The Americleft Study: An Inter-Center Study of Treatment Outcomes for Patients With Unilateral Cleft Lip and Palate
Part 3. Analysis of Craniofacial Form

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Objective: **To compare craniofacial morphology for individuals with non-syndromic complete unilateral cleft lip and palate between the ages of 6 and 12 years.**

Design: **Retrospective cohort study.**

Setting: **Four North American cleft palate centers.**

Subjects: **A total of 148 subjects with repaired complete unilateral cleft lip and palate who were consecutively treated at the four centers.**

Methods: **The 148 preorthodontic lateral cephalometric radiographs were scanned, scaled, digitized, and coded to blind the examiners to radiograph origin. On each radiograph, 18 (angular and ratio) cephalometric measurements were performed. Measurement means, by center, were compared using analysis of variance and Tukey-Kramer analysis.**

Results: **Significant differences were found for sagittal maxillary prominence among the four centers. The most significant difference was seen between Center B (lowest SNA) and Center C (highest SNA). Similar differences were seen at the soft tissue level, with Center C showing a significantly larger ANB angle compared with Centers B and D. Center C was also shown to have statistically greater mean soft tissue convexity than Centers B, D, and E. The mean nasolabial angle in Center B was significantly more acute than in Centers C, D, and E. No statistically significant differences were seen for mandibular prominence, vertical dimensions, or dental inclinations.**

Conclusion: **Significant differences were seen among the centers for hard and soft tissue maxillary prominence, but not for mandibular prominence, vertical dimensions, or dental inclinations. A modest but statistically significant ($p < .001$) negative correlation was found between Goslon scores and ANB angle ($r = -.607$).**

KEY WORDS: *Americleft, cephalometrics, craniofacial form, intercenter study, maxillary-mandibular relationships, skeletal relationship, treatment outcome measures*

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This part of the Americleft intercenter study focuses on skeletal and soft tissue craniofacial morphology. The purpose was to evaluate and compare the craniofacial morphology and soft tissue profiles of children with repaired complete unilateral cleft lip and palate (CUCLP) treated at four of the original five North American centers participating in the Americleft study (Center A was excluded due to insufficient sample size). Numerous studies in the past have attempted cephalometric comparisons of craniofacial morphology in patients from cleft/craniofacial centers with varied infant management protocols (e.g., Ross, 1987). In these studies, craniofacial morphological differences were found to be associated with different aspects of infant management protocols. However, few evaluations have been done in the context of simultaneously assessing other, equally important outcomes in addition to craniofacial morphology. The landmark Eurocleft study upon which this entire investigation was modeled was the first to attempt such an approach. In those studies as in this, craniofacial morphology was assessed along with dental arch relationships and nasolabial aesthetics in the same cohort of patients (Mølsted et al., 1992; Brattström et al., 2004). Furthermore, although both cephalometric craniofacial morphology data and Goslon Yardstick evaluations were collected in the original Eurocleft study, in that original series there was no attempt to correlate those findings. Therefore, we were interested in evaluating whether the differences in the Goslon scores among the centers would correlate to corresponding differences in craniofacial morphology, thus judging the validity of using the Goslon Yardstick as a means to assess sagittal maxillomandibular relationship.

Methods

Ethics approval was obtained separately from each center's ethics review board. Lateral cephalometric radiographs were largely from subjects whose study models were evaluated in part 2 of the Americleft study. Centers B, D, and E had one, one, and three patients, respectively, for whom usable radiographs were not available. Center C had two patients with no usable dental models for the dental arch relationship study (part 2) but for whom radiographs were available. Thus, the same inclusion and exclusion criteria and demographic characteristics as described in part 1 of the Americleft study apply to this craniofacial morphology study. Center A was excluded due to inability to provide a sufficient sample with the required records. The total resulting sample size was 148 (of the originally presenting 169) (Table 1).

