T.C.
YEDİTEPE UNIVERSITY
INSTITUTE OF HEALTH SCIENCES

SHORT TERM FOLLOW-UP OF NASOLABIAL GROWTH IN PATIENTS WITH CLEFT LIP AND PALATE TREATED WITH NASOALVEOLAR MOLDING

DOCTOR OF PHILOSOPHY THESIS

Dt. BEGÜM DİKMETAŞ

ISTANBUL – 2021

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ISTANBUL – 2021

THESIS APPROVAL FORM

Institute : Yeditepe University Institute of Health Sciences

Programme : Orthodontics PhD Programme

Title of the Thesis : Short Term Follow-Up of Nasolabial Growth in Patients with Cleft Lip and Palate Treated with Nasoalveolar Molding

Owner of the Thesis : Dt. Begüm Dikmetaş

Examination Date : 16.02.2021

This study have approved as a Doctorate Thesis in regard to content and quality by the Jury.

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APPROVAL

This thesis has been deemed by the jury in accordance with the relevant articles of Yeditepe University Graduate Education and Examinations Regulation and has been approved by Administrative Board of Institute with decision dated 01.03.2021 and numbered 2021/02-24.

Prof. Dr. Bayram YILMAZ

Director of Institute of Health Sciences

DECLARATION

I hereby declare that this thesis is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which has been accepted for the award of any other degree except where due acknowledgment has been made in the text.

08.03.2021

Dt. Begüm DİKMETAŞ

ACKNOWLEDGEMENTS

First of all, I would like to thank all my precious professors; Prof. Dr. Fulya Özdemir, Prof Dr. Didem Nalbantgil, Assoc. Prof. Dr. Feyza Eraydın, Assoc. Prof. Dr. Murat Tozlu and Assoc. Prof. Burcu Nur Yılmaz for sharing their knowledge and experience during my educational life.

I would like to express my gratitude to my supervisor, Prof. Dr. Derya Çakan for her guidance and support, who shared all of her knowledge and experience with me during my thesis. I admire her patience and carefulness more and more every day.

My sincere gratitude to Prof. Dr. Hakan Ağır, who shared his intelligence and experience. His support and assessments were precious to me during this study.

I would like to thank all my colleagues in Yeditepe University for all their valuable help and support. I am grateful to have these beautiful friendships.

Finally, I would like to express my love to my dear family, who are always with me, and thank for their endless belief and support. I feel very lucky to have them all.

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LIST OF ABBREVIATIONS and SYMBOLS

2D	: two-dimensional
3D	: three-dimensional
C	: cleft
CAT	: computer-aided tomography
CBCT	: cone-beam computed tomography
CL	: cleft lip
CLP	: cleft lip and palate
CUCLP	: complete unilateral cleft lip and palate
CP	: cleft palate
CT	: computed tomography
DDY	: dudak damak yarığı
NAM:	: nasoalveolar molding
NAŞ	: nasoalveoler şekillendirme
NC	: noncleft
UCLP	: unilateral cleft lip and palate
POT	: preoperative orthopedic treatment

ABSTRACT

Dikmetaş, B. (2021). Short Term Follow-Up of Nasolabial Growth in Patients with Cleft Lip and Palate Treated with Nasoalveolar Molding. Yeditepe University, Institute of Health Science, Department of Orthodontics, PhD Thesis, İstanbul.

The aim of this prospective study was to evaluate the short-term longitudinal nasolabial changes of patients with complete unilateral cleft lip and palate (CUCLP) treated with nasoalveolar molding (NAM) and primary cheilorhinoplasty and to compare the nasolabial characteristics with that of healthy individuals. The study group comprised 20 patients with CUCLP (mean age: 20.60 ± 9.00 months) whereas the control group included 12 children without UCLP (mean age: 20.83 ± 8.96 months). Three-dimensional (3D) stereophotogrammetric records of the study group were taken at the first visit after primary surgeries (T0) and approximately 1 year after the first record (T1). Same records were taken at a similar time interval in the control group. Nasolabial measurements were performed on 3D facial images and statistical tests were performed. At T0, on the cleft side, nostril width and perimeter, alar length and width were significantly greater whereas upper lip transversal length, philtrum and medial lip height were shorter in the UCLP group compared to the control group ($p<0.05$). Nasal tip protrusion and projection angle were higher in the UCLP group ($p<0.001$ and $p<0.01$, respectively). Cleft side nostril height and columella inclination did not differ between groups ($p>0.05$). Nasal base width, alar length, nostril width and height ratios showed significant asymmetry in the UCLP group ($p<0.01$). At T1, significant nasolabial growth changes occurred and the differences between groups observed at T0 were mostly maintained. No significant difference was seen in upper lip transvers length C and columella inclination between UCLP and control groups ($p>0.05$). From T0 to T1, comparable growth changes occurred in both groups. To conclude, children with UCLP had flatter facial profile and more asymmetry in the nasolabial region compared to healthy children. During 1 year of observation period following primary treatments, the nasolabial growth of the patients with UCLP was similar to normal growth, without any relapse.

Key Words: Complete unilateral cleft lip and palate, nasoalveolar molding, extended Mohler technique, nasolabial growth and development, follow-up, noncleft control

ÖZET

Dikmetaş, B. (2021). Nazoalveoler Şekillendirme ile Tedavi Edilmiş Dudak Damak Yarıklı Bireylerde Nazolabial Büyümenin Kısa Süreli Takibi. Yeditepe Üniversitesi, Sağlık Bilimleri Enstitüsü, Ortodonti ABD., Doktora Tezi, İstanbul.

Bu prospektif çalışmanın amacı nazoalveoler şekillendirme (NAŞ) ve primer dudak ve burun operasyonu ile tedavi edilmiş tam tek taraflı dudak damak yarıklı (DDY) hastalarda kısa süreli nazolabial değişikliklerin değerlendirilmesi ve sağlıklı bireyler ile nazolabial özelliklerinin karşılaştırılmasıdır. Çalışma grubu, tam tek taraflı DDY'li 20 bireyden (yaş ortalaması:20.60 ± 9.00 ay) oluşurken, kontrol grubu sağlıklı 12 çocuktan (yaş ortalaması:20.83 ± 8,96 ay) oluşmaktadır. Çalışma grubundaki bireylerin üç boyutlu stereofotogrametrik kayıtları primer dudak operasyonu sonrası ilk randevuda (T0) ve ilk kayıtlardan yaklaşık 1 yıl sonra (T1) ve kontrol grubunda da aynı zaman aralıklarında alınmıştır. Nazolabial ölçümler 3B yüz fotoğrafları üzerinde yapılmış ve istatistiksel analizler uygulanmıştır. T0'da, DDY'li bireyler kontrol grubu ile karşılaştırıldığında yarık taraftaki nostril genişlik ve çevresinin, alar uzunluk ve genişliğinin anlamlı olarak daha uzun olduğu gözlemlenirken, üst dudak transversal uzunluğu, filtrum ve medial dudak uzunluklarının daha kısa olduğu saptanmıştır ($p<0.05$). Burun ucu protrüzyonu ve projeksiyon açısının DDY'li bireylerde daha yüksek olduğu görülmüştür ($p<0.001$ ve $p<0.01$, sırasıyla). Yarık taraftaki nostril yüksekliği ve kolumella inklinasyonu açısından gruplar arasında fark bulunmamıştır ($p>0.05$). Nazal taban genişliği, alar uzunluk, nostril genişlik ve yükseklik oranları DDY'li bireylerde belirgin bir asimetri göstermiştir ($p<0.01$). T1'de, nazolabial yapılarda büyümeye bağlı anlamlı değişiklikler görülmüş ve gruplar arasında T0'da gözlemlenen farklar T1'de de büyük oranda devam etmiştir. DDY ve kontrol grupları arasında yarık taraftaki üst dudak transversal uzunluğu ve kolumella inklinasyonu ölçümlerinde anlamlı bir fark bulunamamıştır ($p>0.05$). T0 -T1 döneminde, her iki grupta da benzer büyüme değişiklikleri meydana gelmiştir. Sonuç olarak, tek taraflı DDY'li çocukların sağlıklı çocuklara göre daha düz bir yüz profiline sahip olduğu ve nazolabial bölgelerinin daha asimetrik olduğu görülmüştür. Primer tedavilerden sonraki 1 yıllık takip döneminde, tek taraflı DDY'li bireylerin nazolabial büyümeleri sağlıklı bireylerinkine benzer bulunmuş ve nüks gözlenmemiştir.

Anahtar Kelimeler: Tam tek taraflı dudak damak yarığı, Nazoalveolar şekillendirme, Extended Mohler tekniği, Nazolabial büyüme-gelişim, Takip, Yarık olmayan kontrol

1. INTRODUCTION and PURPOSE

Cleft lip and palate (CLP) is one of the most common congenital craniofacial deformities. In addition, unilateral clefts are found to be the most common than the other type of clefts (1). Treatment of this deformity requires an interdisciplinary approach from birth to adulthood in order to improve both aesthetics and functions of individuals with CLP (2,3).

Until today, there have been efforts to correct deformations seen in individuals with UCLP and many treatment methods have been developed. In the neonatal period, the unilateral cleft lip and palate (UCLP) is characterised by separated lip segments, enlarged nostril, depressed and concave lower lateral cartilage, deviated columella and a significant nasolabial asymmetry (4). To reduce the severity of this facial deformity, nasoalveolar molding (NAM) is applied to individuals with unilateral cleft lip and palate immediately after birth (5). With NAM treatment, the cleft width is reduced, lips are approximated, the nasal cartilage is molded, the nose is projected and the nasolabial symmetry is improved (6,7). When the configuration of the hard and soft tissues in the cleft area is improved with NAM, the surgical procedure is facilitated. By decreasing the tension of the soft tissue, the surgeon is assisted in the subsequent surgeries and scar tissue is reduced (8). Unfortunately, even if nasoalveolar molding treatment is applied, the normal facial development and symmetry seen in individuals without cleft lip and palate cannot be achieved in individuals with cleft lip and palate. Residual asymmetry following surgery is one of the known stigmas of cleft lip and palate, and secondary surgical intervention may be necessary (9). The rate of asymmetry may affect the surgical and orthodontic approaches in the later stages of treatment (10,11).

The results of various treatment methods on nasolabial asymmetry may be evaluated when previous studies are examined. It has been reported that nasal asymmetry cannot be adequately corrected after primary cheiloplasty in individuals without preoperative orthopaedic treatment (POT) (12). Previous studies have indicated that nasal width on the cleft side is decreased after primary cheiloplasty in individuals not treated with POT but it becomes wider and relapse with time (8). They have also reported that nasal height on the cleft side could not be increased because nasal molding was not performed, and therefore nasal asymmetry has been significantly impaired (12). On the other hand, it has been reported that the nasolabial

asymmetry and deformation have been decreased significantly after primary cheiloplasty in individuals treated with NAM and primary cheiloplasty (13). After NAM and primary cheiloplasty, improvement in columellar deviation, decrease in nasal width and increase in nasal height on the cleft side, and increase in nasal projection have been observed (12,14–16). However, studies examining nasolabial asymmetry following treatments have reported that although nasal asymmetry has been corrected with NAM and primary cheiloplasty, significant relapses have been seen approximately one year after primary cheiloplasty (12,14,15). Therefore, requirement of an overcorrection involving the nasolabial region has been reported (17).

Normally, growth of facial soft tissue often follows the underlying bony structure, but depending on the thickness of the soft tissue, sometimes the facial soft tissue profile and the hard tissue profile may differ (18,19). In children with and without cleft lip and palate, facial soft tissue changes may be affected in different directions. In children without cleft lip and palate, the bone and the facial soft tissue often develop in the same direction depending on the growth of the bone due to various etiological factors and the position of the dental structures (20,21). However, in children with cleft lip and palate, the relationship between the underlying skeletal tissues and the lip contour may differ from the normal. The hypoplasia of the cleft region is one of the most important factors affecting nasolabial growth and development in individuals with cleft lip and palate (22,23). In addition, the surgical correction technique may lead to underdevelopment of the maxilla in all three planes of the space (24–26). Therefore, The follow-up of nasolabial growth and development in individuals with UCLP after NAM and primary cheilorhinoplasty is of utmost importance in terms of observing possible relapses and undesirable changes. Comparison of the growth changes and relapse with healthy individuals helps to determine the necessity and type of secondary surgical interventions to be performed and revising the team approach for necessary adjustments.

The aim of this study was to evaluate the short-term longitudinal nasolabial changes of patients with complete unilateral cleft lip and palate treated with NAM and primary cheilorhinoplasty and compare these changes with that of healthy subjects without CLP. The null hypothesis is that there was no difference in short-term nasolabial changes between subjects with and without CUCLP.

2. LITERATURE REVIEW

2.1. Embryology of Cleft Lip and Palate

Cleft lip and cleft palate (CLP) are one of the most common multifactorial congenital deformities in newborns (27).These deformities occur as a result of faulty growth of the facial processes or inability to fuse properly during the early embryonic development (28).

The basic morphology of the face occurs between 4th and 12th weeks by the development and fusion of five prominences. These prominences are the frontonasal prominence overlying the forebrain, the two maxillary prominences and two mandibular prominences associated with the first pharyngeal arches. In addition, the cranial neural crest cells delaminate and migrate rapidly from the neural placode. The mesenchyme in the frontonasal prominence arises from neural crest cells derived from the midbrain and forebrain, whereas the maxillary and mandibular prominences receive neural crest cell contributions from both the midbrain and hindbrain. The facial clefts result from the failure of some of these facial processes to grow and fuse correctly (29).

Pharyngeal arches develop in the 2nd week and disappear in the 6th week, and they are tissue masses that consist of ectoderm outside and mesoderm inside. Pharyngeal arches approach each other by increasing their volume with cell mitosis. Corresponding pharyngeal arches fuse at the mesodermal level as a result of perforations in the ectodermal layer and this fusion is defined as mesodermization (30).

At the beginning of the fourth week, due to the rapidly growing brain, embryo shows flexion towards oropharyngeal membrane and developing heart at the cephalic end (29,30).

All five facial prominences form at the end of the 4th week. At the beginning, these prominences surround the primitive oral cavity (the stomodeum) which is separated from gastrointestinal tract by the oropharyngeal membrane. During the 5th week, the paired maxillary prominences enlarge and grow ventrally and medially. At the same time, a pair of ectodermal thickenings, called nasal placodes, develop on both sides of the frontonasal prominence. In the 6th week, the ectoderm at the center of each nasal placode invaginates to form an oval nasal pit. This divides the frontonasal

prominence into the lateral and medial nasal processes. The groove between the lateral nasal process and the adjacent maxillary prominence is called the nasolacrimal groove. During the 7th week, the ectoderm at the floor of this groove invaginates into the underlying mesenchyme and it forms a tube called the nasolacrimal duct and lacrimal sac (29).

During the 6th week, the medial nasal processes migrate toward each other and fuse to form the primordium of the bridge and septum of the nose. At the end of 7th week, the inferior tips of the medial nasal processes expand laterally and inferiorly and fuse to form the intermaxillary process with the maxillary prominences. The intermaxillary process gives rise to the philtrum, primary palate and four incisor teeth (29).

Medial nasal prominence, lateral nasal prominence and maxillary prominences fuse to form the upper lip; right and left maxillary prominences and medial nasal prominences fuse to form primary palate. The nasal cavity is separated from the oral cavity anteriorly by formation of primary palate (31,32).

Between 7th and 12th weeks, palatal prominences develop with cell proliferation inside the right and left maxillary prominences. At the beginning, the palatal prominences show vertical growth and then horizontal growth with downward placement of the tongue, forming the secondary palate by fusing with each other and nasal septum at 10th week. Thus, the nasal cavity and the oral cavity are separated at the posterior. Following the formation of the hard palate, the soft palate forms at 10th to 11th weeks, and finally the uvula forms at 12th week (31,32).

All these cellular activities that play a role in the facial development take place due to a specific genetic code and can be easily affected by the external factors. Facial clefts form as a result of inappropriate fusion of facial processes for any reason. Unilateral or bilateral primary cleft lip occurs when medial nasal prominence, lateral prominences and right-left maxillary prominences cannot fuse appropriately. If maxillary prominences cannot fuse appropriately, there can be cleft at the hard palate, soft palate and uvula (30).

2.2. Epidemiology

In previous studies, it has been reported that the incidence of CLP varies upon the races. CLP is most common in Asians and Indians, while it is less common in the

black race (33,34). Vanderas (33) have stated that incidence of cleft lip, cleft palate and CLP are ranged between 0.91 and 2.69 in 1000 in Caucasians. On the other hand, the incidence of cleft lip (CL), cleft palate (CP) and CLP are found to be ranging between 0.18 to 1.67 in 1000 in black race. In Turkey, cleft lip and palate incidence is 0.95 per thousand, while the incidence of isolated cleft palate has been reported as 0.77 per thousand (35).

