Maxillary Development in Patients with Unilateral Cleft Lip and Palate Compared with Individuals Having Skeletal Class I and Class III Malocclusion

Ege Doğan* / Gülen Özses Ergican** / Servet Doğan***

Aim: *To compare maxillary development of individuals with unilateral cleft lip and palate (CLP) to individuals with skeletal Class I and Class III malocclusions.* ***Study design:*** *Cephalometric X-ray films from 90 patients (mean age: 13 ± 2.3 years) were used. The number of samples was determined by Power analysis and three groups consisting of 30 patients (Group 1: Skeletal Class I, Group 2: Skeletal Class III, Group 3: CLP) were formed. A total of 13 cephalometric measurements were performed using Dolphin imaging software 11.7. The Kruskal-Wallis and ANOVA tests were used to calculate the differences. The Dunn test and Bonferroni correction were used in paired group comparisons.* ***Results:*** *SNA, Co-A, A-PTV Horizontal, Na-APog, A-Na-Pog, FH-NA, Sn'-Mx1, MxOP-TVL ($p<0.001$***), U6-PTV Vertical ($p<0.01$**), and NaBa PTV-Gn ($p<0.05$*) values were significantly different between the three groups. There was no significant difference in Na-ANS, FH-NPog, or Mx1 labial-ULA. SNA, Co-A, A-PTV Horizontal, Na-APog, and A-Na-Pog values between the 1st and 2nd groups and between the 1st and 3rd groups ($p<0.001$***) were significantly different. FH-Na-A, Sn'-Mx1, MxOP-TVL ($p<0.001$***), and U6-PTV vertical were different between groups 1 and 3 ($p<0.01$**), while FH-Na-A ($p<0.001$***), Sn'-Mx1, MxOP-TVL ($p<0.01$**), A-PTV Horizontal, and A-Na-Pog ($p<0.05$*) were significantly different between groups 2 and 3.* ***Conclusion:*** *Maxillary development in CLP differs from skeletal Class I but is similar to skeletal Class III. Considering the delay in maxillary development in the CLP patient, maxillary protraction and maxillary expansion are important treatment protocols in the early period.*

Keywords: *Unilateral cleft lip and palate, maxillary development, skeletal class I, skeletal class III*

INTRODUCTION

Cleft lip and palate (CLP) is the most common congenital anomaly in the craniofacial region. CLP is formed as a result of the facial processes not fusing at the right time and it is typically caused by a combination of genetic and environmental factors. CLP occurs in approximately 1 in 700 live births, with wide variability across geographic origin as well as racial and ethnic groups. It affects craniofacial growth, especially in the mid-face area, resulting in functional, aesthetic, and psychosocial disturbances. The high incidence of CLP creates a need to investigate the anomaly's features and treatments[1-7].

The structure, relative positions, and effect of growth on the maxilla in individuals with CLP is an important issue. During craniofacial growth of the patients with CLP, generally there is growth inhibition of the maxilla, which restricts transverse and sagittal maxillary growth. In studies of the facial growth in patients with CLP, natural variations in craniofacial form are also evident. Each patient with CLP shows an individual hereditary growth pattern that can cause different treatment needs. CLP affects craniofacial growth through many factors, including intrinsic developmental deficiencies, functional distortions, and iatrogenic consequences[7-12].

* Ege Doğan, Private practice, Orthodontics.
** Gülen Özses Ergican PhD student, Ege University Faculty of Dentistry Department of Orthodontics .
*** Servet Doğan Professor, Ege University Faculty of Dentistry Department of Orthodontics.

Send all correspondence to:
Ege Dogan
Ali Cetinkaya Bul. Servet Apt. k:1 d:1 Alsancak / Izmir/ Turkey.
E-mail: dtegedogan@hotmail.com

Although primary surgery is the most important iatrogenic effect, there are clinical differences in technique and timing. One of the biggest challenges of researching this issue is the wide variety of clinical protocols in current use. Unfortunately, systematic attempts to compare the dentofacial results reported in the literature are unlikely to be reliable because of methodological biases. As a result of comparative studies conducted between centers, the reliability of the data has increased, which shows us the importance of the multidisciplinary approach. However, differences in both surgical skills and the underlying craniofacial form are important considerations.