For this study, the lateral cephalograms (digital or conventional films) had to be taken at the same time (corresponding age) as the models used in part 2—Dental Arch Relationships (average age of 8 years 8 months; range, 6 to 12 years). The cephalograms were obtained with the teeth in occlusion, using the cephalometric equipment available at the respective centers. Dentofacial Planner™ version 8.05 cephalometric software (http://www.dentofacial.com/) was used for all cephalometric analyses. Lateral cephalograms received in digital file format (JPEG or Digital Imaging and Communications in Medicine [DICOM]) were imported into the software. The resolution was adjusted to resize and calibrate the radiographs to a standardized dimension of 8.5 × 11.7 inches so that relative uniformity of the images was achieved. When the radiographs submitted were not in DICOM or JPEG format, a film scanner (Epson model 1680) was used to convert the films into JPEG format, at a resolution of 262 dots per inch, so they could be imported into the analysis software. The digital radiographs were subsequently coded, so that the digitizer and examiners were blinded to the origin of the radiographs. All radiographs were digitized on screen by a professional digitizer with 30 years of experience in the interpretation of radiographs of patients with cleft lip and palate.

Sixteen hard tissue and 12 soft tissue cephalometric landmarks were digitized per radiograph (Fig. 1 and

TABLE 1 Demographics of the Sample in the Craniofacial Morphology Study

Center Code	*N*	*Cleft L:R*	*M:F Ratio*	*Mean Age*
B	39	33:6	27:12	8 y 5 mo
C	40	24:16	24:16	8 y 8 mo
D	37	29:8	28:9	8 y 9 mo
E	32	20:12	20:12	9 y 1 mo
Total	148	106:42	99:49	8 y 9 mo

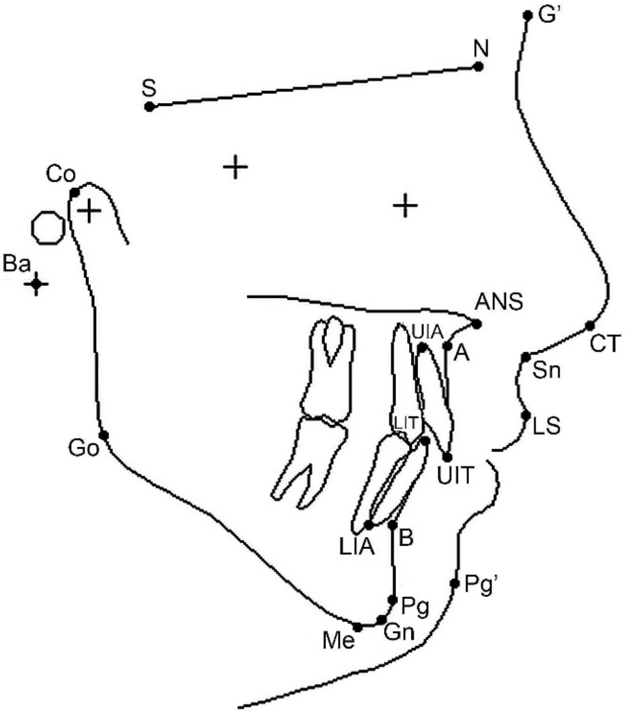

FIGURE 1 The reference landmarks are shown on a sample lateral cephalometric tracing.