Cleft lip, cleft palate, cleft lip and palate are also seen in different frequencies. The cleft palate, associated with cleft lip, is secondary to the lip defect. This situation is thought to be the secondary effect of the problem in the fusion of the facial processes leading to the palate formation. As a consequence, cleft palate is found in half of the individuals with cleft lip (34,36,37).

In addition, unilateral cleft lip and palate are more common than bilateral cleft lip and palate. It has been found that unilateral clefts affect the left side more than the right, and this is irrelevant to race, severity or gender (34,37–40).

In studies evaluating the relationship between sex and CLP, it has been reported that the cleft lip is more common in males and the cleft palate is more common in girls (32,34,36,37,39).

In approximately one third of patients with cleft lip and palate, other malformations have been detected. This group of patients is also called as syndromic CLP. It is accepted that CLP is involved in more than 300 syndromes in different ways. Pierre Robin Syndrome, Treacher-Collins syndrome, DiGeorge syndrome, Van der Woude syndrome are examples of these syndromes (39,41,42).

2.3. Etiology

The etiology of cleft lip and palate is multifactorial and complex. Moreover, both genetic and environmental factors may cause CLP (39).

In 1942, the existence of the effect of the genetic mechanism on the etiology of orofacial cleft was first demonstrated by Fogh-Andersen (40) in human studies. The effect of genetics in the development of CLP appears in many cases. Patients with cleft lip and palate often have a family history, usually there are more than one cleft lip and cleft palate case in the family. Individuals who already have a child with CLP have more risk of having a child with CLP. Along with these examples, the high incidence of CLP in both babies in monozygotic twins compared to dizygotic twins reveals that

genetics has an important effect. In addition, CL or CLP increases with consanguineous marriage. In consanguineous marriages; the similarity of the gene structure increases the possibility of encountering the recessive genes that carry the disease. However, explaining the etiology of this malformation is not always possible only by genetics. Both genetic and environmental factors are thought to be effective (36,39,41,43–46).

Embryological development of the face is a complex chain of biological events involving cell differentiation, cell proliferation, cell migration, intercellular interaction, cell death and tissue fusion. Transcription factors, signaling molecules and proteins that are effective in the eventuating of all these events are produced by a specific genetic coding. As a result of mutations in genes, problems occur in the production of active molecules and when the biological chain breaks, facial clefts may occur (29,47).

Ardinger et al. (48) firstly reported that transforming growth factor-alpha (TGFA) contributes to the formation of orofacial clefts. Since then, many researches have been conducted and the effective genes in CLP development have been investigated. Findings of linkage studies have suggested various loci could have a causal role in cleft lip and palate including regions on chromosomes 1, 2, 4, 6, 14, 17, and 19. Furthermore, 2p13 (TGFA), 2q35-36, 6p21.3-21.1, 17q12 (RARA), TCEB3, KIF7, T-box (TBX10, TBX22), MTHFR, MSX1, MSX2, PAX2, PAX9 and 1q22 (IRF6) genes mutations may play a role in the development of cleft lip and palate without syndrome (41,43,44,48–52).

The presence and effect of more than one gen and environmental factors in the development of cleft lip and palate makes it difficult to find the key gene or gene groups. The fact that the number of families participating in the researches is few and heterogeneous structure reduces the significance of the results obtained. Therefore, a gene with a fully proven efficacy is still not available today.

The first 3 months of pregnancy is the organogenesis phase. Some environmental factors effective in this period may cause the development of CLP in the newborn. Malnutrition (deficiency of folic acid, vitamin A and vitamin B), some drugs used during pregnancy (anticonvulsants, benzodiazepines, steroids, overdose vitamin A, antihypertensive drugs), maternal and paternal age (to become a father 40 years and older, a mother 35-39 years), infections (toxoplasmosis, rubella), alcohol or smoking, exposure to radiation and excessive stress have been reported among the main factors (43,53–57).

2.4. Classification

Cleft lip and palate is seen in different types depending on the predisposing factor that disrupts the facial development. Classification is important in order to clearly identify the severity and type of anomaly during communication between professionals and to make accurate diagnosis and treatment planning since CLP requires a multidisciplinary treatment approach. The cleft lip and palate classification should be informative about severity of deformations, premaxilla protrusion, collapse of alveolar arches, deviation of nasal structures and velopharyngeal function deficiency. It should also be simple and understandable.

This deformity, which is as old as human history, has been named differently in every age. Most of the first written sources compare the cleft lip with the animal features, and because of the similarity to the hare mouth, the most popular term used was "harelip" (labium leporinum). At the meeting of the American Medical Association in St. Louis in 1922, a call was made for an explanation to stop using the harelip term. John Staige Davis and Harry P. Ritchie said that the term congenital cleft of the lip should be used instead of the harelip term (58).

The previously used harelip term was stopped using, at the beginning of the 20th century, different CLP classifications were made. In 1922, Davies and Richie (58) classified the clefts into three simple groups as prealveolar, alveolar, postalveolar, and accepted the alveolar process as a dividing line. In 1923, Brophy (59) wanted to identify all the muscle and bone tissue involved in this deformity, and his classification included 16 different morphological cleft palate forms with or without cleft lip. Brophy's classification was considered as overly complex and unpractical by many surgeons. In 1932, Veau (60) defined a classification that based on anatomical structures consist of four groups as clefts of the soft palate, clefts of the soft and hard palate extending through the incisive foramen, clefts of the soft and hard palate extending unilaterally through alveolus, clefts of the soft and hard palate extending bilaterally through alveolus.

In 1942, Fogh-Andersen (40) suggested an alternative classification based on embryological formation and proposed that it would be better to use incisive foramen as a reference instead of using the alveolar process as a dividing line. His classification consists of four group as harelip (single or double), harelip with cleft palate, isolated cleft palate, rare atypical cleft (median cleft lip). In 1958, Kernahan and Stark (61)

described a classification based on the theory of embryological formation instead of anatomical structures and this classification is still being used today. In this classification, the incisive foramen was referenced instead of the alveolar crest. The anterior part of the incisive foramen was named as the primary palate (upper lip, philtrum, premaxilla and 4 incisors) and the posterior part was named as the secondary palate (hard and soft palate). They stated that a cleft could only affect the anterior or posterior part, as well as both parts.

It was stated that the classifications made up to this time are inadequate during communication among professionals. Therefore, in 1960, the American Association for Cleft Palate Rehabilitation appointed a Nomenclature Committee to formulate a classification system. Thereupon, in 1962, Harkins et al. (62) also defined a new classification.

In 1966, Pfeifer (63) made the first symbolic classification. In Pfeifer's classification, lines and dots were used to indicate the complete and incomplete cleft. In 1971, Kernahan (64) made a new symbolic classification which was based on the basis of the classification they had previously defined and it was called 'the striped Y'. In this classification, the arms of Y represent the primary palate and the base part represents the secondary palate, and the circle at the conjunction of these two regions is the incisive foramen. The primary palate is divided into two as right and left. Cleft segments are indicated by dots. The presence of a submucous cleft or Simonart band is indicated by horizontal lines and the median cleft indicated by a vertical straight line drawn between the arms of the Y. In 1973, Elsahy (65) created a modified striped Y classification due to the inability to clearly define the severity of cleft on the lip, to define premaxillary protrusion and alveolar arch collapse, to code function, and to define velopharyngeal insufficiency. In 1977, Millard (36) modified the striped Y scheme slightly and added two inverted triangles to the top of Y to define the nose wings and included the nose in the classification. In 1991, Friedman et al. (66) combined Elsahy (65) and Millard's (36) schemes to form a new Y-scheme. In their classification, they made coding with numbers and letter instead of dots, crossing and drawing lines. Thus, it was aimed to facilitate a standardized classification for clinical and epidemiological investigations by establishing medical data and transferring the standardized data. In 1998, Smith et al. (67) created a new classification in which the deformity is described more easily and digital coding is made by using the stripped Y-diagram. Premaxilla and velopharyngeal functions were not taken into consideration in

this classification. Unlike the stripped Y-diagram, the secondary palate was divided into two as right and left.

In the symbolic classifications, the presence of the cleft and which tissues are affected have been stated, but sufficient objective information has not been given about its severity. Tough, the clear definition of the severity of deformity is an important criterion for determining the type of preoperative orthopedic or surgical treatment. Therefore, in 2001, Ortiz et al. (68) defined a new classification that also shows the severity of deformity and the amount of tissue affected. However, this classification had a large and complex structure including multiple schemas. In 2009, Rossell-Perry (69) created a new classification called "The Clock Diagram" based on the definition of the degree of distortion to create a simpler and more understandable classification. This classification method was created based on the surgical results of 1043 patients who were selected by Rossell-Perry (69) and this method includes 4 basic structures (nose, lip, primary palate, secondary palate). Rossell-Perry (69) compared his own classification with Kernahan diagram in this study. In the classification of two patients with including the same tissue but with different cleft severity, the Kernahan diagram indicated that both patients had the same CLP status but it could be coded differently by defining the cleft severity in the clock diagram.

In 2012, Coşkuner Gönül (70) determined the severity of the cleft type in infants with CLP according to a new classification created by numerical models. In this classification, the coding is composed of 3 digits. In this coding, digit of hundreds indicate the cleft type, digit of tens represents the cleft width, and digit of units indicates the degree of dislocation (soft-hard palate cleft's length).

2.5. Maxillofacial Characteristics of Complete Unilateral Cleft Lip and Palate in Newborns before NAM and Primary Cheiloplasty

Complete cleft lip and palate is a complex deformity that includes not only the lip and palate but also the nasal tissues. The presence of deformity unilaterally or bilaterally affects distortion, dislocation and tissue deficiency in the maxilla and nasal region in different ways (36,71).

In individuals with CUCLP, the maxilla is divided into two parts as greater and lesser segment. Due to the neuromotor activity of the tongue and the interrupted orbicularis oris muscle, morphological deviations are observed in the maxillary

alveolar segments. It is observed that the greater segment rotates anterolaterally in the transversal plane, while the lesser segment shows more heterogeneous (medial or lateral) morphological deviations (72) (Figure 2.5.1.).

In the complete unilateral cleft lip and palate, the alar cartilage on the cleft side is depressed and concave, the alar cartilage on the noncleft side is closer to the nose tip and in the higher position. On the cleft side, the nostril base width is increased. The nose is flat, the columella and nasal septum are deviated towards the noncleft side. The alveolar segments and lips are not in contact (4,5,36) (Figure 2.5.1.).



Figure 2.5.1. Initial extraoral and intraoral views of CUCLP

2.6. Preoperative Orthopedic Treatment and Surgical Approaches in CLP

Preoperative orthopedic treatment (POT) has been emerged to reduce the severity of the initial cleft deformity, to restore the normal anatomy, to stimulate palatal growth or to guide growth and development of the maxillary alveolar segments. Therefore, a number of orthopedic techniques have been developed over the years to improve nasolabial deformations and to overcome problems that may arise in patients with cleft lip and palate. Preoperative orthopedic treatments first started around the 16th century. Surgeons have tried to retract the protrusive premaxilla in order to achieve a better surgical outcome by reducing the severity of the initial deformity (73). Until today, many preoperative orthopedic treatment methods have been developed such as lip band application, lip adhesion, active and passive plate treatments and nasoalveolar molding (NAM) (74–80).

Neonatal maxillary orthopedics has emerged with the goals of restoring normal anatomy and guiding the growth and development of the maxillary segments. Besides these purposes, other purposes of use are as follows; normalizing the swallowing pattern, correcting the tongue position and arc form by preventing the tongue from entering the cleft area, improving the alar base positions, facilitating surgery and

improving the results of surgery, reducing the cleft width, preventing postoperative collapse, facilitating nutrition, correction of nasal septum deviation, transition to nasal breathing, better speech development, preventing middle ear infections, prevention of crossbite, the need for more limited orthodontic treatment in the following years and providing positive psychological support to families (26,72,81–87).

There are many techniques developed and presented until the 20th century, but most of these techniques are primitive and insufficient. Surgeons and dentists, who were dissatisfied with the long-term results of presurgical orthopedic treatment methods in the past, sought new ways to achieve more appropriate results until today. In 1561, Franco (88) suggested some suture methods to close the gap of lips. In 1686, Hoffmann used a head cap with arms extended to the face to retract the premaxilla and to narrow cleft (89). In 18th century, Louis, Chaussier and Desault used bandages on the prolabium to simulate muscle retraction and compress the premaxillary region. By the 19th century, after the development of medical adhesive tapes, treatment methods were changed and improved (90).

In 1950, McNeil (91) was the first person who described modern preoperative orthopedic treatments. In McNeil method, the displaced maxillary segments are repositioned with a series of orthopedic plates to narrow the cleft area and achieve a normal maxilla. In plaster models that were taken from infants with CLP, segments are cut and separated from each other, then these segments are brought gradually to desired position and fixed. The maxillary plate fabricated on the created plaster model is applied to the baby. For the purpose of lengthening and approximating the lip muscles, extraoral tapes can be applied. With McNeil plates, active force is applied to the segments so that leveling is achieved and the arc form is corrected. According to McNeil, the pressure resulting from the gentle contact of the plates to the palatal mucosa has a growth enhancing potential, and also ideal leveling of the palatal segments stimulates the palatal growth, corrects bone deficiency and allows a normal maxillary development (2,91).

Latham (92) suggested the use of an active maxillary plate that is fixed to the palate with pins. The activation of the plate is achieved by turning a screw and increasing the tension of the elastic chain applied to the alveolar segments. The appliance produces anteriorly directed forces to the lesser segment and posteriorly and medially directed forces to the greater segment in unilateral cases whereas expansive forces to the posterior segments and retractive forces to the premaxilla are created in

bilateral cases. Latham appliance is a fixed appliance, so that there is limited need of cooperation of the parents. And also, the reduced number of control appointments is advantage. However, this method is an invasive method that requires general anesthesia for fixing the appliance. In the previous studies, it was stated that a significant decrease in the initial cleft width was achieved in POT applied with Latham apparatus (92–96).

In active orthopedic applications, as well as screws, U-springs added to the appliances were also used to approximate the segments. In 1995, Ball et al. (81) examined transversal changes in the maxillary arch following POT with active maxillary plates in infants with CUCLP. The active plates consist of two acrylic parts which can easily slide over each other, these acrylic parts are connected and activated by a U-shaped wire in the middle. After lip operation, acrylic parts are fixed to each other and continued to be used passively until the palate operation. Although there was no collapse of the arch during correction of the maxillary segments, it was reported that the expected increase in the arch dimensions did not occur. It was also reported that the width of the cleft decreased as the segments grew in the transverse direction (towards the cleft area) and became more horizontal. The reason for the growth of the alveolar segments in this way is thought to be the removal of the tongue from the cleft area with plate. On the other hand, in their study, Adali et al. (97) stated that the active plates, are recommended by Ball, did not have a significant effect on the arch form and that lip operation caused the movement of the segments.

In 1976, Hotz and Gnoinski (74) produced passive maxillary plates which there is hard acrylic on the outside and soft acrylic on the inside. Unlike active plates, these passive plates do not apply active force to the segments. Segments are guided by reduction of hard acrylic and adding soft acrylic to the plates during certain periods of treatment. With the growth, the segments are brought to the desired positions. This method has been called Zurich technique. In the Zurich technique, the extraoral elastic tapes are not applied because it is thought that the sagittal development of the maxilla may be affected negatively (25,75). According to Hotz and Gnoinski, the primary aim of neonatal orthopedics is not to facilitate the surgery or to stimulate the growth as postulated by McNeil, but to take advantage of intrinsic developmental potentials. The benefits of the method have been listed as helping feeding, maintaining the width of the maxilla, enabling the palate to increase spontaneously in all three dimensions

without impeding its growth potential and permitting the soft palate to grow to its maximum length prior to surgery (25,74,75).

Lip adhesion is a surgical method that is done before the last lip operation. Lip cleft edges are joined and lip integrity is ensured. The principle behind the lip adhesion is to create a narrower cleft, thus facilitating the definitive repair under more favorable conditions as less tension and a minimum of undermining. With this procedure, complete CLP is converted into incomplete CLP and tissue tension that may occur during final lip repair is reduced (93,98).

The application of lip tapes aims to approach the lip edges with extraoral tape without surgical intervention. Therefore, it has the same purpose as the lip adhesion (77). Lip taping requires patient cooperation and long-term controlled force cannot be applied with the tapes. Despite these disadvantages, lip tape is preferred because it is not an invasive method. It is widely used with POT appliances (5,78,80).

2.6.1. Nasoalveolar Molding (NAM)

Preoperative orthopedic applications were based on alveolar molding for many years and no intervention was made to the nasal region. A paradigm shift occurred at the end of 20th century about POT. Dr. Grayson and Dr. Cutting (78) introduced a new concept called nasoalveolar molding (NAM), where presurgical orthopedic treatment was applied not only to align the alveolar segments but also to mold the depressed alar cartilage and reshape the nose. The rationale behind this concept lies on the plasticity of the neonatal cartilage (5,79).

