0.47 at A point to 4.77 $\pm$ 1.59 at Gonion. The degree of asymmetry increased with the increasing laterality of the landmark from the midsagittal plane. In the UCLP group, the values of AI significantly increased compared to the control group at nearly all measured landmarks. The extent of the asymmetry to involve the upper, middle, and lower facial skeleton varied widely with the individual patient with UCLP.

Conclusion: The asymmetry index is capable of capturing the 3D facial asymmetry of subjects with UCLP and as a basis for classification of the extent of the asymmetry. We found the index to be applicable in surgical planning and in measuring the outcome in improving the symmetry in patients who have undergone orthognathic surgery.

Keywords

unilateral cleft lip and palate, facial asymmetry, 3D anthropometric analysis

Introduction

Children who are born with unilateral cleft lip and palate (UCLP) present with facial asymmetry. A fundamental goal of reconstruction is to restore the symmetry 3-dimensionally (3D) to within a clinically acceptable range of the general population. There is a need to accurately define the extent of facial asymmetry using a quantitative measuring tool that is clinically applicable.

The asymmetric facial features have been well documented in the literature (Atherton, 1967; Laspos et al., 1997; Mølsted and Dahl, 1990; Mølsted et al., 1995; Ras et al., 1994; Smahel and Brejcha, 1983). The vast majority of these studies have utilized 2-dimensional photographs to qualitatively characterize the cleft lip and nasal regions, and the skeletal studies have utilized 2-dimensional lateral and frontal cephalometric radiographs, limiting the analysis to only the sagittal and vertical relationships. However, in recent years, the increasing availability of surface imaging, computed tomography (CT), and low-dose cone beam computed tomography (CBCT) has given investigators a tool by which to quantitatively assess cleft deformities in 3 dimensions (Choi et al., 2013; Li et al., 2011; Stauber et al., 2008).

In terms of the underlying skeletal framework, the few studies that have been published suggest that the skeletal asymmetry remains "local" to the piriform region, with conflicting reports as to the extent of the midfacial skeletal and mandibular involvement (Choi et al., 2013; Kurt et al., 2010; Laspos et al., 1997; Li et al., 2011). The vast majority of the reported studies have not approached quantitatively measuring the degree of asymmetry in comparison to a clinically relevant population.

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The objectives of this study were to utilize an applicable quantitative asymmetric index for facial skeletal asymmetry, to establish the range of acceptable degrees of facial skeletal asymmetry in a "comparative, unaffected" population, to compare the extent of 3D asymmetry of the facial skeleton with UCLP against the noncleft (control) population, and to illustrate the applicability of an asymmetry index as a quantitative tool to guide treatment planning and a quantitative measure of the outcome of treatment in UCLP.

Materials and Methods

Subjects

The University of Illinois Institutional Review Board for human studies approval was obtained prior to the study. Two groups of study subjects between the ages of 15 and 20 who had available CBCT scans were used for this study. Group 1 (Control Group) consisted of 50 patients (25 females, 25 males) who had only orthodontic treatment and were treated to class I occlusion. Patients with clinically identifiable cleft, craniofacial, and maxillofacial anomalies or history of trauma were excluded in group 1. There were no patients in group 1 who required orthognathic surgery as they were skeletally class 1. Group 1 patients were used to establish the background range of asymmetry that exists in the "normative" population with the caveat that this study used patients who only needed orthodontic treatment for occlusal coordination. Group 2 (UCLP Group) consisted of 25 patients (12 females, 13 males) with complete unilateral cleft lip and palate and who had available CBCT archived scans. Patients who had a UCLP within the context of a syndromic condition or who have had cleft orthognathic surgery were excluded. Separate from these 2 groups of patients, this study also included a cleft patient who underwent orthognathic surgery to illustrate a practical application of the AI as an outcome measure before and after surgical treatment.

Data Acquisition and Analysis

The anatomic data of the facial skeletal anatomy was imaged using a CBCT scan (iCAT Next Generation, Imaging Sciences International, Inc, Hatfield, PA). The patients were in an upright position with the Frankfort Horizontal plane parallel to the horizon and in centric occlusion. The CBCT scan data were imported into Mimics v.16 (Materialise, Leuven, Belgium) and then thresholded and segmented to create a volumetric 3-dimensional facial skeleton. The data were then imported into Simplant Pro Crystal (Materialise, Leuven, Belgium). The sagittal, transverse, and coronal planes established an internal coordinate system. First, the midsagittal plane was constructed using the following landmarks: nasion, sella, and basion. Next, the transverse plane was constructed through sella and nasion and perpendicular to the midsagittal plane. Finally, the coronal plane was constructed through the basion and perpendicular to the midsagittal and axial planes. The intersection of all 3 planes at the basion established the origin of the coordinate system. Skeletal landmarks (Phulari, 2013) for this study were then identified (Table 1). Each anatomic landmark was uniquely identified by its coordinate location (x, y, and z) in a euclidean system. Ten randomly chosen CBCT from each group were selected and landmarked at a 2-week interval to ensure reliability. All landmarking was conducted by a single individual (D.S.P.). Test-retest reliability was evaluated via intraclass correlation (ICC) using 2-way random model with measures of absolute agreement. For all 10 cases, the ICC value was 0.999, indicating that there was a high reliability with the landmarking.