TABLE 2 Cephalometric Landmark Definitions

Hard Tissue Landmarks	
A-point	The deepest point on the anterior contour of the maxillary alveolar process
ANS	Anterior nasal spine: the tip of the osseous anterior nasal spine
B-point	The deepest point on the anterior contour of the mandibular alveolar process
Ba	Basion: the most anteroinferior point on the margin of the foramen magnum
Co	Condylion: the most posterosuperior point on the head of the mandibular condyle
Gn	Gnathion: the most anteroinferior point on the outline of the chin
Go	Gonion: the most posteroinferior point on the angle of the mandible
LIA	Lower incisor apex: the apex of the most labially placed mandibular central incisor
LIT	Lower incisor tip: the incisal tip of the most labially placed mandibular central incisor
Me	Menton: the most inferior point on the outline of the chin
N	Nasion: the most anterior point of the fronto-nasal suture
Pg	Pogonion: the most anterior point on the outline of the chin
S	Sella: the geometric center of sella turcica
UIA	Upper incisor apex: the apex of the most labially placed maxillary central incisor
UIT	Upper incisor tip: the incisal tip of the most labially placed maxillary central incisor
PNS′	Point of intersection of the palatal plane and a line drawn downward from PTM* in a direction perpendicular to a plane constructed 7° up from SN
Soft Tissue Landmarks	
CT	Columella tangent: the point of intersection with the nasal outline of a tangent to the columella from Sn
G′	Soft tissue glabella: the most prominent point on the soft tissue drape of the forehead
LS	Labrale superius: the most prominent point on the vermilion border of the upper lip
Pg′	Soft tissue pogonion: the most anterior point on the soft tissue outline of the chin
Sn	Subnasale: the point where the base of the columella of the nose meets the upper lip
Me′	Soft tissue menton: the soft tissue point overlying menton
LI	Labrale inferius: the most prominent point on the vermilion border of the lower lip
N′	Soft tissue nasion: the deepest point of the frontonasal curvature
P	Pronasale: the most prominent point on the apex of the nose
B′	Soft tissue supramentale: the point of greatest concavity in the midline of the lower lip
A′	Soft tissue subspinale: the point of greatest concavity or convexity in the midline of the upper lip
UNT	Upper nasal tangent point: from N′

* PTM = The lowest point of the pterygomaxillary fissure.

Table 2). A total of 11 hard tissue and seven soft tissue cephalometric measurements were evaluated: 16 angular and two ratios (Tables 3 and 4). The measurements used were based on those used in the original Eurocleft study (Mølsted et al., 1992). Because the lateral cephalograms from each center were produced using various types of radiographic equipment incorporating different enlargement factors, no linear measurements were included. To avoid error from differential magnification of the films, only angular and ratio measurements were undertaken. The means of the numerical outcomes for each cephalometric measurement were calculated and then compared.

The use of a cohort of patients on whom dental arch relationships were compared using the Goslon Yardstick in part 2 of this study provided an opportunity to assess the degree to which assessment of dental arch relationships using dental models corresponded to the cephalometric measures presumed to measure apical base relationship. Therefore, as a final part to this investigation, the correlation coefficient between Goslon Yardstick scores on individual patients and their corresponding cephalometric measures of SNA, SNB, and ANB were determined. In addition, the average Goslon scores for each center were compared with the average of the cephalometric measure

TABLE 3 Mean Values for the Hard Tissue Measurements; Bold Numbers Are Statistically Significantly Different From One Another

Measurement	*Center B*	*SD*	*Center C*	*SD*	*Center D*	*SD*	*Center E*	*SD*
SNA (°)	**76.30*****^{C}	0.62	**79.80*****^{B}	0.62	77.82	0.64	77.70	0.69
SNB (°)	73.90	0.58	74.38	0.57	74.47	0.60	74.33	0.64
ANB (°)	**2.40*****^{C}	0.52	**5.42*****^{B}*^{D}*^{E}	0.52	**3.34***^{C}	0.54	**3.37***^{C}	0.58
Ba-N-ANS′ (°)	**59.93****^{C}	0.55	**62.77****^{B}*^{D}*^{E}	0.55	**60.68***^{C}	0.57	**60.57***^{C}	0.61
Ba-N-Pg (°)	56.53	0.51	56.70	0.51	56.99	0.53	56.48	0.57
ANS′-N-Pg (°)	**3.39***^{C}	0.60	**6.07***^{B}*^{D}	0.59	**3.69***^{C}	0.61	4.09	0.66
SN-MP (SN-GoGn) (°)	33.98	0.80	36.51	0.79	34.65	0.82	34.63	0.89
Lower face height ratio (ANS′-Me/N-Me) (%)	54.88	0.37	55.61	0.37	55.01	0.38	55.09	0.41
UI-PP (UI-ANSPNS′) (°)	95.19	1.57	98.06	1.55	93.73	1.61	95.49	1.74
LI-MP (LI-GoGn) (°)	89.67	0.94	87.68	0.92	89.34	0.96	89.14	1.03
Md axis angle (BaN-CoGn) (°)	75.76	0.65	76.40	0.65	75.89	0.67	76.59	0.72