In 1984, Matsuo et al. (99), in his study on the treatment of auricular cartilage deformations, reported that cartilaginous formability was higher in newborns because of high maternal estrogen and hyaluronic acid levels. As the level of hyaluronic acid gradually decreases towards the 6th month, the molding ability of the cartilage decreases and its form becomes stable. When it was seen that auricular cartilage molding could be done at early neonatal period without the need for any surgical intervention, it was understood that nasal cartilage deformation could be corrected at neonates with cleft lip and palate taking advantage of this formability feature because the nasal cartilage is similar to the auricular cartilage (100). In this way, a new treatment method based on the leveling of the maxillary segments and molding of the nasal region has emerged in infants with CLP (5,101). Matsuo (100) made a stent

containing a pair of silicone tubes to shape nostrils. However, as this method required a solid nasal base, Simonart band had to be present or lip adhesion had to be made first. These limitations were overcome by the NAM since the nasal molding was performed by a stent attached to the alveolar molding plate (5,79).

In the operation of individuals with large alveolar cleft, the surgeon is forced to stretch the tissues to bring them closer. Therefore, a stretched and wide scar tissue may develop after surgery. This scar tissue and increased tissue tension can cause collapse of the segments by creating a strong and uncontrolled force on the alveolar segments (102). In order to reduce the severity of the initial deformity and allow the surgeon to repair a minimal deformity, NAM has been advocated. Thus, it is suggested that a good aesthetic appearance can be achieved with minimal scar tissue because the tissue tension is reduced before surgery.

The aim of NAM is to decrease the cleft width by leveling alveolar segments, to correct deformed nasal cartilage, to correct the deviation by extending the columella, to provide nasal projection and to approximate the lip muscles. When the relationship of the alveolar structures improves, a subsequent improvement is observed in the nasal region. The alar edge, which was stretched over a wide cleft, is brought to a more symmetrical and convex structure as a result of the increase in the laxity of the tissue by approaching the alveolar and lip segments. The projection of the nose is increased by supporting its tip with a nasal stent. The molding plate, extraoral tapes and the nasal stent enable the clinicians to correct some of these nasolabial deformations to some extent in NAM (4,7,103) (Figure 2.6.1.1.).

Proper use of extraoral tapes is crucial for the treatment success. Horizontal tapes reduce the tension in the lip muscles, while the lip muscles extend, they bring the lip segments closer. The deviated columella tends to improve with the horizontal force exerted by the horizontal tape (4,79).



Figure 2.6.1.1. Initial and posttreatment extraoral and intraoral views of CUCLP

In patients with UCLP, first step of NAM treatment is taking intraoral impression to fabricate the NAM plate. This impression is taken in the operating room with a silicone-based impression material under the supervision of anesthesiologist by providing oxygen support (104). Plaster model is obtained from the impression. Cold acrylic plate is fabricated on the plaster model. The retention button is fixed with cold acrylic to the anterior side of the plate at an angle of 45° to the horizontal plane in order to stabilize the NAM plate with extraoral elastic tapes (Figure 2.6.1.2). However, it should be noted that the button must not press on the lower lip and it must be exactly in the cleft line. After fabrication of the plate, extraoral elastic-tape combination is applied to generate approximately 2 oz. of force (Figure 2.6.1.4.). Selective abrasions and soft denture liner additions are made at weekly appointments to orient the alveolar segments. In this process, hard acrylic reductions are made on the inner part of the greater segment and soft denture liner additions are made on the outer part in order to correct the anterolateral rotation of the greater segment and bring it closer to the midline. In order to provide anterolateral movement of the lesser segment, hard acrylic removal is made from the outer and anterior parts of the segment. In addition, in order to prevent the contact of the plate with the pharyngeal tissues, the posterior part of the plate is trimmed gradually. During NAM, extraoral horizontal tape is also used to approximate the lip segments. Skin barriers are applied to prevent irritation of the infants' cheeks when using extraoral tapes. These barriers are changed once or twice a week when necessary (4).

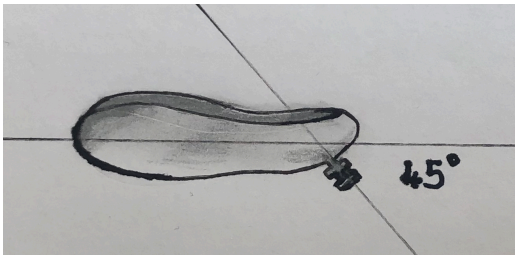


Figure 2.6.1.2. Position of the retention button

Nasal molding begins when the alveolar cleft width is less than or equal to 5 mm to prevent meganostril development. There is no need to take nasal impression from the baby in order to prepare the nasal stent. The nasal stent is bent from a 0.8 mm thick round stainless-steel wire in the form of a swan's neck. When performing nasal stent bends, a guiding wax template is used. The intranasal part of bend is in the form of a kidney and it is first covered with hard acrylic to increase durability and then with denture liner to prevent soft tissue irritation (Figure 2.6.1.3.). In the consecutive appointments, the nasal stent is activated by bends to the wire or by soft liner addition (4,79).

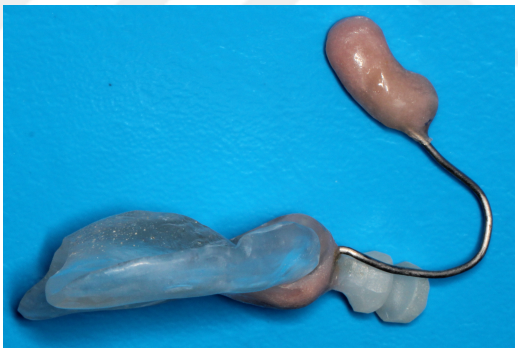


Figure 2.6.1.3. NAM appliance with nasal stent



Figure 2.6.1.4. A unilateral cleft patient undergoing NAM treatment with plate, lip tapes and nasal stent

2.6.2. Surgical Approaches in UCLP

Primary cleft lip and nose reconstruction is one of the most challenging surgical procedures in plastic surgery. The ideal cleft lip repair should ensure a symmetrical Cupid's bow, natural philtral columns, a philtrum dimple, a well-aligned continuous white roll, minimum visible scar in the line of the philtral column and an ample vermilion and mucosa with a slight philtral tubercule. The function should also be provided while the aesthetics is provided. Therefore, this intervention should also ensure a normally functioning orbicularis oris muscle with harmonious symmetry. Moreover, there should also be symmetry of the nostrils and nostril sills (105). In addition to reconstructing form and function in individuals with unilateral cleft lip and palate, primary operations contribute to the improvement of the psychosocial health of the individuals and their parents (106). Therefore, the results of primary operations become crucial.

Until today, many methods have been tried to provide an ideal symmetry and aesthetics outcome. Ralph Millard pioneered the surgical techniques developed by defining innovative principles in cleft lip and palate surgery. In 1957, Millard (107) presented the concept of rotation advancement for unilateral cleft lip repair. He developed his own technique by adding various refinements over the years (36,108,109). In this procedure, a symmetrical scar can be produced with the philtral column on the normal side only with the lower two-thirds. On the other hand, the lip length also may be short because of inadequate rotation on the medial lip segment. In 1987, Mohler (105) made modification of the rotation advancement flap. In this modification, the rotation flap and back cut are shifted from the superior border of the upper lip onto the columellar skin. The defect that is created by the downward rotation of Cupid's bow is filled with the columellar flap. The resulting upper lip scar is placed along the entire length of the philtral column on the cleft side. However, this technique limits the lengthening of the lip. Cutting (110) modified Mohler's technique to eliminate the disadvantage of this technique. In the Extended Mohler technique, the apex of the flap is extended higher on the columella and the back cut is extended to junction of the columellar base and noncleft sided philtral column. This modification improved downward rotation of the medial lip segment. Nowadays, the Extended Mohler unilateral cleft lip repair is one of the commonly used techniques.

The ideal cleft palate repair should not adversely affect speech development, maxillary development and hearing. Unfortunately, there is no ideal palatoplasty technique yet. Moreover, palatoplasty should be performed between 6-12 months of age before speech development (2).

In 1861, Bernard von Langenbeck described a method of palatoplasty. In this technique, mucoperiosteal flaps are used for the repair of the hard palate region (111). Another palatoplasty technique is Veau-Wardill-Kilner palatoplasty. In this technique V-Y procedure is performed, the whole mucoperiosteal flap and palate are retroposed and the palate is lengthened. However, this technique leaves an extensive raw area anteriorly and laterally. The use of this technique decreased due to its disadvantage (2). In 1995, Bardach (112) defined a new technique that was a modification of the von Langenbeck technique. In this technique, the incision is made along the cleft margin and the alveolar margin. These are joined anteriorly to free the mucoperiosteal flaps. This technique is commonly used.

2.7. Preoperative, NAM induced nasolabial changes in patients with Complete Unilateral Cleft Lip and Palate

In the nasolabial region of patients with complete unilateral cleft lip and palate, asymmetry and deformations decrease after nasoalveolar molding. The results of the previous studies revealed that the nostril width on the cleft side decreases, nostril height on the cleft side increases, the columellar deviation improves, the nasal projection increases, the nasal symmetry improves and the cleft width decreases (113–115).

In a study by Liou et al. (14) the nasal asymmetry and the growth of 25 individuals with UCLP were examined. The authors photographed each individual at the initial appointment, after nasoalveolar molding, and 1 week, 2 years and 3 years after the cheiloplasty. They made linear measurements on 2D photographs and evaluated the asymmetry by subtracting the measurements of the noncleft side from the measurements of the cleft side. The differences of nostril height and nostril width measurements between cleft and noncleft sides significantly decreased after NAM. According to the results of this study, there was an improvement in the nasal asymmetry after NAM.

Pai et al. (15) evaluated the nasal symmetry of 57 individuals with UCLP on 2D photographs taken at the initial appointment, after NAM, 1 month after primary cheiloplasty and at 1 year of age. Linear measurements were calculated as a ratio of affected side to nonaffected side, in an attempt to minimize method-related errors. They observed that the ratio of nostril width and the ratio of nostril height were improved after NAM. In addition, they stated that there was an improvement in columellar inclination after NAM. Based on their results, they stated that NAM therapy has a positive effect on nasal symmetry.

Ezzat et al. (116) examined the results of the presurgical nasoalveolar molding using plaster models. They included 12 individuals with UCLP and observed that there was an improvement on columellar deviation, increase in nostril height on the cleft side, and an insignificant increase in nostril width after NAM.

Keçik and Enacar (117) scanned 22 individuals' plaster models in their study to evaluate changes in the nasal region. Same as previous studies, they found that alar width on the cleft side decreased and alar width on the noncleft side increased after NAM. Furthermore, an improvement in columella deviation was observed. On the other hand, they observed that there was an increase in the nostril area on the cleft side. As the reason for the increase in the nostril area, they attributed that the nostril width decreased with NAM while the nostril height increased with nasal stent. They also found that the alar cartilage was protruded.

Gomez et al. (118) also evaluated nasal changes after presurgical nasoalveolar molding in 30 individuals with UCLP. They evaluated the results of NAM on 2D photographs that were obtained from plaster models. They found that there was an increase in columellar length and nostril height on the cleft side.

In his thesis, Anderepoulos (119) examined the effects of NAM in 24 individuals with UCLP using scanned extraoral plaster models and stated that columellar length increased after NAM.

Nur Yılmaz and Germeç-Çakan (87) used stereophotogrammetric records obtained from nasal plaster models to evaluate nasolabial morphology of 42 individuals with UCLP after NAM. According to results of this study, there were increases in nasal width, lip gap, nostril height on the cleft side, nasal projection and lip vertical length. Moreover, they stated that the nasal symmetry improved after NAM.

In none of these studies performed in the past, extraoral recordings were obtained from individuals by using 3D stereophotogrammetry directly.

Previous studies evaluated the nasolabial morphology using 2D photographs or 3D model, which have their own limitations. In 2019, Mancini et al. (16) took extraoral records from individuals with UCLP by using 3D stereophotogrammetry. They observed significant improvements in nasal projection, columella length, nasal deviation, nasal symmetry and nasal width after NAM. Moreover, they also observed that the nasal form was significantly corrected at nasal tip projection and columella angle. However, in this study, as a control group, they used normal nasal anthropometric measurements from 13 noncleft infants aged 0 to 5 months, which were previously published by Farkas (120). The use of historic groups was interpreted as confusing for reasons such as differences in craniofacial size or form, different examiners and measurement techniques.

In 2019, Birli (7) evaluated the effects of NAM using 3D stereophotogrammetry. A control group composed of age-matched, healthy individuals was also included to compare nasolabial morphology between individuals with and without UCLP. According to the results of this study, nostril base width decreased on the cleft side, nostril height increased, columella inclination improved, nose projection increased, lip gap reduced after NAM treatment. When the results were compared with the control group after NAM, it was stated that nasolabial deformity and asymmetry seen in individuals with UCLP decreased and approached to that of the healthy individuals in the control group. However, it was stated that individuals with UCLP had residual deformity and asymmetry in the nasolabial region even after NAM treatment.

2.8. Postoperative Nasolabial Changes in Patients with Complete Unilateral Cleft Lip and Palate

The residual asymmetry and deformations after NAM treatment are corrected by surgical interventions. In previous studies, it has been stated that an improvement in the nasolabial asymmetry and the deformation is observed in individuals with UCLP after surgical treatments (Figure 2.8.1 and Figure 2.8.2) (14–16,121,122). However, some studies have shown that the asymmetry and deformation increased again later in life (14,15,123).



Figure 2.8.1. Extraoral and intraoral views of patient with CUCLP after primary lip operation



Figure 2.8.2. Extraoral and intraoral views of patient with CUCLP after palate surgery

Mancini et al. (16) observed significant improvements in nasal width, nasal projection, columella length and nasal symmetry after NAM and primary cheiloplasty. Single-stage cheilorhinoplasty technique was used for reconstruction of UCLP in this study. When they compared individuals with UCLP to healthy individuals, nasal morphology was corrected with notable overcorrection of nasal projection, columella angle and nasal width.

Williams et al. (124) evaluated the nasal symmetry between individuals who treated with NAM and treated without NAM. 42 nonsyndromic patients with UCLP were selected. 28 patients treated with NAM and 14 patients were not treated with NAM. Lip repair was performed according to Millard procedure in this study. According to the results of this study, nostril height-width ratio is statistically significantly different between groups postoperatively and this ratio is closer to “1” in the NAM group. Therefore, they stated that in the NAM group more symmetrical nostril is achieved with treatments.

In their study, Liou et al. (14) applied modified rotation-advancement cheiloplasty without nasal cartilage dissection to reconstruct UCLP. They stated that the residual nasal asymmetry after NAM was significantly improved and the maximum level of nasal symmetry was reached after primary cheiloplasty. However, they also

stated that there was a significant relapse in the first year after primary cheiloplasty and the nasal asymmetry remained stable in the following years.

Similar to the results of the study conducted by Liou et al., Pai et al. (15) stated that nasal symmetry was at the maximum level after primary cheiloplasty applied after NAM. But again, they observed relapse rates of 10% in height, 20% in width, and 5% in columella angle at 1 year of age.

Knight et al. (125) conducted a prospective study to evaluate nasolabial changes. In this prospective study, two follow-up periods were included. First phase was from infancy to early childhood and included 50 children with complete or incomplete unilateral cleft lip and palate. Second phase was from early childhood to late childhood and included 50 children from first phase. The deformity was corrected by one surgeon and the rotation-advancement technique was used. Before surgery, preliminary dentofacial orthopedics was applied. They stated that the heminasal width (sn-al) grew faster on the cleft side over time, but could not reach the heminasal width on the noncleft side. In the measurements of the lip area (sn-cph, sbal-cph), it was stated that there was no difference in the growth rate of the cleft and noncleft sides, but the measurements differed on the cleft side and noncleft side.

In 2018, Hosseinian et al. (121) examined the results of two technique to reconstruct UCLP. In this study, which included 23 patients, 12 of the patients were treated using only the rotation advancement technique, while the other 11 patients were treated with rotation advancement after NAM treatment. Nasal plaster models, obtained from the nasal impressions taken from the patients, were scanned. According to the results of this study, when dome height, nasal projection, alar base width measurements were examined, it was observed that nasal asymmetry healed more in individuals who received NAM treatment before surgery.

Ayoub et al. (126,127) conducted two studies in 2011. They examined nasal and lip morphology in individuals with UCLP were at 3 years of age and evaluated the difference between individuals with UCLP and healthy subjects. Passive feeding appliance with lip strapping was applied up to the lip surgery in 21 individuals with UCLP included in the study. A modified Millard cheiloplasty and a McComb primary rhinoplasty were performed at the age of 3 months to the individuals with UCLP included in this study. 96 age matched healthy individuals were included for comparison. They stated that the nasal widths measurements remained greater, the upper lip were remained at posterior position, the upper lip transversal length remained

longer and the philtrum remained wider in individuals with UCLP compared with healthy individuals.