Table 1. Asymmetry Index in Group 1 Noncleft Patients (N = 50).

	Landmarks	Mean	Standard Deviation
Upper-facial landmarks	Frontomaxillary-nasal (FMN)	1.81	0.79
	Orbitale (O)	2.41	0.70
	Frontozygomatic (FZ)	2.48	1.03
	Porion (Po)	4.26	2.06
	Anterior nasal spine (ANS)	0.78	0.44
Midfacial landmarks	A	0.72	0.47
	Maxillary incisor (MxI)	0.73	0.54
	Maxillary Canine (MxC)	1.72	0.65
	Maxillary molar (MxM)	2.52	0.75
	Zygoma (Zy)	3.25	0.99
Lower-facial landmarks	Mandibular incisor (MdI)	0.91	0.65
	B	1.05	0.69
	Pogonion (Pog)	1.38	0.93
	Menton (Me)	1.44	0.96
	Mandibular canine (MdC)	2.40	0.79
	Mandibular molar (MdM)	3.16	1.15
	Gonion (Go)	4.77	1.59
	Condyle (Co)	4.31	1.31

The difference between the corresponding right and left anatomic landmark was calculated using the following equation:

$$\text{Asymmetry Index} = \sqrt{}(Rdx - Ldx)^2 + (Rdy - Ldy)^2 + (Rdz - Ldz)^2$$

The equation, utilized by Katsumata et al., calculates (Figure 1) the difference between the bilateral landmarks relative to each reference plane. For solitary midsagittal landmarks, the asymmetry index only consisted of a dx value as there is no significance in the dy and dz values. The result is an asymmetry index number that corresponds to the skeletal asymmetry in 3 dimensions for that landmark.

Statistical Analysis

The data were entered into Microsoft Office Excel 2011 (Microsoft, Redmond, WA) and were analyzed using the Student t test in the statistical package. The difference of asymmetric index (AI) at each landmark between group 1 (control) and group 2 (UCLP), and the difference between gender within each group were compared. We used the 95% confidence level with a P value less than .05 as statistically significant. All statistical analysis was performed using IBM SPSS Statistics 20 (IBM Corporation, Armonk, NY).