* $p < .05$, ** $p < .01$, *** $p < .001$ denotes the level of significance in comparison with other centers specified.

TABLE 4 Mean Values for the Soft Tissue Measurements; Bold Numbers Are Statistically Significantly Different From One Another

Measurement	*Center B*	*SD*	*Center C*	*SD*	*Center D*	*SD*	*Center E*	*SD*
A′N′B′ (°)	**4.65**^{**C}	0.43	**6.95**^{**B*D}	0.42	**5.32**^{*C}	0.44	5.59	0.47
Nasolabial angle (CT-Sn-LS) (°)	**96.40**^{**C**D***E}	1.99	**107.10**^{**B}	1.96	**106.75**^{**B}	2.04	**107.87**^{***B}	2.20
Soft tissue convexity (G′-Sn-Pg′) (°)	**3.67**^{***C}	0.93	**9.47**^{***B***D**E}	0.92	**3.64**^{***C}	0.95	**4.33**^{**C}	1.03
Nasal projection angle (G′-P-Pg′) (°)	31.19	0.81	29.80	0.80	28.68	0.83	29.30	0.90
Nasal bridge angle (S-N′-UNT) (°)	111.08	1.05	110.19	1.03	111.00	1.07	108.91	1.15
Nasoform angle (N′-P-Sn) (°)	**79.01**^{***C*E}	0.95	**73.03**^{***B}	0.94	76.11	0.98	**74.60**^{*B}	1.05
Soft tissue face height ratio (N′-Sn/Sn-Me′) (%)	72.73	1.46	70.05	1.44	73.59	1.50	73.29	1.62

* $p < .05$, ** $p < .01$, *** $p < .001$ denotes the level of significance in comparison with other centers specified.

demonstrating the strongest correlation to the Goslon scores for each center to see whether the ranking of centers for sagittal jaw relationship, from best to worst, was similar for both methods of determination.

Statistical Analysis

The means of the cephalometric measurements for each center were compared using analysis of variance (ANOVA). Variance terms also were included in the model to account for between-subjects variation. Pairwise comparisons of means were performed using the Tukey-Kramer analysis to account for multiple comparisons (Kramer, 1956). Goslon Yardstick scores were compared with SNA, SNB, and ANB measurements for each patient included in both part 2 and part 3 of this series to determine the correlation coefficient (R and r^2) between the methods. The statistically significant level was set at $p < .05$.

Error of the Method

Of the cephalograms from each center, 20% were randomly selected and redigitized 12 months after the original digitization. An intraclass correlation coefficient (ICC) was calculated from the double determination of each cephalometric landmark to determine the landmark identification error using a one-way ANOVA for repeated measures.

Results

The error of the method analysis for the hard tissue measurements resulted in ICCs ranging from .899 to .990; whereas, for the soft tissue measurements, the ICCs ranged between .909 and .990. Both ranges indicate very good to excellent agreement.

The results of the cephalometric comparison of the four centers are shown in Tables 3 and 4. Significant differences were found for sagittal maxillary prominence among the four centers. The most significant difference was seen between Center B (smallest maxillary prominence) and Center C (highest maxillary prominence). The differences for the mean SNA and ANB angles between these two centers, as well as the differences between the mean Ba-N-ANS and ANS-N-Pg angles, were significantly different. Centers D and E also had significantly lower mean ANB and Ba-N-ANS angles than Center C had.