It is obvious that patients with a significant deficiency of maxillary tissue are most at risk for post-operative maxillary distortion and restraint. Although the specific cause of growth disturbance is unclear, lip and palate closure has been explained. Experimental animal studies report that increased pressure from the repaired cleft lip is the primary cause of maxillary growth restraint. Lip pressure in children with CLP has been measured after lip repair and is significantly higher than in a non-cleft control group[14].

Cephalometric studies have shown differences in maxillomandibular spatial relationships in children with and without CLP. There is a tendency for relative retrusion of the anterior portion of the maxilla, a steeper mandibular plane, larger mandibular length, and increased facial height in CLP. These differences in facial morphology may be attributed to the surgical repair of the lip and palate, functional changes resulting from the mechanical presence of the cleft, inherited traits such as genetic influences on size and form, or a combination of these factors[6,8,10].

In the literature, some studies aimed to eliminate changes in growth and development by comparing skeletal Class III malocclusion treatment with untreated Class I or Class III malocclusion controls. It is unethical that individuals with skeletal anomalies such as Class III malocclusion should remain untreated in order to form a control group[15-19].

Few studies assess the skeletal development pattern of CLP patients. In randomized controlled studies, the necessity to use a Class I or Class III group as a control group for better assessment of the condition of the CLP patients has not been specified. The null hypothesis of this study was established in comparative studies related to CLP patients as there is no difference in using Class I or Class III patients as the control group. The purpose of the study is to evaluate the maxillary development of individuals with CLP and to compare it with individuals with skeletal Class I and Class III disorders.

MATERIALS AND METHODS

The study was approved by the Ege University Faculty of Medicine Clinical Research Ethics Committee dated 20.02.2019; 99166796-050.06.04.

In this study, cephalometric X-ray films routinely taken from 90 patients who were referred to the Ege University Faculty of Dentistry, Department of Orthodontics were used. Patients were separated into three groups of 30 each. Group 1 consisted of 30 individuals with skeletal Class I malocclusion (mean age 13 ± 2.3), Group 2 consisted of 30 individuals with skeletal Class III malocclusion (mean age 13 ± 2.3), and Group 3 consisted of 30 individuals with CLP with skeletal Class III malocclusion (mean age 13 ± 2.3). Lateral cephalometric films taken from the individuals between 13 and 15 years of age were evaluated. A total of 13 cephalometric measurements were performed using Dolphin imaging software 11.7 in 6 dimensions and 7 angles (Figure 1, Figure 2).

The inclusion criteria of the study are as follows:

- Lateral cephalometric films taken from patients with CLP between 13 and 15 years of age
- Lateral cephalometric films taken from patients with Class I closure between 13 and 15 years of age
- Lateral cephalometric films from patients with Class III closure between 13 and 15 years of age

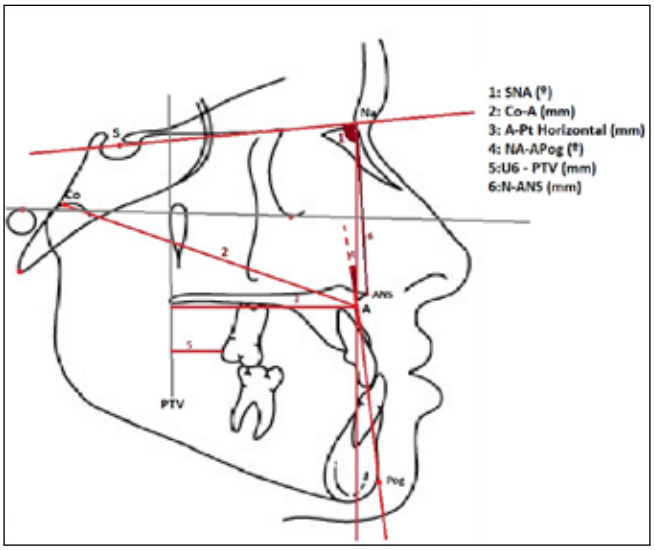
Exclusion criteria of the individuals for the study are as follows:

- Lateral cephalometric films taken from patients with syndrome

Cephalometric measurements:

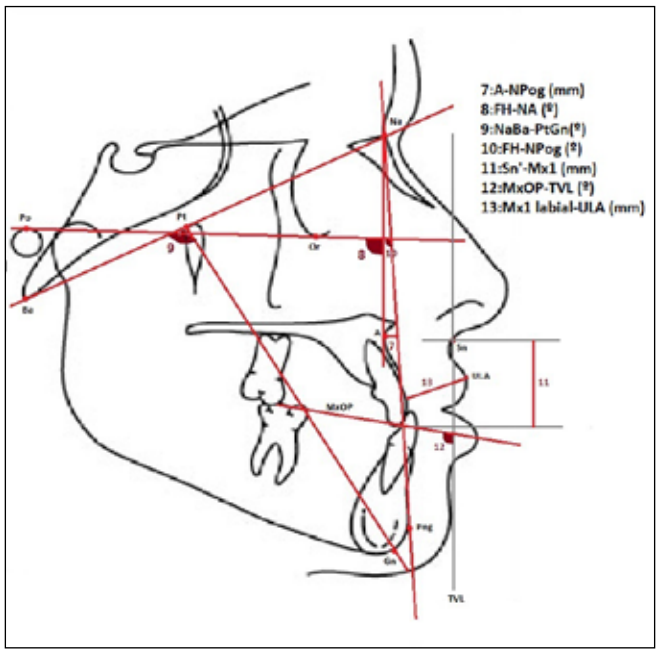
Figure 1- Cephalometric measurements: SNA (º), Co-A (Medium face length) (mm), A-PTV Horizontal (mm), Na-APog (Convexity) (º), U6-PTV Vertical (mm), Na-ANS (Upper face height) (mm)

SNA (º): the angle indicating the position of the maxilla in the sagittal direction relative to the anterior cranial base. Co-A (Medium face length) (mm): the distance between the condyle and point A that specifies the middle face length. A-PTV Horizontal (mm): the distance from point A to PTV. Na-APog (Convexity) (º): the angular value of skeletal convexity. U6-PTV Vertical (mm): the distance from the upper 1st molar to the PTV. Na-ANS (Upper face height) (mm): the distance between the Anterior Nasal Spina that specifies the upper face height.



A-Na-Pog (Convexity) (mm): skeletal convexity in millimeters. FH-Na-A (Maxillary depth) (º): the angle between the Frankfurt Horizontal plane and the Nasion-A plane that specifies the maxillary depth. NaBa-PTV-Gn (Facial Axis-Ricketts) (º): the angle between the Nasion-Basion plane and the Pterigoid-Gnathion plane. FH-NPog (Facial angle) (º): the angle between the Frankfurt Horizontal plane and Nasion-Pogonion plane. Sn'-Mx1 (Front maxillary height) (mm): the vertical distance between the subnasal and the incisal of the maxillary incisor that specifies anterior maxillary height. MxOP-TVL (Maxillary occlusal plane) (º): the angle with TVL that specifies the direction of rotation of the maxillary occlusal

Figure 2- Cephalometric measurements: A-Na-Pog (Convexity) (mm), FH-Na-A (Maxillary depth) (º), NaBa-PTV-Gn (Facial Axis-Ricketts) (º), FH-NPog (Facial angle) (º), Sn'-Mx1 (Front maxillary height) (mm), MxOP-TVL (Maxillary occlusal plane) (º), Mx1 labial-ULA (Upper lip thickness) (mm).



plane. Mx1 labial-ULA (upper lip thickness) (mm): the distance between the anterior of the upper lip and the labial of the maxillary 1st incisor that specifies the thickness of the upper lip.

Statistical Analysis

Statistical analyzes were performed using STATA 11 and MEDCALC software. The number of patients needed for the study was determined by Power analysis carried out using the G Power analysis software. A level of 0.05 was accepted as statistically significant.