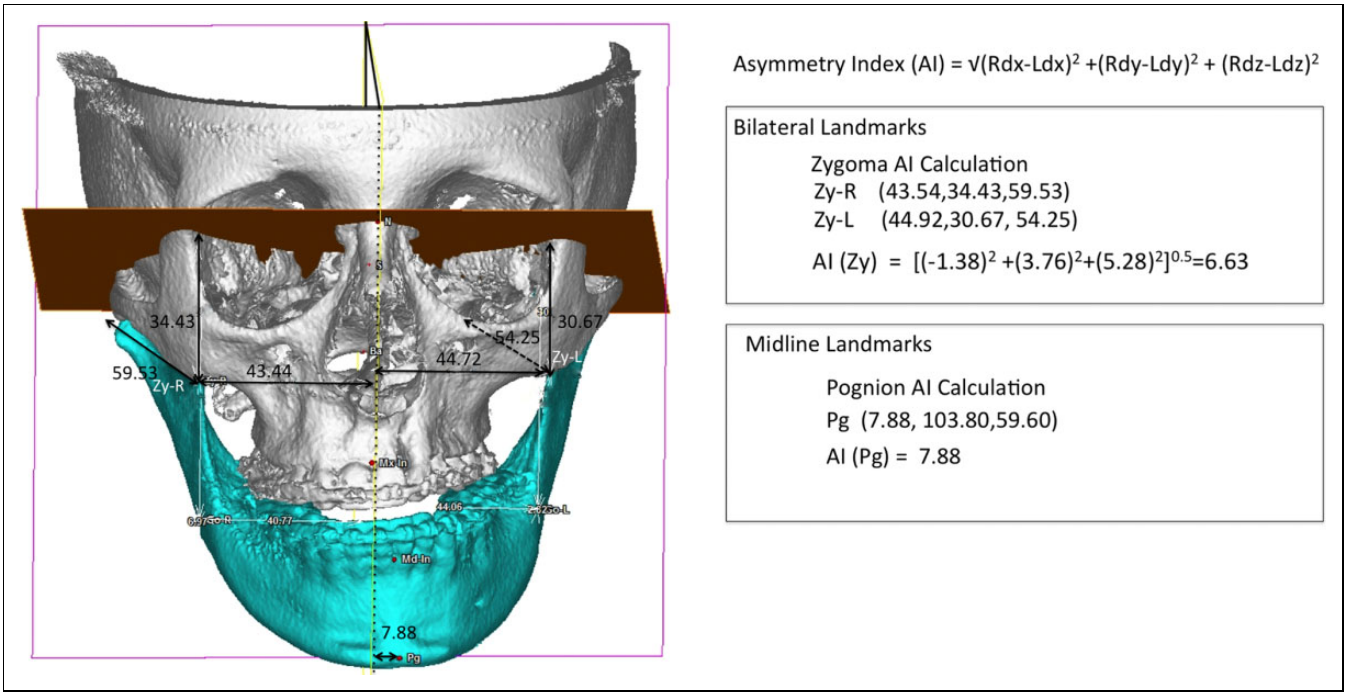

Figure 1. Orthogonal planes defined by cranial base landmarks: sella, nasion, and basion. Asymmetry Index (AI) calculation is shown for the bilateral and midline (single) landmarks (Katsumata et al., 2005).

Results

Control Group Asymmetry Index

The mean asymmetry index value with standard deviation of each of the anatomical landmarks in control subjects are shown in Table 1. The value of the index, as a reflection of the degree of asymmetry, increased with increasing laterality from the midsagittal plane (Figure 2). We did not find any significant difference in the asymmetry index for each of the landmarks based on gender. For the gender comparison, the *P* values of the AI at the landmarks ranged from 0.10 to 0.98.

Assessing UCLP Asymmetry Compared to the Control Population

We found that there was a significant difference between the extent of asymmetry in subjects with UCLP compared to the control population (Figure 2). This difference was statistically significant at each of the landmarks with the exception of FMN, FZ, Go, and Po. As with group 1 (control), we found no statistically significant gender bias with the UCLP group. For the gender comparison, the *P* values of the AI at the landmarks ranged from 0.31 to 0.88.

Asymmetry Classification

Using control group 1, we defined the symmetrical range, Grade 0, as the mean plus 1 standard deviation for each landmark. We defined grade 1 asymmetry as the region between mean plus one standard deviation and mean plus 2 standard deviations. Grade 2 asymmetry as marked asymmetry that exceeded mean plus 2 standard deviations. This is illustrated in Figure 3 as the background classification.

Regional Variation

In this sampling of patients with facial clefts, we found that the facial skeletal asymmetry in subjects with UCLP extended to involve the upper, middle, and lower facial skeleton as illustrated in case examples (Figure 3). In this limited sampling of 25 UCLP patients, we found 2 patients that were symmetrical based on the AI, 10 patients whose facial asymmetry was limited to the midface, 8 patients whose asymmetry extended beyond the midface to involve the mandible, 3 patients whose asymmetry involved the midface and upper face but not the mandible and 2 patients whose asymmetry involved all 3 regions. Thus, the index can regionally identify the asymmetry and quantifiably define the extent of asymmetry.

Discussion

Children who are born with facial clefts visually present with an obvious facial asymmetry as a result of their underlying congenital deformity. Such asymmetries have been difficult to assess quantitatively with 2-dimensional (2D) photography and 2-dimensional radiographic studies. However, increasing advances in 3-dimensional surface imaging (3D stereophotogrammetry) have allowed valid quantitative assessment of the regional variations in surface anatomy (Bell et al., 2014; Bugaighis et al., 2014; Duffy et al., 2000; Kuijpers et al., 2015; Plooij et al., 2009; Ras et al., 1994; Stauber et al.,