Similar differences were seen at the soft tissue level, with Center C showing a significantly larger ANB angle compared with Centers B and D. Center C also was shown to have statistically greater mean soft tissue convexity than Centers B, D, and E. The mean nasolabial angle for Center B was significantly more acute than that for Centers C, D, and E. No statistically significant differences were seen among the centers for mandibular prominence, vertical dimensions, or dental inclinations. A representative superimposition of the mean tracings of Centers B and C is shown in Figure 2.

The correlation statistics between parts 2 and 3 of the Americleft project showed weak but statistically significant correlation between Goslon score and each of the following: SNA ($r^2 = .081$) and SNB ($r^2 = .064$). A significant ($p < .001$) moderate negative correlation was found between Goslon rating and ANB angle ($r = -.607$, $r^2 = .369$) (Fig. 3).

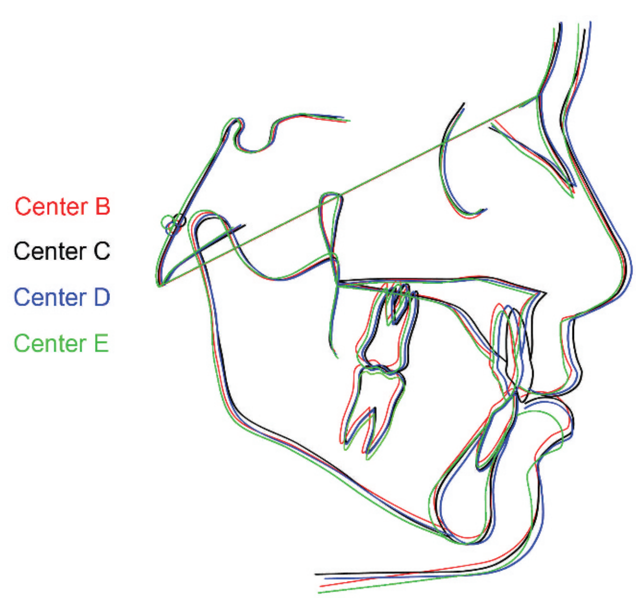

FIGURE 2 Representative superimpositions of the mean tracings of the four centers.