For comparison of three groups, Kruskal-Wallis analysis was used to compare the non-normally distributed data, while the ANOVA test was used when the data was normally distributed. The paired group comparisons were made with the Dunn test (Bonferroni correction).

In addition, cephalometric analyses were reconducted on randomly selected radiographs of 15 patients after an interval of 1 month, and intra-observer reliability was evaluated using intraclass correlation coefficients (ICC). Also, another examiner measured all the parameters, and the inter-examiner error was determined. A level of 0.05 was accepted as statistically significant.

RESULTS

The method errors ranged from 1.4° to 3.2°, intra-examiner agreement was excellent (ICC range: 0.956-0.995), and inter-examiner agreement represented high reproducibility (ICC range: 0.872-0.923). Means, standard deviations, and statistical results of tests comparing the measurements of three groups are given in Tables 1-4. The power analysis showed that 18 patients were required. To increase the power of the study, it was decided to include 30 patients to achieve a representation rate of over 90%.

SNA (º), Co-A (Mid-face length) (mm), A-PTV Horizontal (mm), Na-A-Pog (Convexity) (º), U6-PTV Vertical (mm), Na-ANS' (Upper face height) (mm), A-Na-Pog (Convexity) (mm), FH-Na-A (Maxillary depth) (º), NaBa-PTV-Gn (Facial Axis-Ricketts) (º), Sn'-Mx1 (Anterior maxillary height) (mm), and MxOP-TVL (Maxillary occlusal plane-True vertical line) (º) values were evaluated using the Kruskal-Wallis Test. FH-Na-Pog (Facial angle) (º) and Mx1 labial-ULA (Upper lip thickness) (mm) values were evaluated with the ANOVA Test.

In the present study a significant difference was found in SNA between the three groups, between groups 1 and 2, and between groups 1 and 3 ($p<0.001$***). When we evaluated the Co-A (Mid-face length) value between the three groups, a significant difference was found ($p<0.001$***). A significant difference was also found between groups 1 and 2 ($p=0.001$***) and between groups 1 and 3 ($p<0.001$***). A significant difference was found when we evaluated the A-PTV Horizontal value between the three groups, group 1 and group 2, group 1 and group 3 ($p<0.001$***), and group 2 and group 3 ($p<0.05$*). A significant difference was found in the Na-A-Pog (Convexity) value between the three groups, group 1 and group 2, and group 1 and group 3 ($p<0.001$***). When we evaluated the U6-PTV Vertical value between the three groups, a significant difference was found ($p<0.01$**) and there was a significant difference between group 1 and group 3 ($p<0.01$**). A significant difference was found in the A-Na-Pog (Convexity) values between the three groups, between group 1 and group 2, group 1 and group 3 ($p<0.001$***), and group 2 and group 3 ($p<0.05$*). When we evaluated the FH-Na-A (Maxillary depth) value between the three groups with the Kruskal-Wallis Test, a significant difference was found between the groups ($p<0.001$***). A significant difference was found between group 1 and group 3 and between group 2 and group 3 ($p<0.001$***). A significant difference was found between the three groups in the NaBa-PTV-Gn (Facial Axis-Ricketts) value ($p<0.05$*). No significant difference was found between any two groups. When we evaluated the Sn'-Mx1 (Anterior maxillary height) value, a significant difference was found between the three groups, group 1 and group 3 ($p<0.001$***), and group 2 and group 3 ($p<0.01$**). When we evaluated the MxOP-TVL (Maxillary occlusal plane) value between the three groups, a significant difference was found ($p<0.001$***). A significant difference was found between group 1 and group 3 ($p<0.001$***) and between group 2 and group 3 ($p<0.01$**). No significant difference was found when we evaluated the Na-ANS' (Upper face height) ($p=0.926$), FH-Na-Pog (facial angle) ($p=0.068$), and Mx1 labial-ULA (Upper lip thickness) ($p=0.338$) values between the three groups.