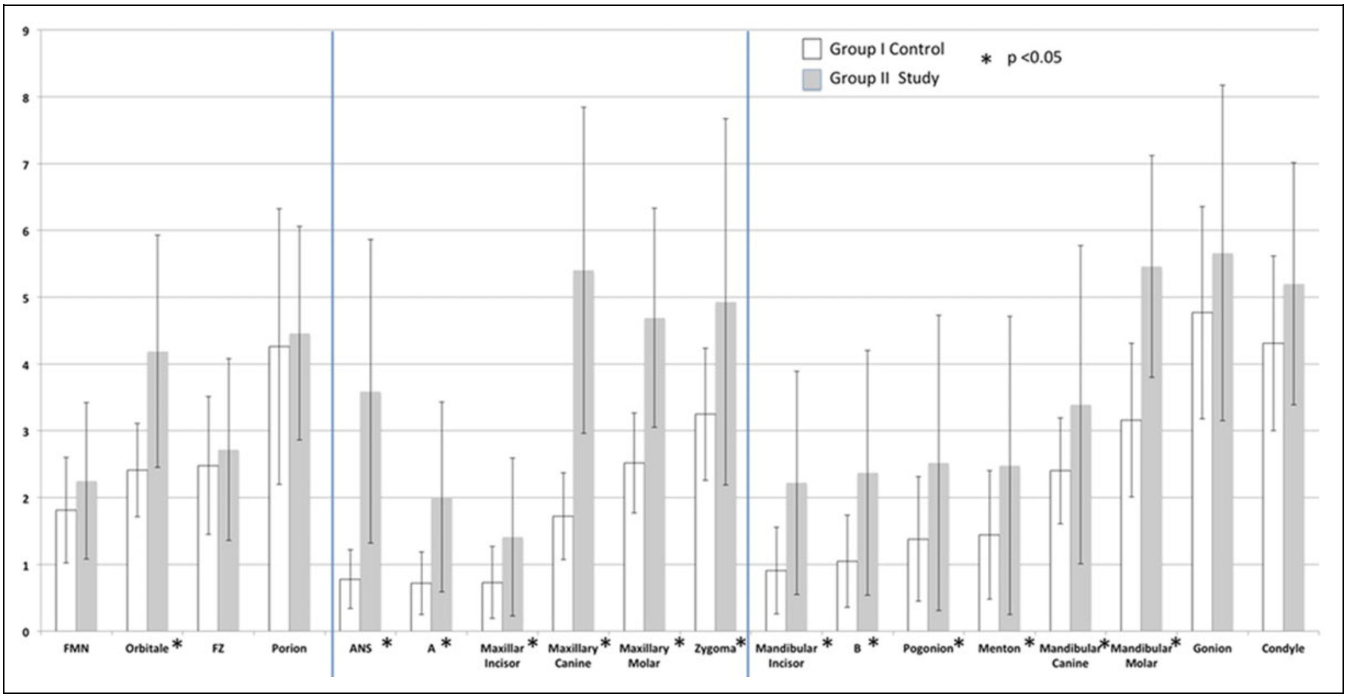

Figure 2. Asymmetry Index measurement at each landmark (mean plus 1 standard deviation) for group 1 noncleft patients (control) and for group 2 unilateral cleft patients. The landmarks that are statistically significant at *P* < .05 are indicated with an asterisk.

2008). Similarly, the advent of low-dose radiation CBCT has increasingly replaced the traditional 2D lateral and frontal cephalometric radiographs that define the underlying skeletal anatomy (Choi et al., 2013; Nur et al., 2016; Yang et al., 2016). Technological advances such as these have given clinicians and researchers the ability to quantitatively study patients with UCLP at a 3-dimensional form—at various anatomic levels—to provide quantitative longitudinal monitoring for growth and development and for quantitative measure of the outcome with surgical and/or orthodontic intervention (Bell et al., 2014; Suri et al., 2008).

Cleft orthognathic surgery allows the surgeon to reposition the maxilla and mandible in all 3 dimensions. The osteotomy patterns can be varied asymmetrically so that the final position not only achieves appropriate facial proportions in the sagittal plane but also improves the facial left-right symmetry. A valuable "tool" would be to develop a simple methodology for measuring the asymmetry before the surgical intervention to guide the surgeon. It is important to note that despite the surgical intervention, there is always a degree of residual asymmetry: The question is whether this residual is within the general population norm of acceptable asymmetry.

In comparison to 2D skeletal cephalometry, 3D anthropometry results in a myriad of linear and angular measurements. As the number of anatomic points increases, the analysis becomes bewildering and clinically impractical. The 3-dimensional asymmetry that can be visually grasped becomes an enigmatic series of values. Several approaches have been proposed. Historically, Habits et al. proposed a simple difference formula, $|[(R - L)/R + L]] \times 100\%|$, for 2-dimensional orthopanorex study of the ramal height symmetry (Habets et al., 1988). This difference formula was more recently extended to a 3-dimensional CBCT study by Yang et al. as a comparative study of patients with UCLP and a control group (Yang et al., 2016). Each landmark required 3 values with respect to the distance to each of the planes. Choi et al.'s (2013) approach was to set up a series of vertical and horizontal planes that would allow measurement comparison between the cleft and noncleft sides at the intersection points of the lattice. This provided an internal assessment of the difference between the 2 sides, but could not be practically utilized as a comparison to a noncleft population. In both studies, the significant differences were seen only in the region of the nasal piriform. In contrast, we found significant differences that extended beyond the nasal piriform region that included the zygoma and mandible in significant number of cleft patients. The studies by Yang, Choi, and others were averaged cross-sectional comparisons; thus, the individual patient asymmetry significance may have diminished as the distance from the cleft region increases. We, as well as others, have found that there is a wide variability that exists in patients with UCLP. Cross-sectional comparison with means becomes less clinically applicable to the individual patient seeking restoration of their facial proportions and symmetry and to the surgeon as well as orthodontist, who must develop a patient-specific treatment plan that optimizes the outcome.