Funayama et al. (128) examined effects of nasal stent with PNAM and postsurgical nasal retainer. 23 individuals with CUCLP were included in this retrospective study. They made evaluations on 2D photographs taken when the individuals included in the study were 4 years old. All patients were treated with same surgical technique. They stated that although PNAM or postsurgical nasal retainer were applied, asymmetry was observed in individuals in the nasal area at the age of 4. On the other hand, more symmetrical results were obtained in individuals who were applied PNAM or postsurgical nasal retainer compared to those who did not.

Al-Rudainy et al. (123) evaluated the facial asymmetry of the 15 infants from the beginning of treatment to age of 4. In this study, preoperative nasoalveolar molding was not applied to reconstruct, modified Millard cheiloplasty and McComb primary rhinoplasty were applied as surgical technique. They took 3D recordings from infants by using stereophotogrammetry and used the facial mesh method instead of the landmark method to evaluate asymmetry. They found that although the asymmetry significantly improved following the primary lip operation, a residual asymmetry was evident at upper lip, nostrils and paranasal area. The philtrum was deviated toward the scar tissue. They concluded that the scar tissue resulted in unequal growth of the lip mediolaterally. The inadequate approximation of the orbicularis oris muscle fibers during primary surgery causing a tension and scar on the lip led to a significant lip and philtrum shift to the cleft side. Furthermore, the noted anteroposterior asymmetry was explained by the scarring of the lip and palate as well as intrinsic factors leading to growth deficiency.

In a retrospective study, Chang et al. (12) examined nasal asymmetry in individuals with UCLP to define the most successful treatment modality. Seventy six patients were divided into four groups according to treatment methods (Group I: primary rhinoplasty alone, Group II: nasoalveolar molding alone, Group III: nasoalveolar molding + primary rhinoplasty, Group IV: nasoalveolar molding + primary rhinoplasty + overcorrection). Modified rotation advancement cheiloplasty with a Mohler incision and Noordhoff vermilion flap techniques were used in this study. Photographic records were taken when individuals were 5 years old. According to the results of this study, the best results in nasal symmetry were observed in Group IV. In addition, the worst nostril height ratios were observed in Group I, worst nostril

width ratios were observed in Group II, worst nostril area in Group I, worst inner nostril height width ratio on the cleft side in Group II. Therefore, they stated that the best nasal symmetry results were obtained after primary cheiloplasty following NAM. In addition, the authors emphasized the need for overcorrection.

In individuals with CUCLP, palatoplasty and lip operations cause major scar and overstretched tissue. Accordingly, the development of the maxilla is restricted in three dimensions of space. Maxillary retrognathia appear in the sagittal direction, maxillary constriction appears and posterior cross bite in the transversal direction, open bite appears in the vertical direction (2). These deformations are corrected with orthodontic treatment and orthognathic surgeries in later ages.

2.9. Extraoral Recording Methods in Cleft Lip and Palate

Treatment of individuals with cleft lip and palate involves a long period from infancy to adulthood. In this anomaly, which requires a multidisciplinary treatment approach, clinical records have great importance in order to fully identify the problem, to make the correct diagnosis and to establish treatment planning. In addition, these records allow to evaluate physiological development and treatment results. Thus, indirect contribution is made to the psychological health of the patients and their families. Moreover, performing these evaluations is important for comparing individuals with CLP and normal individuals in terms of facial aesthetics. In order to make these evaluations properly, the records should reflect the textures exactly.

Both intraoral and extraoral photographs and intraoral impressions are routinely taken from the newborns who are referred to the orthodontic clinics in order to determine the initial treatment requirements, to fabricate the NAM appliance and to evaluate the treatment results in the future (129).

Direct clinical evaluation, also known as anthropometry, has been used by clinicians for many years (130). Today, this method is used in the first examination when the patient first applies to the clinic. But this method has some disadvantages. In this method, while performing detailed analysis and measurements, the patient should be present in the clinic and should remain stationary for a long time. It is almost impossible to apply this method, which requires patient cooperation, especially in newborns, children and patients with mental retardation.

Until today, many techniques have been used to study craniofacial growth, such as two-dimensional facial photographs, lateral cephalometry, facial plaster models, and 3D facial images obtained by laser scanning, computed tomography, or stereophotogrammetry (7,14,15,116,131,132). The methods containing X-rays have decreased because of the harm to the individuals. Noninvasive methods have been developed instead of these techniques. Furthermore, new methods have been developed due to the fact that two-dimensional recording methods are insufficient in the evaluation of three-dimensional structures. But again, some of the three-dimensional recording methods also contain harmful radiation and the applicability of methods such as facial impression is difficult. Today, there are three-dimensional recording methods such as stereophotogrammetry, which are noninvasive and easy to apply.

2.9.1. Two-dimensional Imaging Methods

There are two main two-dimensional methods; cephalometric radiographs and two-dimensional photographs. These methods are routinely used in orthodontic clinics as a recording method for older patients. However, lateral cephalometry is not used in newborns because of the harmful effects of x-rays.

Previous studies have used conventional lateral and anteroposterior cephalometric radiographs to examine the craniofacial growth, skeletal and facial soft tissues (18,131,133,134). Lateral and anteroposterior cephalometric radiographs are often used in orthodontics for diagnosis and treatment planning. But they are inadequate in the evaluation of a 3-dimensional structure, especially in the evaluation of asymmetries in individuals with unilateral cleft lip and palate.

Another traditional recording method is facial photography which delivers two-dimensional data. Two-dimensional facial photographs are often used nowadays and there are many studies that used 2D photographs to evaluate facial features ([22,135–145]). It is quite advantageous that 2D photographs are low cost so they are commonly used in daily practice. However, this method has some disadvantages. Photographic records are taken from different aspects of face such as frontal, lateral and oblique. Metric calibration is required to make precise evaluations, but this is not possible in this method (146–149). It is difficult to standardize facial photographs, especially in patients with craniofacial deformities. The quality of photo recordings is important.

The person should be well trained and experienced in photograph taking for better qualified photos. The ability of the photographer to capture a good image, especially in newborns, depends on the performance of the photographer. Furthermore, facial photographs are insufficient for tracking three-dimensional growth and it is not easy to be capture from younger individuals (150).

2.9.2. Three-dimensional Imaging Methods

Until today, many three-dimensional methods have been developed. With the help of these methods, changes in nasolabial structures could be evaluated in three dimensions. There are many old and new three-dimensional methods including facial impression method, computed tomography, laser surface scanning, stereophotogrammetry. With technological improvements better three-dimensional methods have been developed; they can be applied more easily and less harmful with shorter capture time. Thus, distortions caused by the patient's motion were prevented, patients were protected from harmful x-rays, the records were stored in the computer environment, data losses were prevented and the analyzes could be done in the computer environment. In addition, a series of independent studies have shown that various 3D surface analysis techniques have high precision and accuracy (151–162).

2.9.2.1. Facial Impression Method

The facial impression method allows three-dimensional examination of anatomical structures. Particularly, in patients with craniofacial deformity, the clarity of the recordings is very important, but there may be deterioration in the recordings due to the tension and weight of the impression. Holberg et. al. (163) have stated that impression with alginate might cause 1 to 3 mm of soft tissue deformations. Germec-Cakan et al. (164) have also stated that face morphology may be deteriorated due to the pressure of the impression material when facial models are taken and thus the reliability of this method is reduced. The resulting impression errors with alginate are most evident in the areas that are important for the assessment of the facial esthetics such as lower facial third, the nasal tip, the subnasal region, and the cheeks. Whereas, the impression errors at the forehead, the glabella and the nasal base are moderate. These disadvantages can be avoided by using lighter impression materials and by

placing patients in the upright position during the impression. In addition, movement artifacts caused by breathing during impression, led to large inaccuracies particularly in the areas of the lips and the nose. Therefore, respiration tubes may be used, but it is likely that the nasal or oral tubes also distort the soft tissues, which may influence the accuracy of the measurements. In infants, it might be a hazardous technique and may require an emergency intubation kit and the presence of a neonatologist (104,164,165).

After the impressions are taken, they are filled with hard plaster to produce plaster casts. The problems with casts include the production, data loss due to the fragility of the models, archiving, costs of models, and need of extra space for storage. Accessibility to these casts for communication between professionals is difficult (164).

2.9.2.2. Conventional Computed and Cone-Beam Computerized Tomography

Conventional computed tomography (CT), also known as computer-aided tomography (CAT), is an imaging modality that uses x-rays and computational and mathematical processes to generate detailed image data of a scanned subject (166). While this scan especially contains 3D information about hard tissues, it also contains information about soft tissues. Computed tomography can be obtained by a fan-beam or a cone-beam. Conventional tomography is fan-beam tomography. This system has some disadvantages such as having high radiation, being expensive and not being available in every hospital. Because of high radiation, routine use of this system is not possible in orthodontic treatment. On the other hand, the true color of the skin and soft tissue images cannot be determined with this method (167). Although all these disadvantages of this system, it provides precise and clear information and therefore it has an important role in dentistry (168). On the other hand, the most important advantage of this method is that images taken from patients can be saved on computers, transmitted between professionals and measurements can be made on these images.

Craniofacial cone-beam computerized tomography (CBCT) has been developed to overcome some of the limitations of conventional CT (169). CBCT has some advantages over CT, such as being less costly and having a lower radiation level than CT (170–172). However, the lower radiation dose is still much higher than conventional 2D imaging systems and other 3D imaging systems.

CBCT allows realignment of 2D images in coronal, sagittal, oblique, and various inclined planes. All raw data are obtained in a single turn with CBCT devices so the capture time is short.

3D imaging is quite useful for pretreatment evaluation of orthognathic surgery cases and the patients with craniofacial deformities such as CLP, syndromes, and facial asymmetries (173,174). Nur et al. (175) reported that facial hard and soft tissue asymmetries can be measured accurately using CBCT.

Until today, CBCT and soft tissue studies have focused more on soft tissue thickness and changes as a result of treatment. Since CBCT can show soft tissues as much as hard tissues, it has helped the researcher to understand the cause of soft tissue changes (176–181). In addition, methods such as lateral cephalometry and stereophotogrammetry are insufficient to provide information about soft tissue thickness. However, CBCT usage is limited due to high radiation exposure.

2.9.2.3. Laser Scanning Methods

Laser scanning is one of the first three-dimensional surface-imaging technologies. This method is non-invasive to capture facial morphology and soft tissue (182). The laser scanner consists of a laser beam source, object and optical sensors that detect and transmit the reflected beam to the computer. The light scattered by the object is collected at a triangulation distance from the laser, and x, y and z coordinates of the surface point are calculated. In recent studies, validity of laser scanning method has been proven (158,182–187). According to Kau et al. (158), laser scanning provides quality 3D data as well as low cost and easy to use. In addition, the 3D laser scanners can produce digital models.

Laser scanning method has been used in many studies to evaluate facial asymmetry, to evaluate soft tissue changes after orthognathic surgery and to evaluate the effects of treatments on individuals with CLP (132,188). Furthermore, Kuijpers et al. (180) have reported that laser scanner and stereophotogrammetry are reliable soft tissue imaging systems with a maximum measurement error of <1 mm.

However, this technique has several disadvantages for 3D scanning. The capturing time in this technique is very long. During scanning, patients should remain stable for one minute or longer, otherwise there may be distortions in the scanning. Distortional problems due to movement may occur during scanning of the infants

(185). Another disadvantage of this technique is the safety problem. The laser beam exposure of the eyes during scanning may be inconvenient in infants. In addition, patients are scanned with their eyes closed, which may interfere with the natural facial expression. There is an inability to capture soft tissue surface texture, which results in difficulties in identification of landmarks due to surface color (166,189,190).

2.9.2.4. Stereophotogrammetry

The method of creating a 3D image with images taken from different angles on the same plane of an object is called stereophotogrammetry. This technique is based on the principle of stereoscopic vision in all living creatures. The brain uses images from two eyes that take images from different angles to create a perception of depth in the image. The fact that the eyes are in the same plane and take images from different angles creates a 3-dimensional perception. 3D image of the object is obtained by reconstructing the images obtained with at least two calibrated cameras on the same plane at equal distance from the object. Similar to the living creatures, the images captured by two cameras in the same plane and obtained from different angles, are reconstructed in computer environment and 3D images are obtained (191,192). The 3dMDface system has two modular units with six vision cameras and an industrial-grade flash synchronized system in a single capture (Figure 2.9.2.4.).



Figure 2.9.2.4. Stereophotogrammetry device with two camera pods and flashes.

In 1944, Thalmaan (193) was one of the first to try to capture 3D images. It was also the first attempt to use stereophotogrammetry in clinics. This technique was based on the measurements from photographs. Thalmaan examined an adult with facial asymmetry and a baby with Pierre Robin syndrome. Images of the subject from two different views were taken and inserted into a plotting machine to draw 3D contour maps. In 1967, Burke and Beard (194) improved on Thalmaan's method by using simpler and less-expensive cameras. They improved and shortened the time-consuming method through applying a multiplex plotting system. The methods were used to demonstrate craniofacial deformities and soft tissue growth in children, and to measure preoperative and postoperative faces in children. In 1995, Ras et al. (191) concluded that stereophotogrammetry is an appropriate 3D registration method for quantifying and detecting development and changes in facial morphology. In 1999, Deacon et al. (195) improved the stereophotogrammetric technique. They replaced the precalibrated metric cameras and film emulsion with low-cost charge coupled device (CCD) cameras, which offered the advantage of digitized image capture for 3D automatic analysis, drastically shortening the manual analysis of stereophotogrammetry.

In stereophotogrammetry systems, it is possible to capture images in 1.5 milliseconds. In this way, disturbances that may occur as a result of patient movement are prevented and the need for patient cooperation is reduced. One of the biggest advantages of this system is the ability to capture images quickly, especially in young children, where it is difficult to achieve cooperation. The combination of fast image acquisition and wide scene coverage (up to 360 degrees) offers significant advantages over older surface imaging methods such as laser scanning (154,155,196,197).

In stereophotogrammetry systems, the ability to accurately reflect the morphology of the anomaly in patients with soft tissue deformity such as CLP and trauma patients makes possible to accurately determine the degree of asymmetric formations on the face of patients. Superimposition of preoperative and postoperative records of surgery patients can be used by orthodontists and surgeons to determine treatment planning and treatment outcomes. It also helps to evaluate postoperative changes in facial morphology (151,198,199).

Stereophotogrammetry method is noninvasive due to the absence of radiation. Therefore, this makes possible to capture images frequently from patients and provides a more detailed examination of changes in the soft tissue (162,191,192).

In 2008, Schwenzer-Zimmer et al. (200) remarked another advantages of 3D stereophotogrammetry. In stereophotogrammetry method, after capturing image, it is possible to analyze preoperative and postoperative facial features in the absence of the patient. Unlike the direct measurements, evaluation of facial morphology is easier, no time limitation and not disturbed because of patient. It facilitates data transfer especially in CLP which requires a multidisciplinary treatment approach.

The most important disadvantage of stereophotogrammetry systems is the high cost compared to standard anthropological measurement techniques. Usually, a special room and a large space are needed to use this system. This space requirement varies depending on the width of the area to be displayed, brands and hardware specifications. The precision calibration of the cameras is very important for the reliability of the images taken in these devices working with multi-camera system. In stereophotogrammetry systems, distortions may be observed during image acquisition due to dark areas (interlabial region), shaded and bright areas (eyes and eyelashes), and very indented anatomical structures (the inside of the ear). This reduces the reliability of measurements made in these regions (148,166,196).

Stereophotogrammetry systems are divided into active and passive systems. Active systems are similar to the structural lighting method. The light beam is distributed to the scanned area on the object by means of projection. High resolution 3D geometry is obtained by capturing as many algorithms as possible of the cameras and combining these algorithms from images generated by randomly transmitted rays on the object. These systems do not need an extra light source from outside, and other external lights have no effect on the system. In passive systems, no light source is needed. It is sufficient for these systems to be bright and visible with natural light. 3D images are created with images obtained from different angles. In passive systems, high-resolution digital cameras are generally needed to achieve error-free and reliable images. The normal level of ambient light to prevent distortion of the images will be advantageous to avoid glare on the surface of the scanned object (192).

The position of the individual should be adjusted so that the entire face can be seen. First, the vertical position is adjusted so that the patient’s entire face is in the viewing area. This can be done with an adjustable seat or adjustable tripods. The subnasal and submental regions are prone to loss of data or artifact formation due to lack of visualization by cameras. Proper head positioning allows these areas to appear on the image sensors. Raising the individual’s head a few degrees up makes these

areas visible. Especially in individuals with cleft lip and palate, if the nostril region is wanted to be examined in detail, the perception of the nostril region by the device can be increased by slightly tilting the head of the individual backwards (196,197,201,202).

The accuracy and reliability of 3D stereophotogrammetry have been evaluated in many studies by using different brands and types of devices (147,155,157,162,180,194,203–206). In the studies, the differences between 3D image acquisition techniques and methods, differences between the people measuring in the same device and the differences in self-repeated measurements were evaluated. The difference was generally less than 2 mm and this was not considered clinically significant (157,162,204,207). In 2006, Krimmel et al. (208) evaluated 3D stereophotogrammetry in their study on plaster casts and stated that 3D stereophotogrammetry method is accurate and reliable, it is advantageous to use especially in infants with its rapid imaging feature, and facial development can be better understood with its superimposition feature. In 2012, Sforza et al. (206) also made a research on plaster casts and stated that 3D stereophotogrammetry systems are sufficiently accurate and reliable. In 2010, Germec-Cakan et al. (164) reported that stereophotogrammetry method is better than laser scanning method to visualize the deeper tissues such as nostrils and to identify color between mucocutaneous junctions of the lip region.