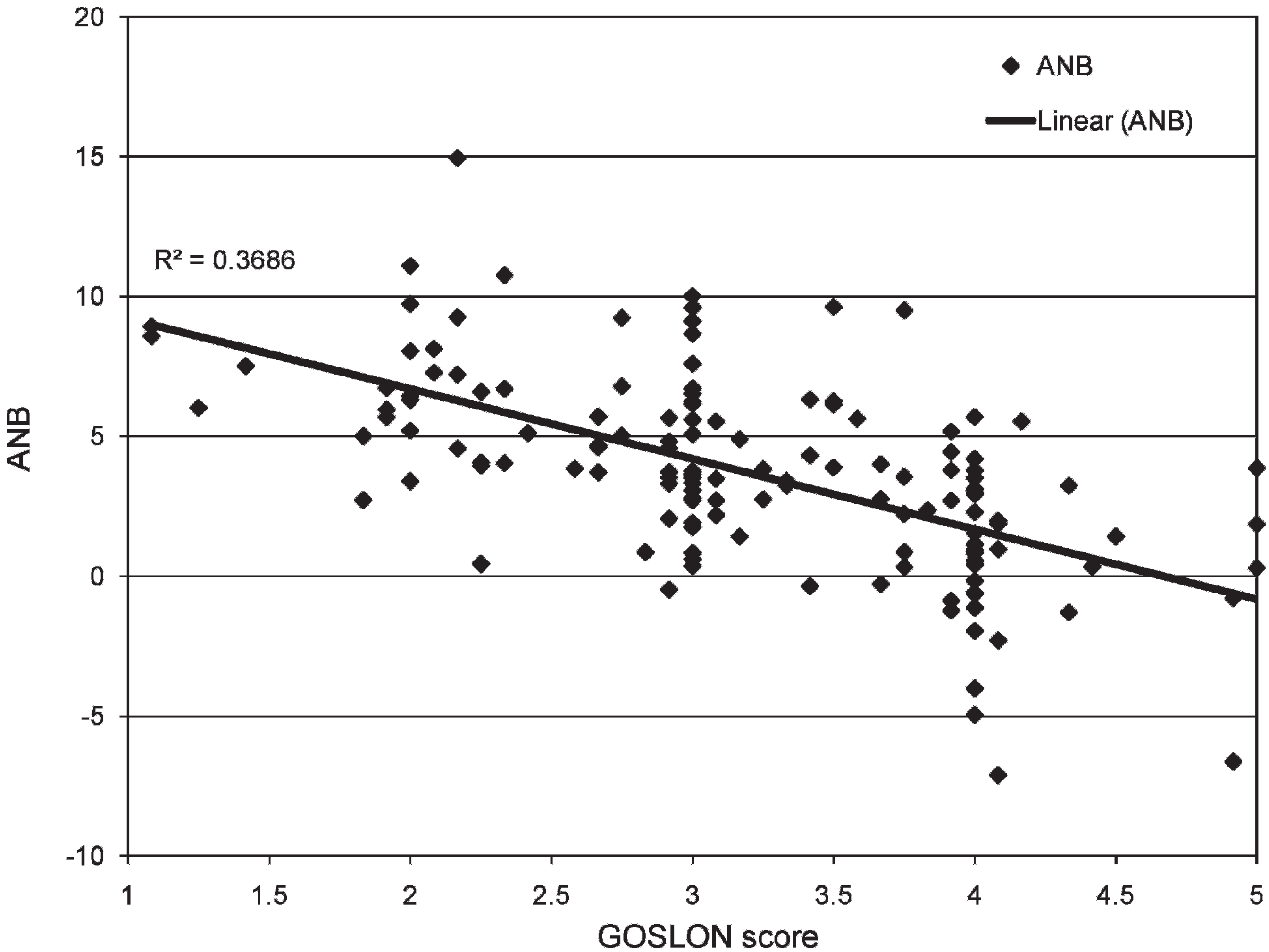

FIGURE 3 **Chart illustrating negative correlation between the Goslon score and ANB (data from the entire Americleft sample).**

Discussion

Significant morphologic differences could result not only from variations in treatment protocols but also from dissimilar populations having ethnic, genetic, and age differences (Ross, 1987; Trenouth et al., 1999; Daskalogiannakis et al., 2006). Despite the relative apparent homogeneity of nonsyndromic CUCLP, considerable between-patients variation may still exist within a population diagnosed with CUCLP, making reasonably large samples a requirement for statistical comparison (Shaw et al., 2005). This is especially true in centers where the population is extremely heterogeneous, as with many of the centers in the Americleft study. Thus, this study was restricted to only white patients with no exceptions to this inclusion criterion. However, given the cultural and ethnic melting pot of present-day North American cities, any white sample is likely to be more culturally or ethnically diverse (an additional source of genetic variability) as compared with the more segregated genetic makeup of smaller Northern European cities of the 1980s. Therefore, some of the differences seen in the cephalometric measurements may not be totally attributable to different surgical interventions, given there may have been significant differences in the genetic makeup of these samples from the outset. To address this possibility, a sample size of between 30 and 40 patients was deemed essential for this study to minimize susceptibility bias (case selection) and was met by four of the five centers.