For the questions we were interested in answering, the approach taken by Katsumata et al. and Maeda et al. proved to be the most useful (Katsumata et al., 2005; Maeda et al., 2006). The complexity of 3D anthropometric analysis was

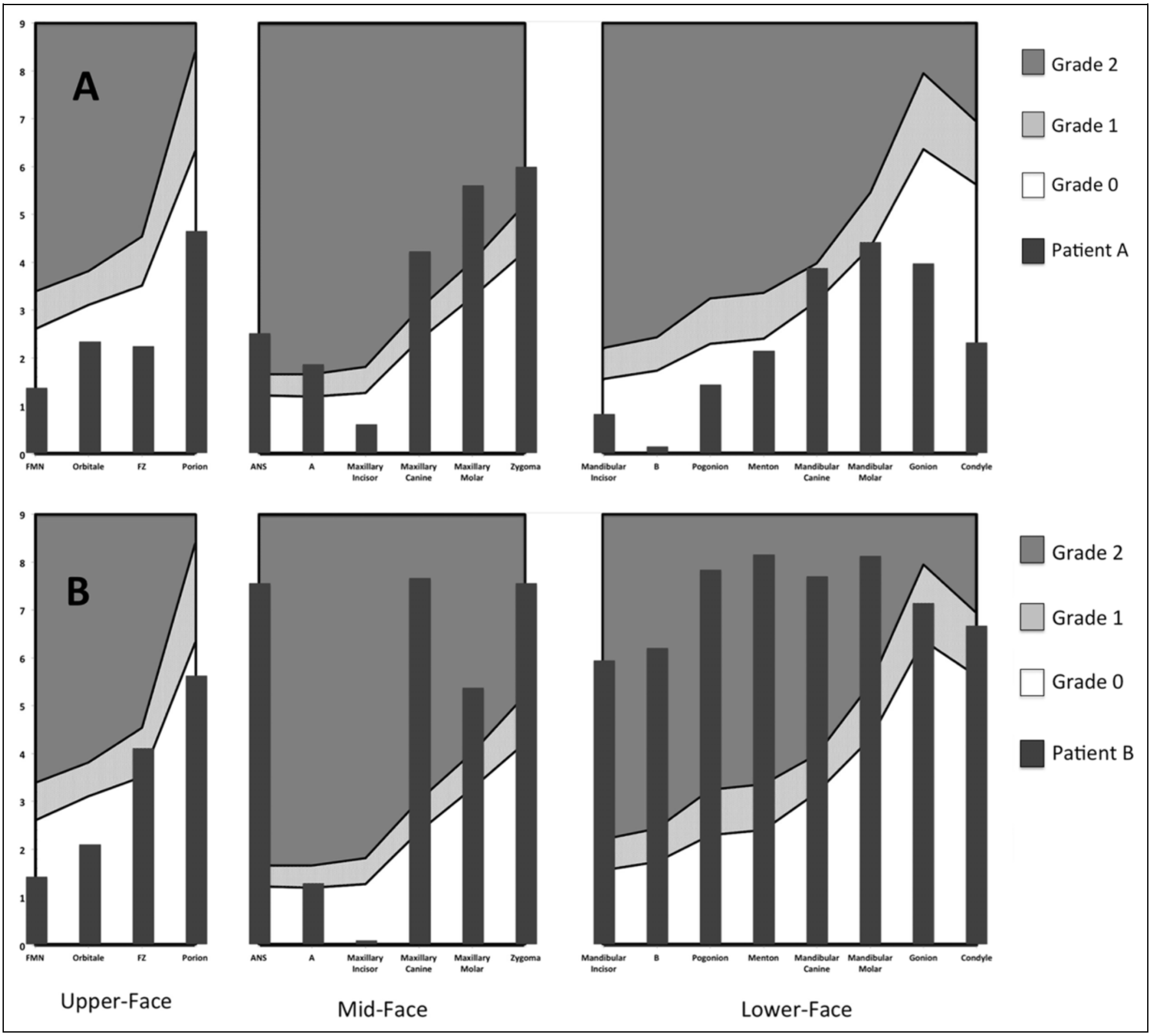

Figure 3. Proposed asymmetry classification grading system based on the mean value at each landmark and standard deviation. Illustrative cases of the range of Asymmetry Index of UCLP patients compared to the control (background population). In case A, the asymmetry is limited to the midface. In case B, the asymmetry involves the midface and extends to involve the mandible.

reduced to calculating an asymmetry index for each relevant anatomic paired landmark with a more intuitive interpretation. Each landmark was then assigned a single value based on the Euclidean distance formula utilizing the coordinate differences between the corresponding left and right landmarks.