3. SUBJECTS and METHODS

Our study was approved by Yeditepe University Faculty of Medicine Clinical Research Evaluation and Ethics Committee (Decision no: 895, Date: 27/09/2018). The parents of all individuals who were willing to be involved, signed the Informed Consent Form after receiving information about the study.

3.1. Subjects

This prospective clinical study was carried out on patients with CUCLP treated by NAM and primary surgeries and healthy children without CLP. As controls, 12 healthy infants who did not have CLP were included. 3D extraoral records of these individuals were taken.

3.1.1. UCLP Group

Of 41 infants with CUCLP treated by NAM at Orthodontics Clinic of Yeditepe University, Faculty of Dentistry and followed between years 2014-2019, 20 infants meeting the criteria whom parents were willing to participate were enrolled in the study group of this prospective clinical study.

The selection criteria were as follows:

- Nonsyndromic patients with complete unilateral cleft lip and palate treated by NAM by the same orthodontists (D.G.Ç. and B.N.Y.) and operated by the same surgeon (H.A.) with the same surgical procedure.
- NAM treatment started between 1-30 days
- Regular attendance for all treatment visits and follow-ups
- Cheiloplasty carried out at about 3-4 months old, palate operation at 9-10 months old.
- Patients attaining first orthodontic follow-up appointment after the surgeries within the first two years following primary surgeries.

All of the patients included in the study were treated by nasoalveolar molding therapy by two senior and experienced orthodontist according to the technique of Grayson et al. (4,5,78,79). Following NAM, the primary lip operation was carried out by a single, experienced surgeon using extended Mohler modification of rotation and

advancement technique at approximately 4 months of age. At 9 months of age, the patients were operated by the same surgeon using Sommerlad modification Bardach's Two Flap palatoplasty with radical intravelar veloplasty for palatal repair.

After primary operations, patients are routinely seen in the orthodontic clinic for annual follow-up visits. The first visit is scheduled within the first years after surgeries. In our study, the patients were evaluated at the first and second follow-up visits, with an interval of approximately 1 year (Fig. 3.1.1.). No active orthodontic treatment was applied to the patients aged between 10 and 36 months but individuals' development, dental eruptions and oral hygiene controls were performed during this observation period.

In UCLP group, the mean age of the 20 infants with complete unilateral cleft lip and palate (9 females, 11 males) at the beginning of the observation period and at the end of the observation period was given in Table 3.1.1.1. There were 11 males and 9 females (Table 3.1.1.2.). The distribution of the cleft side was shown in Table 3.1.1.3..

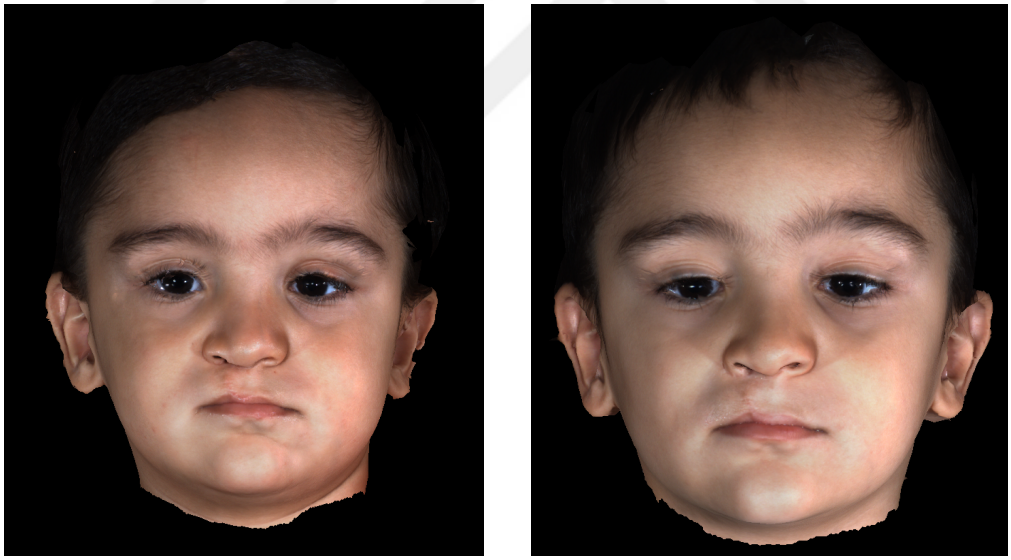


Figure 3.1.1. 3D image of an infant from UCLP group at T0 and T1

Table 3.1.1.1. The mean age of UCLP group at T0 and T1

	UCLP Group (n:20)		
	Mean ±SD	**Min**	**Max**
T0 (Month)	20.6±9.00	10	36
T1 (Month)	32.5±10.17	19	50
T1-T0 (Month)	11.9±1.83	9	15

Table 3.1.1.2. Distribution of gender in UCLP group

Gender	UCLP Group (n:20)	
	n	**Percentage**
Male	11	55%
Female	9	45%

Table 3.1.1.3. Distribution of cleft side in UCLP group

Cleft Side	UCLP Group (n:20)	
	n	**Percentage**
Right	8	40%
Left	12	60%

3.1.2. Control Group

To be able to compare the nasolabial changes of the UCLP group, an aged matched control group was composed. The inclusion criteria for individuals in the control group were as follows:

- Healthy individuals without any craniofacial deformity or syndrome, systemic or genetic disorders.
- Infants aged 10-36 months at T0 in accordance with the age of onset of follow-up diagnostic records of the UCLP group (Table 3.1.2.1.)

The control group (7 females, 5 male) consisted of 12 healthy infants who met the inclusion criteria. The parents of the individuals were informed about the aim of our study and the stereophotogrammetric recording which is not an invasive method. The parents who were willing to participate in the study were asked to bring their

babies for the 3D records to be taken at T0 and T1 (a matching observation period to that of UCLP group). The parents of infants signed a consent form and they voluntarily agreed to be a part of this study.



Figure 3.1.2. 3D image of an infant from control group at T0 and T1

Table 3.1.2.1. The mean age of the control group at T0 and T1

	Control Group (n:12)		
	Mean ±SD	**Min**	**Max**
T0 (Month)	20.83±8.96	10	35
T1 (Month)	33.25±11.08	19	50
T1-T0 (Month)	12.42±3.20	9	16

Table 3.1.2.2. Distribution of gender in the control group

Gender	**Control Group (n:12)**	
	n	**Percentage**
Male	5	41.67%
Female	7	58.33%

3.2. Methods

3.2.1. Acquisition of three-dimensional images

Three-dimensional facial images were taken from the subjects in UCLP group at two time periods, T0 (at first follow-up visit in the orthodontic clinic within the first years following the primary surgeries) and T1 (approximately 1 year after the first follow-up visit). In the control group, two consecutive records were taken with one-year intervals in accordance with the observation period of UCLP group. 3dMDface system (3dMD LLC, Atlanta, USA) was used in order to capture 3D facial images.

Before image capturing, the stereophotogrammetry device was calibrated. Calibration required two images of a specially designed panel and the software guides the operator through the process. After calibration, the child was taken to the imaging room alone or with the caregiver. The child sat alone or with the caregiver in the seat which was set 1 meter away from the cameras of the stereophotogrammetry device. The child was held in an upright position, facing towards the cameras. By controlling the image of the infant from the computer screen, the position of the chair was changed when needed. Care was given to capture natural facial expression of the children at rest position, without crying or smiling. A 3D image was obtained within 1.5 milliseconds and the captured image was controlled on the computer screen by a single operator (B.D.). The 3D image was retaken if there were distortions or missing areas on the image. The captured image was saved in the patient file in .tsb format.



Figure 3.2.1. Acquisition of an image from a child with CUCLP

3.2.2. Refinement of the Images

The 3D images taken from the subjects were imported into 3dMD Vultus software (3dMD LLC, Atlanta, USA) program. The captured images needed to be refined to clearly see the area to be evaluated (Figure 3.2.2.1.). First phase of refinement was cleaning the extrafacial parts of the child in the image. Areas such as the child's body, the parent's face or hand were selected by using the paintbrush tool in the refinement section (Figure 3.2.2.2.) and then the selected areas were deleted. After deletion, the dividing islands selection were used to separate parts that were not connected with the main image (Figure 3.2.2.3.). Afterwards, the residual segments were removed from the objects window.

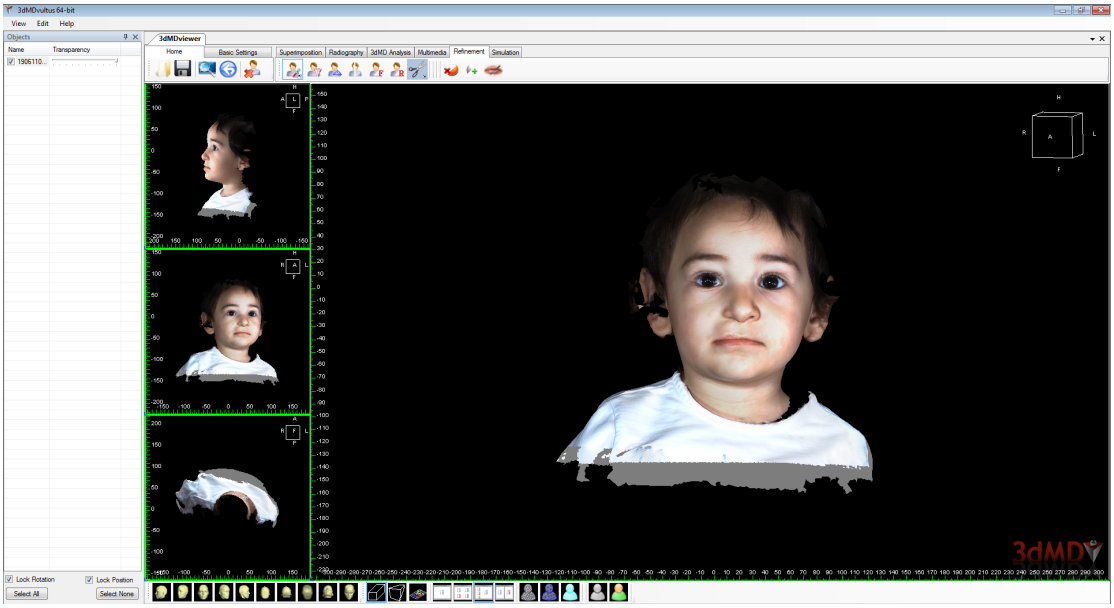


Figure 3.2.2.1. 3D image of a child with CUCLP at the beginning of refinement procedure

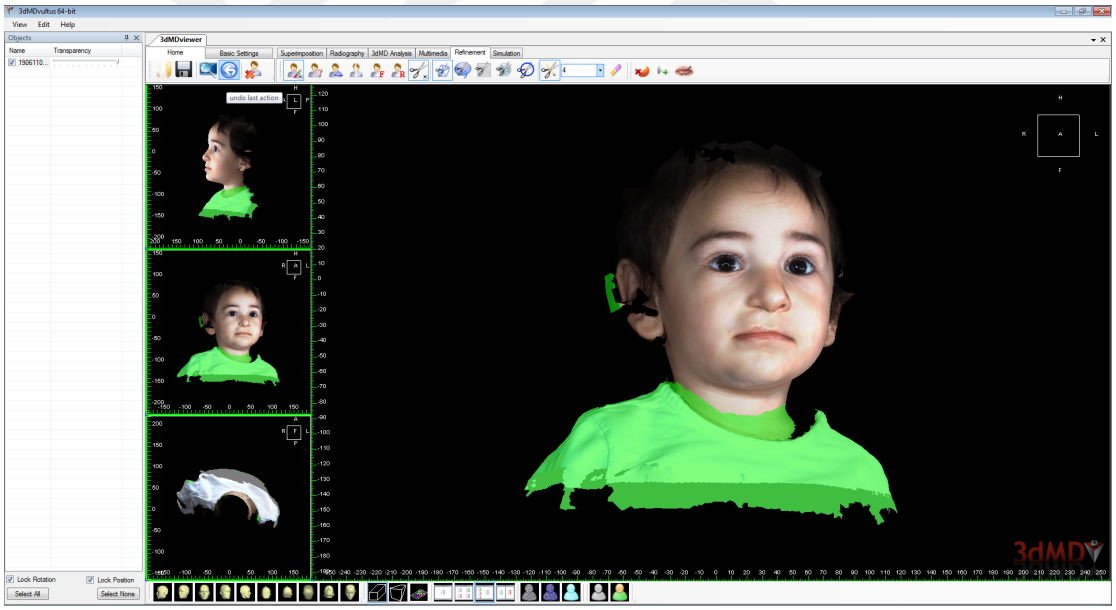


Figure 3.2.2.2. Use of paintbrush tool to select extrafacial structures

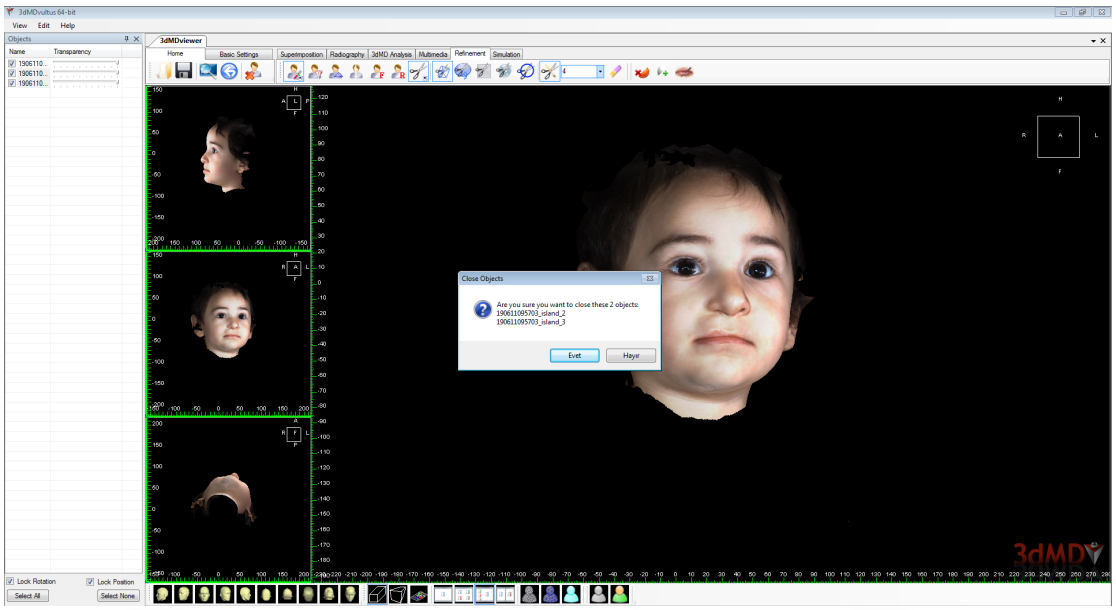


Figure 3.2.2.3. Closing of the residual parts from the objects window

Face orientation was second phase of refinement (Figure 3.2.2.4). In order to make measurements more convenient and all recordings to be in the same position, face orientation had to be adjusted. The position of the image was adjusted separately by unselect the lock rotation and lock position options for each dimension on the x, y, z coordinate system. Soft tissue nasion (N) was set as (0,0,0) point by using grids. Head pitch was adjusted in the sagittal plane by taking the Frankfurt horizontal plane (from tragus to orbital rim) as reference. Head roll was set by using the midsagittal plane as reference. Head yaw adjusted by taking the plane of the forehead from the top-down view. After these steps, the image was saved for future evaluations.