Analysis bias from inherent errors and limitations of cephalometric radiography further cautions one from attributing differences to specific aspects of the treatment protocols. The issue of variable magnification in the radiographs obtained from the different centers is important to address in an intercenter cephalometric comparison study. In the original Eurocleft study, the need for international standardization of the specifications of radiographic cephalometric equipment was identified. In an attempt to reduce error from nonstandardized cephalometric radiographs, our analysis only included ratio and angular measurements. Distortion or disproportionate magnification in the peripheral areas of the radiographs is another inherent source of error that is much more difficult to control. Finally, the use of one expert digitizer allowed

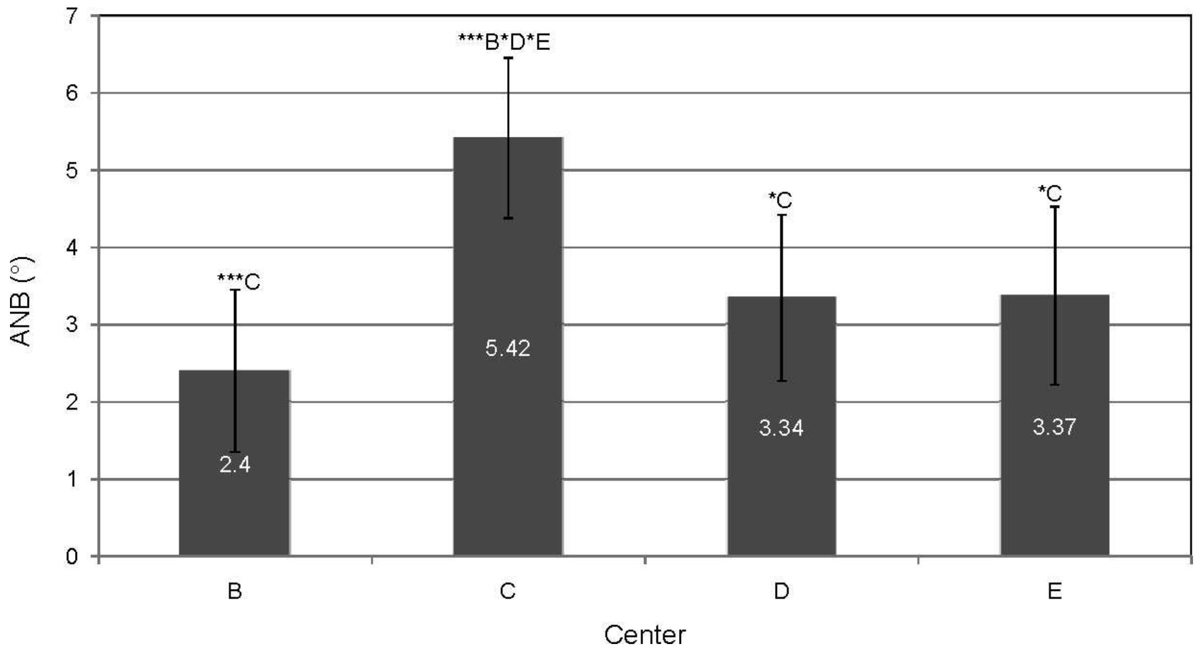

FIGURE 4 Mean ANB angles by center with error bars representing 95% confidence intervals. * $p < .05$, ** $p < .01$, and *** $p < .001$ denote the level of significance in comparison with the other centers specified.

confirmation of negligible random error of the method. It is understood that without a second digitizer for comparison, there is a possibility of systematic error. Given the extensive experience of the digitizer, this is unlikely but cannot be ruled out. Moreover, it was felt that because the intent of this investigation was to compare the relative favorability of outcomes among the various Americleft centers, in the unlikely event of the presence of significant systematic error from one digitizer, all centers' measures would have been affected equally and in the same direction. Although the resultant absolute values obtained may reduce the reliability of a comparison of these data to other stand-alone cephalometric investigations, our primary purpose of relative ranking of the centers in this investigation according to their cephalometric outcomes would not be affected.