The key to defining the left-right asymmetry is to establish a reliable coordinate system where each landmark has a unique position represented by a conventional (x, y, z) coordinate. Although no consensus exists on how to construct reference planes for 3D analysis, we relied on the cranial base landmarks with the assumption that these would be the least distorted. The study by Kyrkanides confirmed that cranial base asymmetry in patients with facial unilateral cleft lip and palate do not differ significantly from the unaffected population (Kyrkanides et al., 2000). Thus, we chose Basion (Ba)-Sella(S)-Nasion (N) to define the midsagittal plane. The transverse plane was then reliably constructed as the plane perpendicular to the midsagittal plane passing through S and N. The third frontal plane was then defined by the plane perpendicular to the midsagittal plane and the transverse plane. The intersection of the 3 planes set the origin of the internal reference coordinate system at the Basion landmark (0,0,0). The midsagittal anatomic landmarks were then measured as the absolute value of the distance from the midsagittal plane. This value is the asymmetry index. Thus, a value of zero for pognion would mean that the chin point was at the midline. With paired landmarks, the equation is the

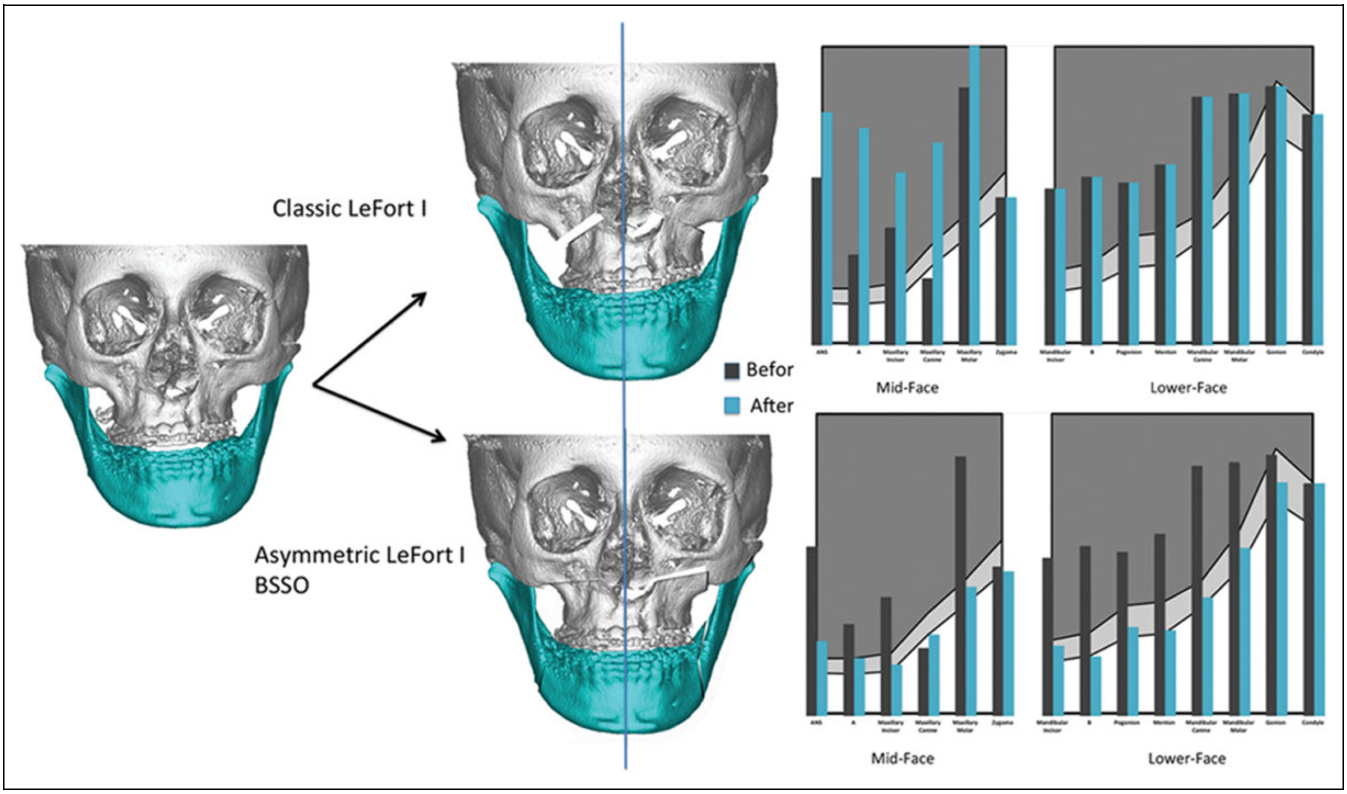

Figure 4. Asymmetry Index before and after virtual surgical simulation of either a single-jaw LeFort I procedure or a 2-jaw asymmetric LeFort I and BSSO procedure. Note that the asymmetry index worsens when the orthognathic procedure is limited to a "classic" LeFort osteotomy pattern. The asymmetry index can be utilized to quantitatively guide the surgical options using 3D digital simulation. BSSO, bilateral sagittal split osteotomy.