Table 1-Mean, standard deviation, median, minimum and maximum statistical results of the measurements in Class III, UCLP and Class I groups

		SNA	Co-A	Apt-horizontal	NA-APo	U6-Pt	N-ANS	A-NPo	FH-NA	NaBa-PtGn	FH-NPo	Sn'-Mx1	MxOP-TVL	Mx1labial-ULA
Class III N:30	**Mean**	76,02	74,38	56,57	-7,55	14,22	48,09	-3,38	87,57	89,70	90,57	20,83	96,19	9,80
	SD	2,26	9,15	7,45	3,66	6,20	6,99	1,81	5,16	4,25	4,74	3,82	4,46	3,25
	Median	76,25	76,90	57,85	-6,90	14,80	49,25	-2,75	88,00	89,80	90,80	21,55	96,00	9,45
	Minimum	71,00	45,70	33,30	-16,20	-1,20	27,40	-7,70	76,30	81,40	81,60	10,60	87,30	4,50
	Maximum	78,50	86,90	68,10	-1,00	27,80	61,80	-0,40	96,10	98,80	99,40	28,90	104,90	15,90
UCLP N:30	**Mean**	73,13	74,38	51,14	-11,08	13,52	49,07	-6,93	81,44	87,65	87,96	17,97	89,46	9,33
	SD	3,94	5,21	5,81	3,88	3,31	4,41	3,34	5,10	3,21	4,17	2,47	7,34	2,32
	Median	71,75	75,10	50,15	-12,50	12,85	47,90	-5,75	82,90	87,30	89,10	17,60	91,05	9,70
	Minimum	68,20	62,80	42,80	-16,30	8,50	42,70	12,60	71,80	80,80	76,80	13,40	74,70	4,10
	Maximum	80,50	85,00	62,70	-2,40	22,60	57,20	-1,60	95,70	94,50	96,40	22,60	102,10	15,70
Class I N:30	**Mean**	81,58	80,60	64,08	2,42	17,27	49,12	1,15	90,67	90,17	89,40	22,04	99,21	10,34
	SD	2,40	8,30	4,97	3,15	4,16	4,39	1,46	3,96	5,07	3,91	3,34	4,45	2,23
	Median	81,15	82,15	63,80	2,65	16,45	49,45	1,15	91,30	90,00	89,10	22,25	99,55	11,00
	Minimum	77,80	48,00	50,30	-3,10	11,00	39,00	-1,40	83,10	80,80	81,60	10,30	89,60	5,30
	Maximum	89,40	93,10	73,10	8,50	31,50	55,90	3,80	99,10	105,90	98,30	28,90	105,90	14,00

Table 2- The comparision of Class I and Class III groups

MEASUREMENTS	Class I N=30	Class III N=30	P value
SNA (º)	81,58±2,40	76,02±2,26	<0,001 ***
Co-A (mm)	80,6±8,30	74,38±9,15	0,001 ***
A- Pt Horizontal (mm)	64,08±4,97	56,57±7,45	<0,001 ***
NA-APo (º)	2,42±3,15	-7,55±3,66	<0,001 ***
U6-Pt Vertical (mm)	17,27±4,16	14,22±6,20	0.072
N-ANS' (mm)	49,12±4,39	48,09±6,99	0,926
A-NPo (mm)	1,15±1,46	-3,38±1,81	<0,001 ***
FH-NA (º)	90,67±3,96	87,57±5,16	0,111
NaBa-PtGn (º)	90,17±5,07	89,70±4,25	1
FH-Npo (º)	89,4±3,91	90,57±4,74	0,068
Sn'-Mx1 (mm)	22,04±3,34	20,83±3,82	0,441
MxOP-TVL (º)	99,21±4,45	96,19±4,46	0,091
Mx1 labial-ULA (mm)	10,34±2,23	9,80±3,25	0,338