Samples in this study also differed with regard to gender ratios. Indeed, the gender distributions varied among the centers because the emphasis during sample collection was placed on approaching consecutiveness rather than matching for gender. Given that the study looked at children in the ages of 7 to 11 years, it was considered appropriate to pool the data for boys and girls because most of the variables that we examined do not exhibit gender differences until adolescence. This was the approach taken in the Eurocleft study. This is also consistent with the findings of Krogman et al. (1982) and of Semb (1991), who were unable to establish a gender difference for angular and/or ratio measurements during longitudinal cephalometric evaluation of patients with unilateral cleft lip and palate in this age range.

The most interesting finding was the significantly larger mean maxillary prominence (SNA) and larger convexity showing a significantly more favorable maxillomandibular relationship (ANB) for Center C compared with the other centers (Fig. 4 and Table 3). In fact, the mean ANB angle of 5.4° for Center C even exceeds the age-matched, noncleft mean of 4° from the Burlington Growth Study (Ross, 1987). Center B, where infant bone grafting was performed, had the lowest mean maxillary prominence (SNA), and the least favorable maxillomandibular relationship (ANB), although no significant difference was found between Center B and the remaining two centers, D and E.

The Goslon scores from part 2 of this series of investigations were shown to correlate weakly with both maxillary (SNA) and mandibular (SNB) cephalometric variables when these were taken separately. However, when a cephalometric index of maxillomandibular sagittal discrepancy was considered (ANB), a stronger negative correlation ($R = -.607$; $r^2 = .369$) was found between it and the Goslon scores (Fig. 3). On a case-by-case basis, Goslon score and ANB angle obviously are not identical measures of dental arch relationship discrepancy. Nevertheless, the variability seems to be random rather than systematic. Thus, when evaluating groups of patients (e.g., the comparison of outcomes from various centers reported in this series), the conclusions and "ranking" of the centers is found to be similar with both methods. In this instance, the ranking of centers included in both part 2 and part 3 of this series and based on the Goslon Yardstick evaluation of dental arch relationship from most favorable to least favorable (see part 2) was C, E, D, and B, which is identical to the ranking found using the cephalometric measure with the strongest correlation to the Goslon Yardstick scores (ANB). As mentioned previously, a similar comparison was not carried out in the original Eurocleft study; although, the centers with the most favorable and least favorable Goslon Yardstick scores in that study were also the centers with the most favorable and least favorable measures of maxillary prominence as measured on lateral cephalometric radiographs.

Although not significantly greater, Center C also exhibited the steepest mean mandibular plane angle and the longest anterior face height. Even though there were no significant differences for any of the mandibular measurements, the combination of a steep mandibular plane angle and long anterior face height could possibly reflect a mandible that is rotated down and back, creating the appearance of a more prominent maxilla. This emphasizes the need to consider underlying skeletal patterns when comparisons are made between different centers in intercenter studies. Such populations may be from different ethnic backgrounds and thus also have intrinsically different and varied underlying skeletal patterns. Although the samples assessed in the Eurocleft study were of a relatively homogeneous origin and were more reflective of an underlying Class II skeletal relationship, the populations of the centers assessed in this Americleft study are more varied due to the multicultural cities involved.

In terms of soft tissue measurements, Center C also exhibited significantly higher mean soft tissue convexity (ANB of 6.9°; soft tissue convexity of 9.4°) than the other centers. Of note, Center B showed a significantly more acute mean nasolabial angle (96.4°) and a more obtuse mean nasoform angle (79.0).

Conclusions

There were significant differences for maxillary prominence among the centers, and these also corresponded to the differences in soft tissue morphology. No differences were found in the mandibular parameters, vertical dimension, or dental inclinations. Correlational statistics demonstrated a correspondence between the results of the Goslon ratings that were based on study models and the cephalometric analysis results, supporting the use of the Goslon Yardstick as a reliable indicator of sagittal maxillomandibular relationship.

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