amplitude of the vector difference between the left and right landmarks. Therefore, a value of zero would imply that both landmarks were symmetrically positioned based on the amplitude of the vector. However, it should be noted that the angular difference is not accounted for in the index.

Katsumata et al. established a normal range asymmetry value in "symmetric" individuals; however, the control group in the Katsumata study consisted of a small sample size of 16 patients (12 males and 5 females) without specifying an age range. The study sample size was understandably limited as they had used available archived computed tomography and not CBCT. We chose to use CBCT because of its significantly lower radiation dose and broad availability in many orthodontic and surgical practices. This allowed us to increase the sample size and to focus the age range for clinical applicability. To establish the normative range of asymmetry, we chose 50 orthodontic patients between the ages of 15 and 20 who have been orthodontically treated to class 1 occlusion but without considerable alteration of maxillofacial skeletal components. Our findings agreed with Katsumata: (1) the midsagittal landmarks increasingly deviated from the midsagittal plane as the landmark distance from cranial base increased from superior to inferior and (2) the asymmetry index of bilateral landmarks increased as the distance of the landmark increased from the midsagittal plane.

These landmarks allowed us to establish a "background" range of skeletal asymmetry against which patients with congenital, developmental, and acquired deformities could be measured against and treated for, as these were post–orthodontic treated CBCTs. Our classification scheme by the severity of asymmetry differs from Katsumata as we use the standard deviation from the mean baseline to establish a simple grading system (Table 1, Figure 3). In contrast, Katsumata preferred classifying asymmetry when the value exceeded the baseline and marked asymmetry when it exceeded twice the baseline value.

In applying this approach, we found the asymmetry index to be an effective tool in quantitatively evaluating the skeletal deformity of patients with unilateral cleft lip and palate. There is a broad range of asymmetry with both regional variation and degree of severity that the index succinctly quantifies. This illustrates wide variation (Figure 4) in the extent of involvement and the need to consider beyond the classic LeFort I procedure to optimize outcome. Although the LeFort I will correct the sagittal discrepancy in occlusion, there is a significant number of patients who would benefit from tailored asymmetric LeFort I osteotomy combined with a mandibular bilateral sagittal split osteotomy (BSSO) to correct rotational asymmetry (Yaw and Roll).

The traditional 2-dimensional lateral cephalometry and analysis guided only the sagittal and vertical treatment objectives of patients needing cleft orthognathic surgery. It gave no