p<0,001 *** p<0,01 ** p<0,05 *

Table 3- The comparision of Class I and UCLP groups

MEASUREMENTS	Class I N=30	UCLP N=30	P value
SNA (º)	81,58±2,40	73,13±3,94	<0,001 ***
Co-A (mm)	80,6±8,30	74,38±5,21	<0,001 ***
A-Pt Horizontal (mm)	64,08±4,97	51,14±5,81	<0,001 ***
NA-APo (º)	2,42±3,15	-11,08±3,88	<0,001 ***
U6 - Pt Vertical (mm)	17,27±4,16	13,52±3,31	0,002 **
N-ANS' (mm)	49,12±4,39	49,07±4,41	0,926
A-NPo (mm)	1,15±1,46	-6,93±3,34	<0,001 ***
FH-NA (º)	90,67±3,96	81,44±5,10	<0,001 ***
NaBa-PtGn (º)	90,17±5,07	87,65±3,21	0,06
FH-NPo (º)	89,4±3,91	87,96±4,17	0,068
Sn'-Mx1 (mm)	22,04±3,34	17,97±2,47	<0,001 ***
MxOP-TVL (º)	99,21±4,45	89,46±7,34	<0,001 ***
Mx1 labial-ULA (mm)	10,34±2,23	9,33±2,32	0,338

p<0,001 *** p<0,01 ** p<0,05 *

Table 4- The comparision of Class III and UCLP groups

MEASUREMENTS	Class III N=30	UCLP N=30	P value
SNA (º)	76,02±2,26	73,13±3,94	0,211
Co-A (mm)	74,38±9,15	74,38±5,21	0,811
A-Pt Horizontal (mm)	56,57±7,45	51,14±5,81	0,013 *
NA-Apo (º)	-7,55±3,66	-11,08±3,88	0,076
U6 - Pt Vertical (mm)	14,22±6,20	13,52±3,31	0,749
N-ANS' (mm)	48,09±6,99	49,07±4,41	0,926
A-Npo (mm)	-3,38±1,81	-6,93±3,34	0,015 *
FH-NA (º)	87,57±5,16	81,44±5,10	<0,001 ***
NaBa-PtGn (º)	89,70±4,25	87,65±3,21	0,095
FH-Npo (º)	90,57±4,74	87,96±4,17	0,068
Sn'-Mx1 (mm)	20,83±3,82	17,97±2,47	0,002 **
MxOP-TVL (º)	96,19±4,46	89,46±7,34	0,002 **
Mx1 labial-ULA (mm)	9,80±3,25	9,33±2,32	0,338

p<0,001 *** p<0,01 ** p<0,05 *

DISCUSSION

Facial form in individuals with CLP is characterized by a progressive retrusion of the profile relative to the cranial base involving the nasal bone, the mandible, and especially the maxilla when compared with the facial form of non-cleft subjects. Both the maxilla and mandible are shorter and retrusive with a severe reduction in the posterior, but only a slight reduction in the anterior, maxillary height and the incisors are retroclined in each jaw. The mandible has an increased gonial angle and a steeper mandibular plane, and there is an increase in lower facial height[6,8-11,16-19].

In the present study, a significant difference was found in Co-A between the control (Class I) and the CLP group and the Class III and the CLP group (p<0.001). This result is in agreement with Tinano et al.[15], which found a significant difference between the control (Class I) and CLP groups (p<0.001). Their aim was to determine the morphological differences in the base of the skull of individuals with CLP and Class III malocclusion in comparison to control groups with Class I malocclusion.

Khanna et al.[17] evaluated the developmental relationship of cervical vertebrae and maxillofacial morphology in complete CLP patients (untreated and surgically treated) and non-cleft patients based on the parameters of lateral cephalograms. They found a significant difference in Co-A between the non-cleft group and the surgically treated CLP group (p<0.001).

In the present study, a significant difference was found in FH-Na-A (Maxillary depth) values between the control (Class I) and CLP groups and the Class lll and CLP groups (p<0.001). Similar to our result, Khanna et al. (41) found a significant difference in FH-Na-A between the non-cleft group and surgically treated CLP group (p<0.001). When we evaluated the FH-Na-Pog (facial angle) values between the three groups, similar to Khanna et al.[17], no significant difference was found.