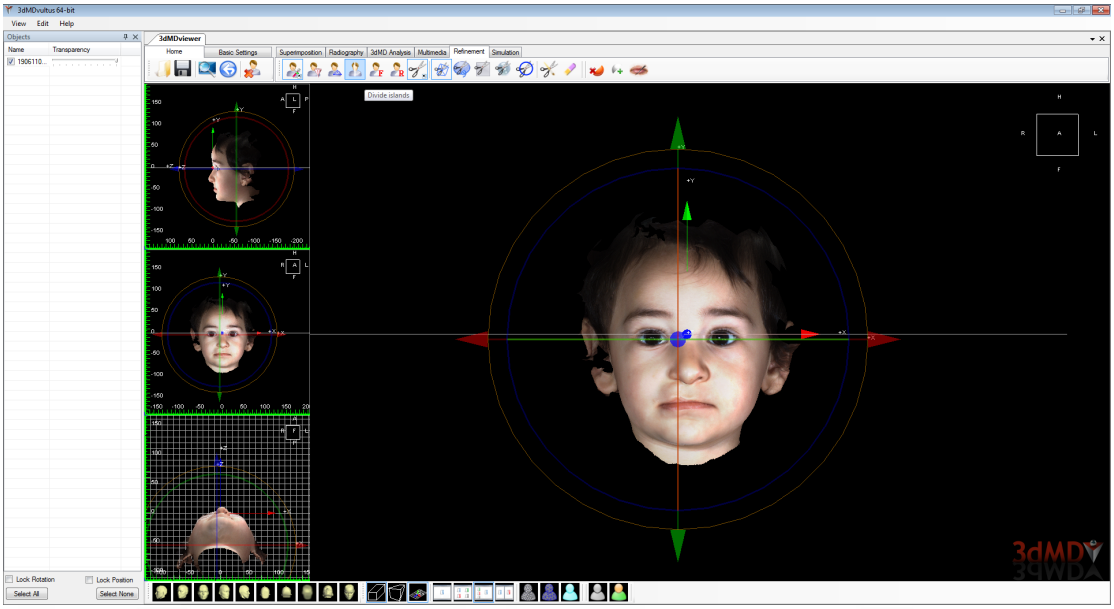


Figure 3.2.2.4. Use of grids for face orientation

3.2.3. Evaluating the Images

While determining landmarks, measurements and proportions suitable for our study, previous studies evaluating the facial development and asymmetry in the cleft patients were examined.

3.2.3.1. Landmarks

In order to prevent possible errors, the position of all landmarks determined on the 3D image was checked separately on each dimension. In total, 18 landmarks were identified. Ten of these landmarks were used twice as cleft side (C) and noncleft side (NC). In the control group, the left side was matched with the cleft side in order not to be confused in the further evaluations.

All landmarks that we used in our study are listed below (Figure 3.2.3.1.):

- **Soft Tissue Glabella Point (G):** The most prominent midline point between the eyebrows, similar to bony glabella on the frontal bone.
- **Soft Tissue Nasion Point (N):** The point in the midline of both the nasal root and the nasofrontal suture, similar to bony nasion.
- **Endocanthion Point (Enc):** The point at the inner commissure of the eye fissure. (C-NC)

- **Exocanthion Point (Exc):** The point at the outer commissure of the eye fissure. (C-NC)
- **Soft Tissue Pogonion Point (Pog):** The most anterior point of the soft tissue chin.
- **Alar Point (Al):** The most lateral point on the alar contour. (C-NC)
- **Nostril Base Point (Nb):** The lowest point of the inner border of the nostril. (C-NC)
- **Nostril Top Point (Nt):** The highest point of the inner border of the nostril. (C-NC)
- **Nostril Medial Point (Nm):** The most medial point of the inner border of the nostril. (C-NC)
- **Nostril Lateral Point (Nl):** The most lateral point of the inner border of the nostril. (C-NC)
- **Subalar Point (Sbal):** The point at the lower limit of each alar base where it disappears into the skin of the upper lip. (C-NC)
- **Pronasale Point (Prn):** The most anterior point of the tip of nose identified on the lateral view and the most upper point of the tip of the nose on the basilar view.
- **Columella Point (C):** The most anterior point of the columella.
- **Subnasal Point (Sn):** The midpoint of the angle at the columella base where the lower border of the nasal septum and surface of the upper lip meet.
- **Cheilion Point (Ch):** The point located at the left and right labial commissure. (C-NC)
- **Crista Philtri Point (Cph):** The point at each crossing of the vermilion line and the elevated margin of the philtrum. (C-NC)
- **Stomion Superior Point (Sts):** The midpoint of the lower border of the upper lip.
- **Labiale Superius Point (Ls):** The midpoint of the upper vermilion line and the most protruded point of the upper vermilion line.

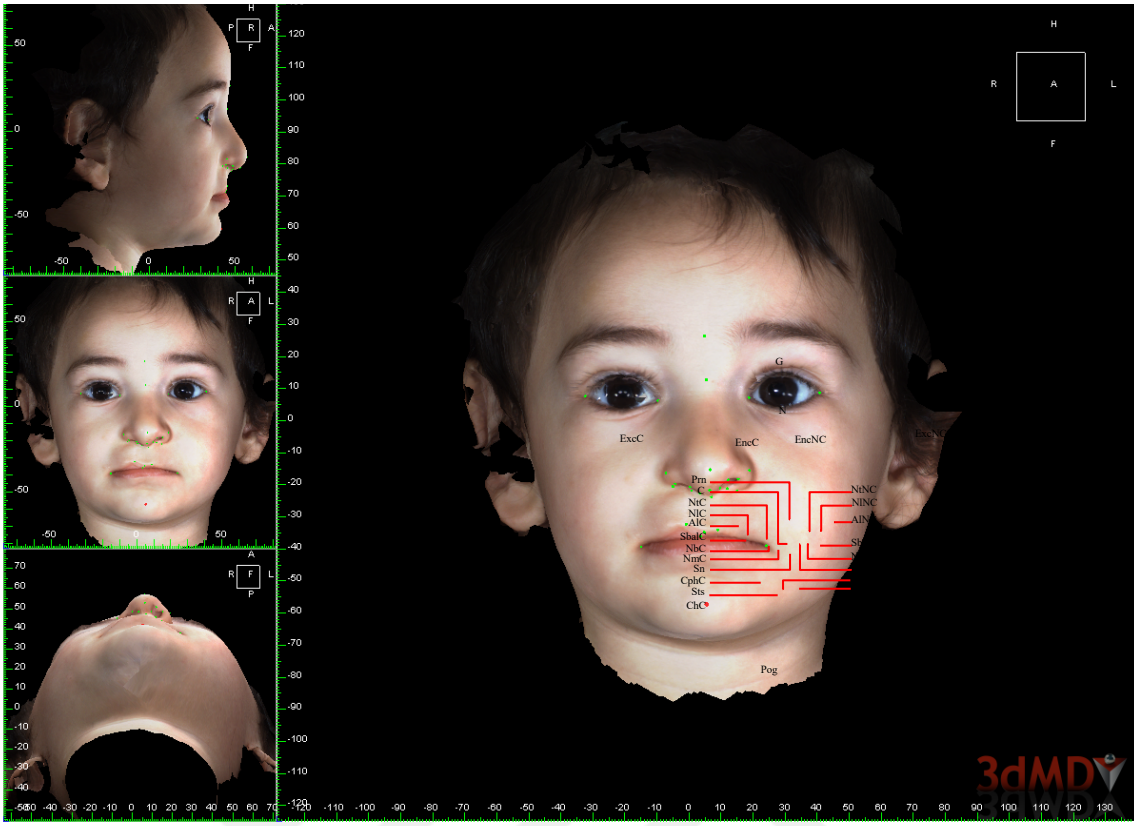


Figure 3.2.3.1. Landmarks

3.2.3.2. Measurements

3.2.3.2.A. Linear measurements

In this study, 38 linear measurements were used.

- **Upper Lip Length (Sn-Sts):** The vertical distance from subnasal to stomion superior. (Figure 3.2.3.2.A.1.)
- **Philtrum Height (Sn-Ls):** The vertical distance from subnasal to labiale superius. (Figure 3.2.3.2.A.2.)
- **Upper Lip Vermilion Height (Ls-Sts):** The vertical distance from labiale superius to stomion superior. (Figure 3.2.3.2.A.3.)
- **Mouth Width (ChC-ChNC):** The distance between cheilions (Figure 3.2.3.2.A.4.)
- **Upper Lip Transverse Length (Ch-Ls):** The horizontal distance between cheilion and labiale superior. (Figure 3.2.3.2.A.5.)

- **Philtrum Width (CphC-CphNC):** The distance between crista philtris. (Figure 3.2.3.2.A.6.)
- **Cupid's Bow Arm Width (Cph-Ls):** The distance between crista phitlri and labiale superior. (Figure 3.2.3.2.A.7.)
- **Crista Philtri Height (Cph-Sn):** The distance between crista philtri and subnasal. (Figure 3.2.3.2.A.8.)
- **Lateral Lip Height (Sbal-Ch):** The vertical distance between subalar and cheilion. (Figure 3.2.3.2.A.9.)
- **Medial Lip Height (Sbal-Cph):** The distance between subalar and crista philtri. (Figure 3.2.3.2.A.10.)
- **Alar Length (Al-Prn):** The distance from alar point to pronasale. (Figure 3.2.3.2.A.11.)
- **Total Alar Width (AlC-AlNC):** The distance between alar points. (Figure 3.2.3.2.A.12.)
- **Right and Left Alar Width (Al-Sn):** The distance between alar point and subnasal. (Figure 3.2.3.2.A.13.)
- **Nasal Dorsum Length (N-Prn):** The distance from nasion to pronasale. (Figure 3.2.3.2.A.14.)
- **Nasal Tip Protrusion (Sn-Prn):** The distance from subnasal to pronasale. (Figure 3.2.3.2.A.15.)
- **Nose Height (Sn-N):** The distance from subnasal to nasion. (Figure 3.2.3.2.A.16.)
- **Total Nasal Base Width (SbalC-SbalNC):** The distance between subalar points. (Figure 3.2.3.2.A.17.)
- **Right and Left Nasal Base Width (Sbal-Sn):** The distance between subalar and subnasal. (Figure 3.2.3.2.A.18.)
- **Nostril Long Axis (Sbal-C):** The distance between subalar and columella. (Figure 3.2.3.2.A.19.)
- **Nostril Width (Nm-Nl):** The distance between nostril medial point and nostril lateral point. (Figure 3.2.3.2.A.20.)
- **Columellar Width (NmC-NmNC):** The distance between nostril medial points. (Figure 3.2.3.2.A.21.)

- **Columellar Apex Width (NtC-NtNC):** The distance between nostril top points. (Figure 3.2.3.2.A.22.)
- **Columellar Base Width (NbC-NbNC):** The distance between nostril base points. (Figure 3.2.3.2.A.23.)
- **Nostril Height (Nt-Nb):** The distance between nostril top point and nostril base point**.** (Figure 3.2.3.2.A.24.)
- **Nasal Tip Projection (Prn-SbalC/SbalNC):** The perpendicular distance of the pronasale point to the line passing between the subalar points. (Figure 3.2.3.2.A.25.)
- **Lateral Nasal Length (Enc-Al):** The vertical distance between endocanthion and alar point. (Figure 3.2.3.2.A.26.)



Figure 3.2.3.2.A.1. Upper Lip Length



Figure 3.2.3.2.A.2. Philtrum Height



Figure 3.2.3.2.A.3. Upper Lip Vermillion Height



Figure 3.2.3.2.A.4. Mouth Width



Figure 3.2.3.2.A.5. Upper Lip Transverse Length



Figure 3.2.3.2.A.6. Philtrum Width



Figure 3.2.3.2.A.7. Cupid's Bow Arm Width



Figure 3.2.3.2.A.8. Crista Philtri Height



Figure 3.2.3.2.A.9. Lateral Lip Height



Figure 3.2.3.2.A.10. Medial Lip Height



Figure 3.2.3.2.A.11. Alar Length



Figure 3.2.3.2.A.12. Total Alar Width



Figure 3.2.3.2.A.13. Alar Width (One Side)

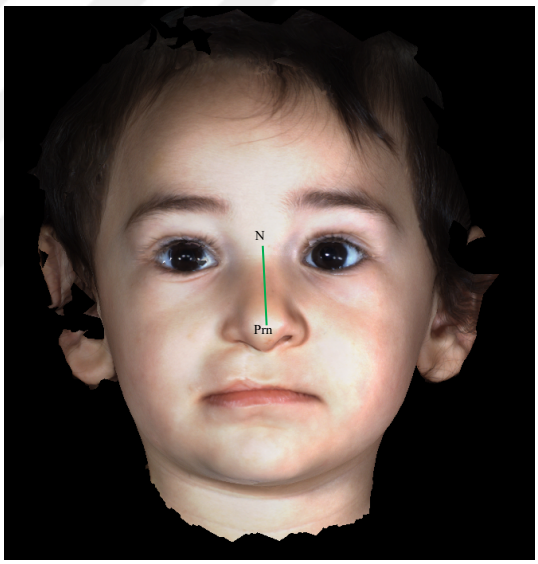


Figure 3.2.3.2.A.14. Nasal Dorsum Length



Figure 3.2.3.2.A.15. Nasal Tip Protrusion

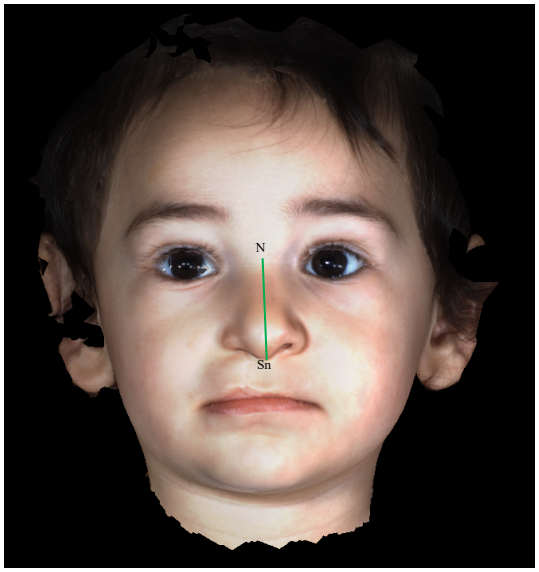


Figure 3.2.3.2.A.16. Nose Height



Figure 3.2.3.2.A.17. Total Nasal Base Width



Figure 3.2.3.2.A.18. Nasal Base Width (One Side)



Figure 3.2.3.2.A.19. Nostril Long Axis



Figure 3.2.3.2.A.20. Nostril Width



Figure 3.2.3.2.A.21. Columellar Width



Figure 3.2.3.2.A.22. Columellar Apex Width



Figure 3.2.3.2.A.23. Columellar Base Width



Figure 3.2.3.2.A.24. Nostril Height

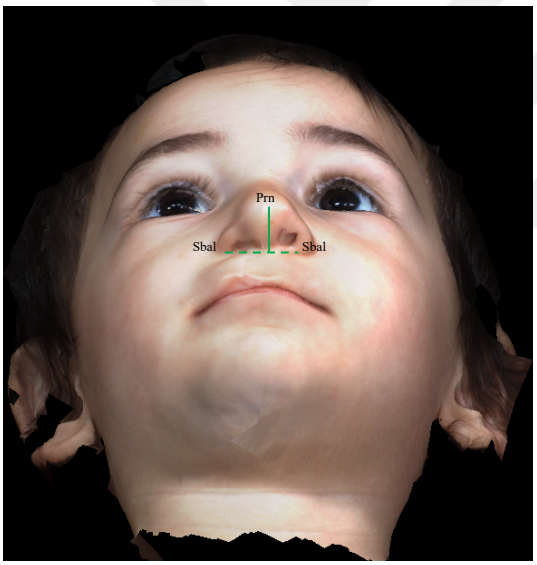


Figure 3.2.3.2.A.25. Nasal Tip Projection



Figure 3.2.3.2.A.26. Lateral Nasal Length

3.2.3.2.B. Angular measurements

In this study, 14 angular measurements were used.

- **Facial Profile Angle (N-Sn-Pog):** The angle between nasion, subnasal and pogonion. (Figure 3.2.3.2.B.1.)
- **Nasofrontal Angle (G-N-Prn):** The angle between glabella, nasion and pronasale. (Figure 3.2.3.2.B.2.)
- **Nasomental Angle (N-Prn-Pog):** The angle between nasion, pronasale and pogonion. (Figure 3.2.3.2.B.3.)
- **Nasal Tip Angle (AlC-Prn-AlNC):** The angle between alar point on cleft side, pronasale and alar point on noncleft side. (Figure 3.2.3.2.B.4.)
- **Lateral Nasal Tip Angle (C-Sn/N-Prn):** The angle between columella-subnasal plane and nasion-pronasale plane. (Figure 3.2.3.2.B.5.)
- **Nasolabial Angle (Prn-Sn-Ls):** The angle between pronasale, subnasal and labial superior. (Figure 3.2.3.2.B.6.)
- **Nasal Projection Angle (Sn-N-Prn):** The angle between subnasal, nasion and pronasale (Figure 3.2.3.2.B.7.)
- **Eyes-Mouth Angle (Exc-Exc/Ch-Ch):** The angle between exocanthion plane and cheilion plane. (Figure 3.2.3.2.B.8.)
- **Cupid's Bow Angle (CphC-Ls-CphNC):** The angle between crista philtri point on the cleft side, labiale superior and crista philtri point on the noncleft side. (Figure 3.2.3.2.B.9.)
- **Alar Wing Angulation (Al-Prn-Sn):** The distance between alar point, pronasale and subnasale. (Figure 3.2.3.2.B.10.)
- **Columella Inclination (Sbal-Sn-Prn):** The angle between subalare, subnasale and pronasale. (Figure 3.2.3.2.B.11.)
- **Upper Lip-Chin Angle (Ls-N-Pog):** The angle between labiale superior, nasion and pogonion. (Figure 3.2.3.2.B.12.)