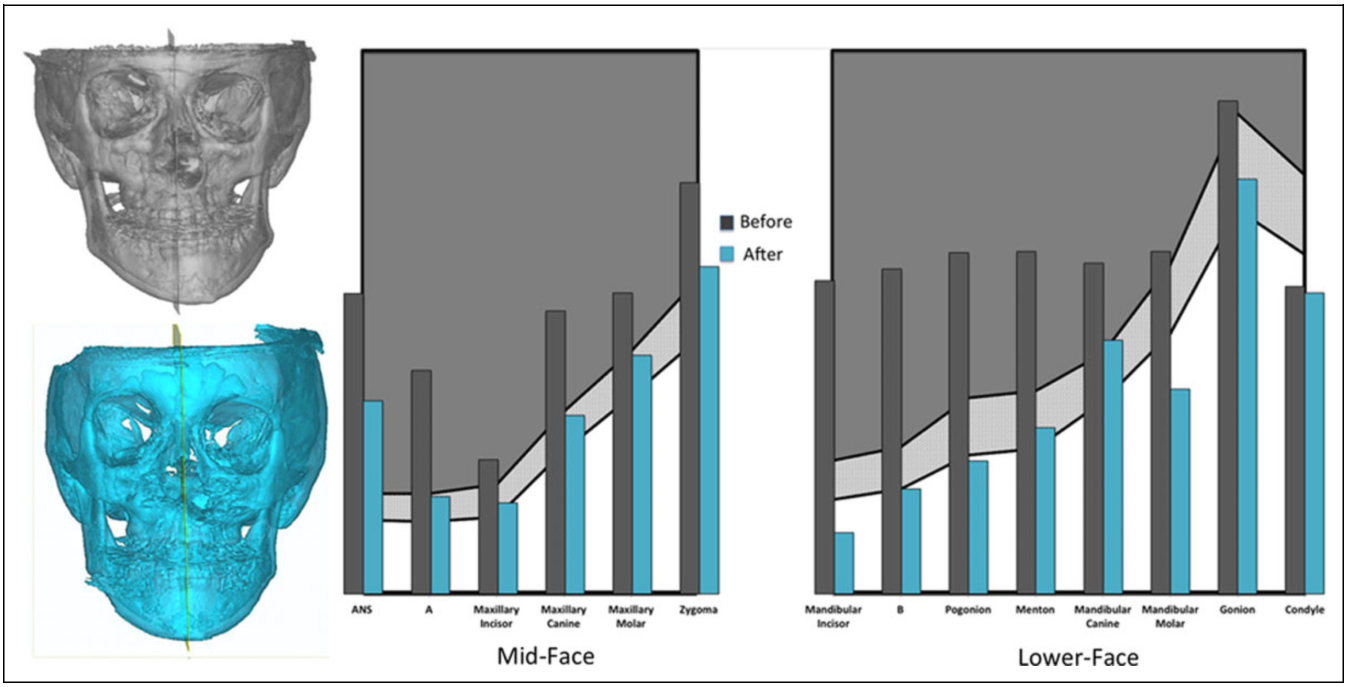

Figure 5. Two-year outcome of UCLP patients who underwent an asymmetric LeFort I and BSSO procedure. Note the quantifiable improvement in the Asymmetry Index Value at the various landmarks. BSSO, bilateral sagittal split osteotomy.

information to the surgeon to address any asymmetry that may have existed between the 2 halves of the face. The value of the asymmetry index approach is in its practical application to refine the surgical options and the specific osteotomy patterns to optimize the surgical reconstruction. This is best illustrated in Figure 4. Although a "classic"-pattern LeFort I osteotomy would allow the surgeon to control the sagittal and vertical position of the maxilla, the asymmetry of the midface worsens and does not address the mandibular asymmetry component that is frequently missed in cleft orthognathic surgery. However, with an asymmetric LeFort I osteotomy pattern and a mandibular BSSO rotation, the asymmetry is also addressed. Additionally, outcome of cleft orthognathic surgery can be quantitatively measured. Figure 5 illustrates the improvement in the Asymmetry Index outcome 2 years after an asymmetric LeFort I and a mandibular BSSO asymmetric rotation.

The impact of our study is that it establishes an acceptable range of asymmetry (Grade 0 region) based on our definition of group 1 noncleft control population. Asymmetric maxillary osteotomy and mandibular surgery, often overlooked, should be an important consideration in cleft orthognathic surgery to not only correct the primary sagittal discrepancy, but also the asymmetry that exists in all 3 planes in regions that extends well beyond the midface.

Utilizing the asymmetry grading system proposed in this study, the surgeon's goal would be to reposition the maxillary and mandibular elements to within Grade 1 level asymmetry. We used the standard deviation as a measure of the severity of the asymmetry. This may not correspond to clinically more relevant visual differences at a perceptual level. Thus, the question that remains to be answered in a future study would be at what level of asymmetry is it perceptually noticeable to the general and professional population. A clinical study correlated with the skeletal asymmetry index would refine the grading system proposed in this study based solely on skeletal assessment. Utilizing the asymmetry index offers the surgeon and the orthodontist a practical approach to guide treatment planning and measuring the outcome of intervention. However, the tradeoff with this approach is that it fails to take into account surface variability that exists between the landmarks such as the convexity and concavity of the noncleft and cleft side.

Conclusion

The Asymmetry Index (AI) is capable of capturing the 3D facial asymmetry of subjects with UCLP and as a basis for classification of the extent of the asymmetry. We found the index to be applicable in surgical planning and in measuring the outcome in improving the symmetry in patients who have undergone orthognathic surgery.

The vast majority of the cleft patients that we studied have a significant degree of midfacial asymmetry (grade 1 and grade 2). Moreover, the asymmetry extended to involve the mandible and upper midface (zygoma) in a percentage of patients. This has relevant implications in the type of orthognathic surgery and the osteotomy pattern. Many patients with UCLP would benefit from mandibular BSSO and modified high LeFort I that would include a component of the zygoma to improve facial asymmetry. While the typical focus is sagittal and vertical correction in cleft orthognathic surgery, the asymmetry index refines the surgical planning to the other planes. Additionally, the index can be utilized as a quantitative measure of the outcome of surgery.

This study defined the background level of skeletal asymmetry in a control group of 50 patients who underwent orthodontic treatment in the age range in which many cleft patients undergo orthognathic surgery. This control group provides a comparative group against which the outcome of surgical and orthodontic management of patients with UCLP can be compared against.

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Declaration of Conflicting Interests

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