Semb (6) showed a small increase between 5 and 18 years of age in the length of the maxilla of 257 subjects with complete CLP. In addition, there was a concomitant reduction in maxillary prominence at the dentoalveolar level. The gradual reduction of maxillary prominence over time has also been described in several long-term studies[9,10,18-21]. According to the studies, the impairment of maxillary development continues into the late teens and early adulthood[6,9,11,18,19,22]. Thus, the anteroposterior jaw relationship worsens over time. However, because there are few publications of longitudinal follow-up beyond age 20, it is not possible to say when this growth differential ends. Enemark et al.[9] followed 57 patients with CLP from birth to 21 years of age and showed that from 16 to 21 years, the maxillary prominence was reduced by 1.1°. A retrusion of maxillary development in the late teens/early adulthood has been reported by Lilja et al.[23], Marcusson and Paulin[16], and Semb et al.[11].

Furthermore, follow-up of partially operated human subjects with CLP where only the lip has been repaired, in comparison to individuals with both lip and palate repair, points to the significant role of lip closure. Indeed, increased lip pressure probably continues to mold the anterior dentoalveolar region and reduce the SNA angle into adulthood. Surgery has a great impact on maxillary growth that becomes progressively apparent as patients reach maturity with reduced prominence of the maxilla[5,11,14,23-28].

In the present study, a significant difference was found in SNA between group 1 and group 2 and between group 1 and group 3 (p<0.001***). When we evaluated the Co-A (Mid-face length) value between the three groups, a significant difference was found (p<0.001***). Also, a significant difference was found between group 1 and group 2 (p=0.001***) and between group 1 and group 3 (p<0.001***). A significant difference was found when we evaluated the A-PTV Horizontal value between group 1 and group 2, group 1 and group 3 (p<0.001***), and group 2 and group 3 (p<0.05*).

CONCLUSION

Maxillary development in patients with unilateral CLP was different from the patients with skeletal Class I, but similar to the patients with skeletal Class III. In this study, the linear and angular measurements of the patients with CLP were similar to the patients with Class III. Especially in the comparison of the development of patients with CLP, the use of a Class III malocclusion group as a control group is more accurate. Considering the delay in maxillary development in the unilateral CLP patients, maxillary protraction and maxillary expansion are important components of the treatment protocol. Especially in the maxilla, we suggest that maxillary protraction occur in the early period.