Figure 3.2.3.2.B.1. Facial Profile Angle



Figure 3.2.3.2.B.2. Nasofrontal Angle



Figure 3.2.3.2.B.3. Nasomental Angle



Figure 3.2.3.2.B.4. Nasal Tip Angle



Figure 3.2.3.2.B.5. Lateral Nasal Tip Angle



Figure 3.2.3.2.B.6. Nasolabial Angle



Figure 3.2.3.2.B.7. Nasal Projection Angle

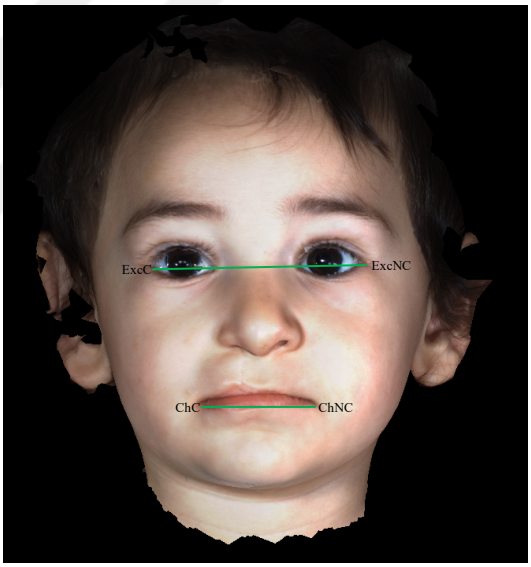


Figure 3.2.3.2.B.8. Eyes-Mouth Angle



Figure 3.2.3.2.B.9. Cupid's Bow Angle

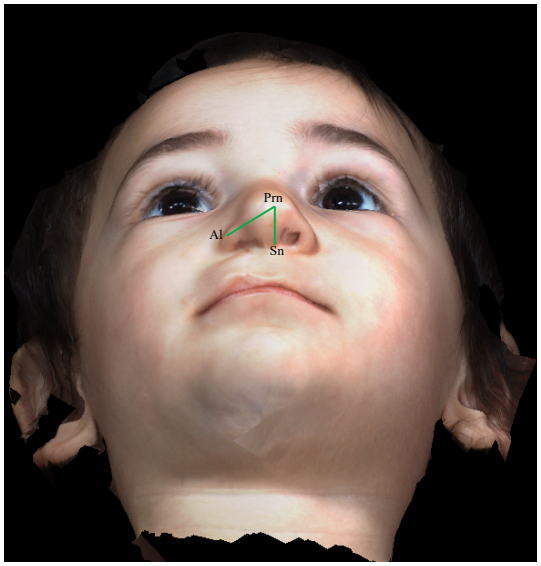


Figure 3.2.3.2.B.10. Alar Wing Angulation



Figure 3.2.3.2.B.11. Columella Inclination



Figure 3.2.3.2.B.12. Upper Lip-Chin Angle

3.2.3.2.C. Proportional measurements

In this study, 11 proportional measurements were used.

- **Cupid's Bow Arm Width NC/C:** The ratio of cupid's bow arm widths between noncleft and cleft side.
- **Alar Length NC/C:** The ratio of alar lengths between noncleft and cleft side.
- **Alar Width NC/C:** The ratio of alar widths between noncleft and cleft side.
- **Nasal Base Width NC/C:** The ratio of nasal base widths between noncleft and cleft side.
- **Nostril Long Axis NC/C:** The ratio of nostril long axises between noncleft and cleft side.
- **Nostril Width NC/C:** The ratio of nostril widths between noncleft and cleft side.
- **Nostril Height NC/C:** The ratio of nostril heights between noncleft and cleft side.
- **Lateral Nasal Length NC/C:** The ratio of lateral nasal lengths between noncleft and cleft side.
- **Upper Lip Transverse Length NC/C:** The ratio of upper lip transverse lengths between noncleft and cleft side.
- **Lateral Lip Height NC/C:** The ratio of lateral lip heights between noncleft and cleft side.
- **Medial Lip Height NC/C:** The ratio of medial lip heights between noncleft and cleft side.

3.2.3.2.D. Perimetric measurements

- **Nostril Perimeter:** The perimeter of the outermost part of the nostril. 13 unspecific points were used for the measurement of the nostril perimeter.

3.2.4. Method Error and Reproducibility

In our study, 38 linear, 14 angular, 11 proportional and 2 perimetric measurements were carried out on 64 three dimensional images. For evaluation of the measurement error and intra-operator reliability, the same investigator repeated the landmark positioning and measurement procedures on T0 and T1 3D images of 10 randomly selected patients and controls, 2 months after the original measurements.

3.2.5. Statistical Methods

In this study, statistical analyses were performed with the NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package program.

In the evaluation of the data, besides descriptive statistical methods (mean, standard deviation, median, interquartile range), the distribution of variables were examined by Shapiro – Wilk normality test. Independent t test in comparison of normally distributed variables of two independent groups, paired t test in T0 and T1 evaluations in each group, Mann Whitney-U test in comparison of non-normally distributed variables of two independent groups, and Wilcoxon test in T0 and T1 evaluations in each group were used. Significance level was determined as $p < 0.05$.

Based on the observed effect sizes, experimental statistical power analyses were conducted to determine the power of the study using G * power 3.1 program (Heinrich Heine Universitat, Dusseldorf, Germany). The sample size was calculated based on the ability to detect 0.82 mm difference for the al-ch measurement in the study group. The expected standard deviation of this difference was taken from the study of Allazzawi et al. (13). The calculation indicated that for a study with a power of 0.80 and an alpha of 0.05, we required a total of 40 subjects (20 patients for the study group, 20 individuals for the control group).

The reliability of the measurements was determined by the intraclass correlation coefficient and 95% confidence interval.

4. RESULTS

4.1. Evaluation of Method Error

In order to evaluate the method error in our study, anatomical points were determined again after 60 days by the same researcher on a total of 40 three-dimensional stereophotogrammetric records of 10 individuals randomly selected from the UCLP and the control groups. Then linear, angular, proportional and perimetric measurements were repeated. In order to evaluate the consistence between the first and second measurements, intraclass correlation coefficient and 95% confidence interval were calculated. When intraclass correlation coefficients are over 0.700, they are evaluated as reliable (209). In our study, the lowest intraclass correlation coefficient was 0.972 (0.947-0.985) and the highest intraclass correlation coefficient was 0.999 (0.998-0.999). For most of the measurements, the intraclass correlation coefficient was found to be above 0.95, and for some of the measurements, it was found to be above 0.90. Thus, the measurements were found to be reliable.

It was observed that intraclass correlation coefficients for the linear measurements ranged from 0.972 to 0.999, which were above the acceptance level of 0.700 (Table 4.1.1.).

Table 4.1.1. Intraclass correlation coefficient for the linear measurements

Linear Measurements	Intraclass Correlation Coefficient	%95 Confidence Interval
Upper Lip Length	0.996	0.993-0.998
Philtrum Height	0.996	0.992-0.998
Upper Lip Vermilion Height	0.999	0.998-0.999
Mouth Width	0.997	0.995-0.999
Upper Lip Transverse Length C	0.997	0.995-0.998
Upper Lip Transverse Length NC	0.997	0.995-0.999
Philtrum Width	0.997	0.995-0.999
Cupid's Bow Arm Width C	0.995	0.990-0.997
Cupid's Bow Arm Width NC	0.984	0.970-0.992
Crista Philtri Height C	0.992	0.985-0.996
Crista Philtri Height NC	0.993	0.986-0.996
Lateral Lip Height C	0.996	0.993-0.998
Lateral Lip Height NC	0.995	0.991-0.998
Medial Lip Height C	0.998	0.996-0.999
Medial Lip Height NC	0.993	0.987-0.996
Alar Length C	0.997	0.994-0.998
Alar Length NC	0.990	0.982-0.995
Total Alar Width	0.995	0.991-0.997
Alar Width C	0.993	0.986-0.996
Alar Width NC	0.996	0.993-0.998
Nasal Dorsum Length	0.996	0.992-0.998

Table 4.1.1. Intraclass correlation coefficient for the linear measurements (continued)

Linear Measurements	Intraclass Correlation Coefficient	%95 Confidence Interval
Nasal Tip Protrusion	0.998	0.996-0.999
Nose Height	0.985	0.973-0.992
Total Nasal Base Width	0.993	0.986-0.996
Nasal Base Width C	0.996	0.992-0.998
Nasal Base Width NC	0.998	0.996-0.999
Nostril Long Axis C	0.994	0.988-0.997
Nostril Long Axis NC	0.997	0.994-0.998
Nostril Width C	0.972	0.947-0.985
Nostril Width NC	0.986	0.973-0.992
Columellar Width	0.997	0.995-0.999
Columellar Apex Width	0.999	0.998-0.999
Columellar Base Width	0.995	0.990-0.997
Nostril Height C	0.997	0.995-0.999
Nostril Height NC	0.996	0.992-0.998
Nasal Tip Projection	0.996	0.992-0.998
Lateral Nasal Length C	0.985	0.972-0.992
Lateral Nasal Length NC	0.993	0.986-0.996

It was observed that intraclass correlation coefficients for the angular measurements ranged from 0.988 to 0.998, which were above the acceptance level of 0.700 (Table 4.1.2.).

Table 4.1.2. Intraclass correlation coefficient for the angular measurements

Angular Measurements	Intraclass Correlation Coefficient	%95 Confidence Interval
Facial Profile Angle	0.996	0.993-0.998
Nasofrontal Angle	0.998	0.997-0.999
Nasomental Angle	0.988	0.978-0.994
Nasal Tip Angle	0.994	0.989-0.997
Lateral Nasal Tip Angle	0.989	0.979-0.994
Nasolabial Angle	0.994	0.990-0.997
Nasal Projection Angle	0.993	0.987-0.996
Eyes-Mouth Angle	0.996	0.993-0.998
Cupid's Bow Angle	0.994	0.988-0.997
Alar Wing Angulation C	0.997	0.994-0.998
Alar Wing Angulation NC	0.994	0.989-0.997
Columella Inclination C	0.997	0.995-0.999
Columella Inclination NC	0.991	0.983-0.995
Upper Lip-Chin Angle	0.996	0.992-0.998

It was observed that intraclass correlation coefficients for the proportional measurements ranged from 0.977 to 0.998, which were above the acceptance level of 0.700 (Table 4.1.3.).

Table 4.1.3. Intraclass correlation coefficient for the proportional measurements

Proportional Measurements	Intraclass Correlation Coefficient	%95 Confidence Interval
Cupid's Bow Arm Width NC/C	0.996	0.992-0.998
Alar Length NC/C	0.998	0.996-0.999
Alar Width NC/C	0.991	0.983-0.995
Nasal Base Width NC/C	0.996	0.992-0.998
Nostril Long Axis NC/C	0.977	0.957-0.988
Nostril Width NC/C	0.988	0.978-0.994
Nostril Height NC/C	0.990	0.981-0.995
Lateral Nasal Length NC/C	0.995	0.990-0.997
Upper Lip Transverse Length NC/C	0.994	0.988-0.997
Lateral Lip Height NC/C	0.997	0.994-0.998
Medial Lip Height NC/C	0.996	0.991-0.998

It was observed that intraclass correlation coefficients for the perimetric measurements ranged from 0.993 to 0.995, which were above the acceptance level of 0.700 (Table 4.1.4.).

Table 4.1.4. Intraclass correlation coefficient for the perimetric measurements

Perimetric Measurements	Intraclass Correlation Coefficient	%95 Confidence Interval
Nostril Perimeter C	0.993	0.989-0.996
Nostril Perimeter NC	0.995	0.988-0.995

4.2. Comparison of Demographic Data of UCLP and Control Subjects

The demographic data of the UCLP group and the control group was evaluated (Table 4.2.1). There was no statistically significant difference in the mean age of the groups at T0 and T1 ($p>0.05$). There was no statistically significant difference in the observation period of groups as well ($p>0.05$). There was no statistically significant difference in gender distribution between groups ($p>0.05$).

Table 4.2.1. Comparison of the mean age and the observation period of the UCLP and the control groups with independent t-test

	UCLP Group (n:20)			**Control Group (n:12)**			**p**
	Mean±SD	**Min**	**Max**	**Mean±SD**	**Min**	**Max**	
T0 (Month)	20.6±9.00	10	36	20.83±8.96	10	35	0.944
T1 (Month)	32.5±10.17	19	50	33.25±11.08	19	50	0.846
T1-T0 (Month)	11.9±1.83	9	15	12.42±3.20	9	16	0.564

Table 4.2.2. Comparison of the gender distribution between groups with chi square test

Gender	**UCLP Group (n:20)**		**Control Group (n:12)**		**p**
	n	**Percentage**	**n**	**Percentage**	
Male	11	55.00	5	41.67	0.465
Female	9	45.00	7	58.33	

4.3. Comparison of Linear, Angular, Proportional and Perimetric Measurements Between the UCLP and the Control Groups at T0

4.3.1. Linear Measurements

The comparison of the linear measurements between the UCLP and the control groups at T0 was given in Table 4.3.1..

At the labial region, there were no statistically significant differences in mouth width, upper lip transverse length NC, philtrum width, cupid's bow arm width C, cupid's bow arm width NC, crista philtri height C, lateral lip height C, lateral lip height NC, medial lip height NC measurements between groups ($p>0,05$). On the other hand, upper lip length, philtrum height, upper lip vermillion height, upper lip transverse length C, crista philtra height NC, medial lip height C measurements were significantly smaller in the UCLP group compared with the control group ($p<0.001$, $p<0.05$, $p<0.001$, $p<0.05$, $p<0.05$, $p<0.01$, respectively).

At the nasal region, there were no statistically significant differences in alar length NC, total alar width, alar width NC, nasal dorsum length, nose height, total nasal base width, nasal base width C, nostril long axis C, nostril width NC, columellar base width, nostril height C, lateral nasal length C, lateral nasal length NC measurements between groups ($p>0,05$). On the other hand, alar length C, alar width C, nasal tip protrusion, nostril width C, columellar width, columellar apex width, nostril height NC, nasal tip projection measurements were significantly greater in the UCLP group compared with the control group ($p<0.001$, $p<0.05$, $p<0.001$, $p<0.05$, $p<0.05$, $p<0.01$, $p<0.01$, $p<0.05$, respectively), whereas nasal base width NC and nostril long axis NC measurements were significantly smaller in the UCLP group compared with the control group ($p<0.001$, $p<0.05$, respectively).

Table 4.3.1. Comparison of the linear measurements at T0 between the UCLP and the control groups with independent t test

Linear Measurements (mm)	T0						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Upper Lip Length	14.73±1.44	11.82	17.46	16.86±1.25	14.49	19.13	**0.0001*** **
Philtrum Height	11.64±1.46	8.90	14.40	14.01±4.03	10.40	26.00	**0.023***
Upper Lip Vermilion Height	3.81±1.17	1.50	5.31	5.89±1.24	3.79	8.29	**0.0001*** **
Mouth Width	34.32±3.65	28.79	39.49	33.7±3.03	29.55	38.08	0.624
Upper Lip Transverse Length C	19.75±2.17	14.67	24.45	21.42±2.39	17.49	24.43	**0.049***
Upper Lip Transverse Length NC	21.24±2.43	16.72	25.19	21.25±2.83	16.48	25.29	0.996
Philtrum Width	8.58±1.48	6.26	11.30	7.81±1.55	5.34	10.64	0.172
Cupid's Bow Arm Width C	4.18±0.84	2.73	6.23	4.90±3.22	2.30	14.74	0.351
Cupid's Bow Arm Width NC	4.72±0.96	3.33	6.27	5.09±2.92	2.98	13.89	0.607
Crista Philtri Height C	11.79±1.53	8.60	14.64	12.26±1.51	9.82	14.68	0.400
Crista Philtri Height NC	11.29±1.39	8.97	14.05	12.41±1.47	9.85	14.93	**0.038***
Lateral Lip Height C	21.08±3.73	15.03	34.30	21.42±2.06	17.85	24.82	0.775
Lateral Lip Height NC	22.12±3.21	17.11	32.64	21.05±2.23	16.40	23.82	0.320
Medial Lip Height C	11.25±2.16	7.97	18.77	13.26±1.02	11.90	15.89	**0.005** **
Medial Lip Height NC	12.79±1.91	10.48	18.91	13.29±1.18	11.73	15.90	0.427
Alar Length C	18.71±2.03	15.25	22.57	15.60±1.29	12.90	17.31	**0.0001*** **
Alar Length NC	15.36±1.87	13.37	20.54	15.72±1.12	13.25	17.28	0.551
Total Alar Width	27.01±2.69	22.10	33.10	25.92±1.74	23.10	28.60	0.220
Alar Width C	15.44±1.98	12.01	19.27	13.78±1.06	11.75	15.31	**0.012***
Alar Width NC	14.45±1.76	12.14	18.54	14.33±1.22	12.65	16.48	0.841

Table 4.3.1. Comparison of the linear measurements at T0 between the UCLP and the control groups with independent t test (continued)

Linear Measurements (mm)	T0						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Nasal Dorsum Length	29.21±2.79	24.29	33.47	28.97±3.66	22.08	33.33	0.837
Nasal Tip Protrusion	13.37±1.64	11.03	16.76	11.23±1.16	8.49	12.72	**0.0001*** **
Nose Height	35.79±2.94	30.73	40.09	34.26±3.64	28.50	38.33	0.202
Total Nasal Base Width	17.94±2.36	14.85	23.21	18.59±1.75	15.68	20.64	0.415
Nasal Base Width C	10.83±1.89	7.69	14.91	9.84±0.93	8.56	11.35	0.103
Nasal Base Width NC	8.29±1.36	6.08	11.43	10.33±1.04	8.41	11.61	**0.0001*** **
Nostril Long Axis C	13.57±2.22	8.33	17.77	12.97±1.32	10.47	14.40	0.403
Nostril Long Axis NC	12.01±1.78	9.53	15.30	13.28±1.16	10.97	14.60	**0.036***
Nostril Width C	9.41±2.05	5.40	15.00	7.71±1.47	6.00	9.70	**0.018***
Nostril Width NC	7.31±1.46	5.20	11.49	8.07±1.50	5.57	9.61	0.171
Columellar Width	6.27±1.67	3.75	10.05	5.07±0.96	3.38	7.17	**0.031***
Columellar Apex Width	15.43±2.72	11.15	20.97	13.07±1.11	11.44	15.62	**0.008** **
Columellar Base Width	12.84±2.17	9.85	17.51	12.00±2.45	7.25	16.16	0.323
Nostril Height C	6.35±1.48	4.06	9.81	6.54±0.97	4.40	8.30	0.694
Nostril Height NC	7.98±1.30	5.64	10.57	6.69±0.72	5.34	7.76	**0.004** **
Nasal Tip Projection	15.82±1.70	13.46	19.43	14.51±1.41	11.36	16.60	**0.032***
Lateral Nasal Length C	26.90±2.03	23.80	30.56	27.83±1.53	25.16	30.69	0.179
Lateral Nasal Length NC	26.62±3.17	15.93	31.15	28.05±1.24	26.37	30.11	0.148

(***) p <0.001, (**) p <0.01, (*) p <0.05

4.3.2. Angular Measurements

The comparison of angular measurements between the UCLP and the control groups at T0 was given in Table 4.3.2..