REFERENCES

1. Cura F, Böhmer AC, Klamt J, Schünke H, Scapoli L, Martinelli M, et al. Replication analysis of 15 susceptibility loci for nonsyndromic cleft lip with or without cleft palate in an Italian population. Birth Defects Res A Clin Mol Teratol 2016;106:81-87.
2. Dixon MJ, Marazita ML, Beaty TH, Murray JC. Cleft lip and palate: understanding genetic and environmental influences. Nat Rev Genet. 2011;12:167–178.
3. Shetye PR. Facial growth of adults with unoperated clefts. Clin Plast Surg 2004;31:361-371.
4. Mars M, Houston WJB. A preliminary study of facial growth and morphology in unoperated male unilateral cleft lip and palate subjects over 13 years of age. Cleft Palate J 1990;27:7–10.
5. Normando ADC, da Silva OG, Jr CL Jr. Influence of surgery on maxillary growth in cleft lip and/or pal- ate patients. J Craniomaxillofac Surg 1992;20:111–118.
6. Semb G, Shaw WC. Facial growth in orofacial clefting disorders. In: Turvey TA, Vig KWL, Fonseca RJ, editors. Facial clefts and craniosynostosis. Philadelphia: W.B. Saunders; 1996;28–56.
7. Berkowitz S. Cleft Lip and Palate Diagnosis and Management, Springer. 2nd Edition, chapter 3: 2006;225-280.
8. Semb G. A study of facial growth in patients with unilateral cleft lip and palate treated by the Oslo CLP team. Cleft Palate Craniofac J 1991: 28; 1-21.
9. Enemark H, Bolund S, Jørgensen I. Evaluation of unilateral cleft lip and palate treatment: long term results. Cleft Palate J 1990;27:354–361.
10. Smahel Z, Betincová L, Mullerová Z et al. Facial growth and development in unilateral complete cleft lip and palate from palate surgery up to adulthood. J Craniofac Genet Dev Biol 1993;13:57–71.
11. Semb G, Rønning E, Åbyholm FE. Twenty years follow-up of 50 patients with unilateral cleft lip and palate. Semin Orthod 2011;17:207–224.
12. Chiu Y-T, Liao Y-F, Chen P K-T. Initial cleft severity and maxillary growth I patients with complete unilateral cleft lip and palate. Am J Orthod Dentofacial Orthop 2011;140: 189–95.
13. Daskalogiannakis J, Mercado A, Russell K et al The Americleft study: an inter-center study of treatment outcomes for patients with unilateral cleft lip and palate. Part 3. Analysis of craniofacial form. Cleft Palate Craniofac J 2011;48:252–258.
14. Bardach J, Bakowska J, McDermott-Murray J et al. Lip pressure changes following lip repair in infants with unilateral clefts of the lip and palate. Plast Reconstr Surg 1984;74:476–479.
15. Tinano, MM, Martins, MA, Bendo, CB, Mazzieiro, E. Base of the skull morphology and Class III malocclusion in patients with unilateral cleft lip and palate. Dental Press J Orthod. 2015;20(1):79–84.
16. Marcusson A, Paulin G. Changes in occlusion and maxillary dental arch dimensions in adults with treated unilateral complete cleft lip and palate: a follow-up study. Eur J Orthod 2004;26:385–390.
17. Khanna R, Tikku T, Verma SL, Verma G, Dwivedi S. Comparison of maxillofacial growth characteristics in patients with and without cleft lip and palate. J Cleft Lip Palate Craniofac Anomal 2020;7:30-42.
18. Paulin G, Thilander B. Dentofacial relations in 1509 young adults with unilateral cleft lip and palate. 1510 A follow-up study. Scand J Plast Reconstr Surg Hand 1511 Surg 1991; 25:63–72.
19. Friede H, Enemark H. Long-term evidence for favourable midfacial growth after delayed hard palate repair in 1267 UCLP patients. Cleft Palate Craniofac J 2001;38:323–329
20. Nollet PJPM, Katsaros C, Huyskens RWF et al. Cephalometric evaluation of long-term craniofacial development in unilateral cleft lip and palate patients treated with delayed hard palate closure. Int J Oral Maxillofac Surg 2008;37:123–130
21. Meazzini MC, Giussani G, Morabito A et al. A cephalometric intercenter comparison of patients with unilateral cleft lip and palate: analysis at 5 and 10 years of age and long term. Cleft Palate Craniofac J 2008;45:654–660
22. Gnoinski WM, Rutz G. A longitudinal cephalomet- 1307 ric study from age 5 to 18 years on individuals with complete bilateral cleft lip and palate. J Craniofac 1309 Surg 2009;20:1672–1682.
23. Lilja J, Mars M, Elander A et al. Analysis of dental arch relationships in Swedish unilateral cleft lip and palate subjects: 20-year longitudinal consecutive series treated with delayed hard palate closure. Cleft Palate Craniofac J 2006;43:606–611.
24. Li Y, Shi B, Song QG, Zuo H, Zheng Q. Effects of lip repair on maxillary growth and facial soft tissue development in patients with a complete unilateral cleft of lip, alveolus, and palate. J Craniomaxillofac Surg. 2006;34:355–361.
25. Liao YF, Mars M. Hard palate repair timing and facial growth in cleft lip and palate: a systematic review. Cleft Palate Craniofac J. 2006;43: 563–570.
26. Liao YF, Mars M. Long-term effects of lip repair on dentofacial morphology in patients with unilateral cleft lip and palate. Cleft Palate Craniofac J. 2005;42:526–532.
27. Richard B, Russell J, McMahon S, Pigott R. Results of randomized controlled trial of soft palate first versus hard palate first repair in unilateral complete cleft lip and palate. Cleft Palate Craniofac J. 2006;43:329–338.
28. Shetye PR, Evans CA. Midfacial morphology in adult unoperated complete unilateral cleft lip and palate patients. Angle Orthod. 2006;76: 810–816.