When the facial angles were evaluated, facial profile angle was found to be significantly greater in the UCLP group compared with the control group ($p<0.001$).

At the labial region, there was no statistically significant difference in eyes-mouth angle between groups ($p>0.05$). Whereas Cupid's bow angle was significantly greater ($p<0.05$) and upper lip-chin angle was significantly smaller in the UCLP group compared with the control group ($p<0.001$).

At the nasal region, there were no statistically significant differences in nasofrontal angle, alar wing angulation NC, columella inclination C, columella inclination NC between groups ($p>0.05$). Nasomental angle, lateral nasal tip angle and nasal projection angle were significantly greater ($p<0.01$, $p<0.05$, $p<0.01$, respectively), while nasal tip angle and alar wing angulation C were significantly smaller in the UCLP group compared with the control group ($p<0.05$).

At nasolabial region, there was no statistically significant difference in nasolabial angle between groups ($p>0.05$).

Table 4.3.2. Comparison of the angular measurements at T0 between the UCLP and the control groups with independent t test

Angular Measurements (°)	T0						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Facial Profile Angle	165.69±5.54	158.14	176.17	157.34±3.06	152.43	162.80	**0.0001*** **
Nasofrontal Angle	147.93±4.64	138.68	156.12	144.46±6.27	131.38	153.56	0.083
Nasomental Angle	137.47±4.69	128.46	149.51	132.8±3.16	127.56	138.38	**0.005** **
Nasal Tip Angle	104.84±7.8	83.75	117.07	112.35±8.26	101.91	129.63	**0.015***
Lateral Nasal Tip Angle	86.74±7.19	75.50	99.26	81.38±4.39	75.19	89.46	**0.027***
Nasolabial Angle	131.64±9.80	114.44	145.96	128.00±8.53	110.55	139.43	0.295
Nasal Projection Angle	20.73±2.38	16.79	24.72	18.21±2.32	15.35	23.13	**0.007** **
Eyes-Mouth Angle	2.51±1.59	0.51	7.36	1.65±0.77	0.91	3.44	0.090
Cupid's Bow Angle	148.86±13.13	110.20	171.20	130.05±31.31	35.70	158.80	**0.024***
Alar Wing Angulation C	54.62±6.27	43.60	68.89	59.3±4.57	52.08	70.75	**0.032***
Alar Wing Angulation NC	58.74±4.15	51.95	65.22	61.8±5.35	55.09	71.25	0.080
Columella Inclination C	105.92±8.36	90.52	120.32	109.74±3.96	102.87	117.39	0.150
Columella Inclination NC	102.46±6.32	88.53	115.28	106.45±4.93	98.72	115.09	0.071
Upper Lip-Chin Angle	6.18±2.68	0.72	11.55	11.82±2.35	6.75	15.73	**0.0001*** **

(***) p <0.001, (**) p <0.01, (*) p <0.05

4.3.3. Proportional Measurements

The comparison of the proportional measurements between the UCLP and the control groups at T0 was given in Table 4.3.3..

At the labial region, there was no statistically significant difference in cupid's bow arm width NC/C ratio. However, upper lip transverse length NC/C, lateral lip height NC/C and medial lip height NC/C proportions were significantly greater in the UCLP group compared with the control group ($p<0.05$, $p<0.01$, $p<0.001$, respectively).

At the nasal region, there was no statistically significant difference in lateral nasal length NC/C proportion between groups ($p>0.05$). Alar length NC/C, alar width NC/C, nasal base width NC/C, nostril long axis NC/C, nostril width NC/C proportions were smaller ($p<0.001$, $p<0.05$, $p<0.001$, $p<0.05$, $p<0.001$, respectively), whereas nostril height NC/C ratio was significantly greater in the UCLP group compared with the control group ($p<0,01$).

Table 4.3.3. Comparison of the proportional measurements at T0 between the UCLP and the control groups with independent t test

Proportional Measurements	T0						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Cupid's Bow Arm Width NC/C	1.15±0.25	0.73	1.59	1.08±0.20	0.71	1.54	0.397
Alar Length NC/C	0.83±0.10	0.63	0.99	1.01±0.06	0.94	1.13	**0.0001*** **
Alar Width NC/C	0.94±0.12	0.76	1.26	1.04±0.06	0.94	1.17	**0.012***
Nasal Base Width NC/C	0.79±0.18	0.50	1.20	1.05±0.08	0.90	1.20	**0.0001*** **
Nostril Long Axis NC/C	0.90±0.18	0.71	1.48	1.03±0.05	0.94	1.11	**0.032***
Nostril Width NC/C	0.80±0.19	0.51	1.29	1.05±0.11	0.92	1.30	**0.0001*** **
Nostril Height NC/C	1.29±0.22	0.91	1.65	1.03±0.10	0.90	1.21	**0.001****
Lateral Nasal Length NC/C	0.99±0.10	0.60	1.10	1.01±0.04	1.00	1.10	0.512
Upper Lip Transverse Length NC/C	1.09±0.14	0.82	1.36	0.99±0.05	0.91	1.10	**0.033***
Lateral Lip Height NC/C	1.06±0.09	0.90	1.30	0.98±0.03	0.90	1.00	**0.008****
Medial Lip Height NC/C	1.15±0.10	0.97	1.34	1.00±0.04	0.92	1.08	**0.0001*** **

(***) p <0.001, (**) p <0.01, (*) p <0.05

4.3.4. Perimetric Measurements

The comparison of the nostril perimetric measurements between the UCLP and the control groups at T0 were given in Table 4.3.4..

At the cleft side, nostril perimeter was significantly greater in the UCLP group compared with the control group ($p<0.001$). However, at noncleft side, no statistically significant difference was found in nostril perimeter between groups ($p>0.05$).

Table 4.3.4. Comparison of the perimetric measurements at T0 between the UCLP and the control groups with independent t test

Perimetric Measurements (mm)	T0						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Nostril Perimeter C	28.20±2.96	23.17	32.55	23.10±3.20	18.32	27.77	**0.0001*** **
Nostril Perimeter NC	25.23±3.24	19.38	29.79	23.46±2.68	18.99	26.97	0.121

(***) p <0.001

4.4. Comparison of Linear, Angular, Proportional and Perimetric Measurements Between the UCLP and the Control Groups at T1

4.4.1. Linear Measurements

The comparison of the linear measurements between the UCLP and the control groups at T1 was given in Table 4.4.1..

At the labial region, there were no statistically significant differences in philtrum height, mouth width, upper lip transverse length C, upper lip transverse length NC, philtrum width, cupid's bow arm width C, cupid's bow arm width NC, crista philtra height C, crista philtra height NC, lateral lip height C, lateral lip height NC, medial lip height NC between groups ($p>0.05$). However, upper lip length, upper lip vermillion height and medial lip height C were significantly smaller in the UCLP group compared with the control group ($p<0.01$).

At the nasal region, there were no statistically significant differences in alar length NC, total alar width, alar width NC, nasal dorsum length, nose height, total nasal base width, nostril long axis NC, nostril width NC, columellar base width, nostril height C, nasal tip projection, lateral nasal length C, lateral nasal length NC between groups ($p>0.05$). Alar length C, alar width C, nasal tip protrusion, nasal base width C, nostril long axis C, nostril width C, columellar width, columellar apex width, nostril height NC were significantly greater ($p<0.001$, $p<0.01$, $p<0.05$, $p<0.05$, $p<0.05$, $p<0.01$, $p<0.05$, $p<0.05$, $p<0.05$, respectively), while nasal base width NC was significantly smaller in the UCLP group compared with the control group ($p<0.01$).

Table 4.4.1. Comparison of the linear measurements at T1 between the UCLP and the control groups with independent t test

Linear Measurements (mm)	T1						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Upper Lip Length	15.63±1.89	12.89	19.29	17.69±0.99	15.97	19.05	**0.002****
Philtrum Height	12.41±1.65	9.43	15.39	14.40±3.90	11.73	26.21	0.053
Upper Lip Vermilion Height	3.91±1.47	1.30	6.10	6.02±1.5	2.99	7.93	**0.001***
Mouth Width	36.66±3.35	31.34	42.54	35.80±3.23	32.12	42.23	0.483
Upper Lip Transverse Length C	21.64±2.34	17.66	26.37	22.09±2.29	18.49	25.72	0.596
Upper Lip Transverse Length NC	21.86±2.43	16.77	26.97	22.24±2.31	17.42	24.71	0.667
Philtrum Width	9.35±1.84	5.94	11.88	8.76±1.84	5.92	11.67	0.390
Cupid's Bow Arm Width C	4.88±1.21	2.88	6.67	5.11±2.99	2.84	13.92	0.754
Cupid's Bow Arm Width NC	4.72±1.00	3.39	6.78	5.67±2.78	3.80	14.05	0.172
Crista Philtri Height C	12.64±1.48	9.65	15.29	12.84±1.30	10.92	15.12	0.705
Crista Philtri Height NC	12.15±1.45	10.26	15.00	12.87±1.35	10.75	15.30	0.175
Lateral Lip Height C	21.43±2.10	17.03	25.58	21.99±1.69	19.27	25.06	0.443
Lateral Lip Height NC	22.49±2.24	18.88	27.08	21.89±1.94	18.42	24.82	0.452
Medial Lip Height C	11.57±1.70	7.53	14.65	13.70±1.48	11.04	17.15	**0.001***
Medial Lip Height NC	13.40±1.30	11.47	15.82	13.47±1.24	11.72	16.52	0.875
Alar Length C	18.92±1.86	14.11	21.72	16.31±1.30	14.30	18.29	**0.0001*****
Alar Length NC	16.12±1.59	12.20	19.10	16.46±1.21	14.40	19.20	0.525
Total Alar Width	27.57±2.74	20.90	32.80	26.54±1.84	23.90	30.30	0.256
Alar Width C	16.01±1.92	11.93	19.51	14.27±0.89	12.97	15.93	**0.006****
Alar Width NC	14.52±1.5	11.22	17.11	14.78±1.41	12.74	18.06	0.642

Table 4.4.1. Comparison of the linear measurements at T1 between the UCLP and the control groups with independent t test (continued)

Linear Measurements (mm)	T1						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Nasal Dorsum Length	31.36±2.52	26.10	35.90	30.78±3.69	23.70	36.50	0.596
Nasal Tip Protrusion	13.68±1.94	10.70	17.60	11.85±1.63	8.50	14.70	**0.011***
Nose Height	37.73±2.85	32.49	42.36	36.35±3.85	29.73	42.53	0.255
Total Nasal Base Width	19.08±2.61	15.95	24.73	18.98±1.94	16.15	21.97	0.910
Nasal Base Width C	11.8±1.98	8.70	17.10	10.19±1.06	8.40	11.60	**0.015***
Nasal Base Width NC	8.82±1.53	6.03	11.69	10.46±1.02	9.00	11.73	**0.003****
Nostril Long Axis C	14.61±1.75	11.69	19.00	13.23±1.34	11.18	15.03	**0.025****
Nostril Long Axis NC	12.54±1.7	9.99	16.32	13.56±0.94	11.79	14.53	0.067
Nostril Width C	10.27±1.94	6.64	14.65	8.30±1.48	5.86	10.47	**0.005****
Nostril Width NC	7.41±1.57	5.03	11.02	8.31±1.60	5.64	10.42	0.128
Columellar Width	6.14±1.38	4.19	9.07	5.16±0.76	4.20	6.49	**0.032***
Columellar Apex Width	15.20±3.12	9.53	21.23	13.10±1.55	10.24	15.15	**0.038***
Columellar Base Width	12.88±1.64	9.86	15.89	12.73±1.55	10.47	15.81	0.790
Nostril Height C	6.88±1.78	3.55	9.27	6.98±0.79	5.47	8.43	0.847
Nostril Height NC	8.26±1.38	5.13	10.68	7.26±0.71	6.04	8.36	**0.027***
Nasal Tip Projection	16.62±1.98	13.30	21.50	15.22±1.74	11.50	17.70	0.052
Lateral Nasal Length C	27.87±2.39	22.70	31.43	28.01±2.77	23.73	33.10	0.877
Lateral Nasal Length NC	27.92±2.59	22.58	32.63	28.34±2.47	24.36	31.42	0.653

(***) p <0.001, (**) p <0.01, (*) p <0.05

4.4.2. Angular Measurements

The comparison of the angular measurements between the UCLP and the control groups at T1 was given in Table 4.4.2..

When facial angles were evaluated, facial profile angle was significantly greater in the UCLP group compared with the control group ($p<0.001$).

At the labial region, there was no statistically significant difference in eyes-mouth angle between groups ($p>0.05$), whereas Cupid's bow angle was significantly greater ($p<0.01$) and upper lip-chin angle was significantly smaller in the UCLP group compared with the control group ($p<0.001$).

At the nasal region, there were no statistically significant differences in nasofrontal angle, nasal tip angle, alar wing angulation C, alar wing angulation NC, columella inclination C, columella inclination NC between groups ($p>0.05$). Whereas, nasomental angle, lateral nasal tip angle and nasal projection angle were significantly greater in the UCLP group compared with the control group ($p<0.05$, $p<0.01$, $p<0.05$, respectively).

At the nasolabial region, there was no statistically significant difference in the nasolabial angle between groups ($p>0.05$).

Table 4.4.2. Comparison of the angular measurements at T1 between the UCLP and the control groups with independent t test

Angular Measurements (°)	T1						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Facial Profile Angle	166.47±5.79	154.73	175.26	158.73±3.42	152.64	165.41	**0.0001*** **
Nasofrontal Angle	149.86±4.73	138.49	158.95	146.03±5.90	137.47	156.14	0.052
Nasomental Angle	137.88±4.52	126.13	144.89	133.96±2.73	129.32	139.42	**0.011***
Nasal Tip Angle	103.67±6.66	89.67	117.46	108.71±7.99	94.38	119.80	0.064
Lateral Nasal Tip Angle	89.40±6.91	77.02	100.64	81.59±5.06	74.32	92.65	**0.002****
Nasolabial Angle	131.76±10.49	113.60	149.10	128.78±9.62	111.40	141.00	0.428
Nasal Projection Angle	20.16±2.56	16.88	26.70	17.95±2.10	14.91	21.25	**0.017***
Eyes-Mouth Angle	2.53±1.71	0.41	6.73	2.03±1.48	0.44	6.03	0.407
Cupid's Bow Angle	154.94±7.87	141.70	168.90	131.92±29.72	41.50	151.50	**0.002****
Alar Wing Angulation C	56.07±5.24	48.90	66.66	58.46±3.19	53.47	65.64	0.164
Alar Wing Angulation NC	57.43±4.77	47.90	64.27	60.38±4.66	52.01	66.63	0.097
Columella Inclination C	106.47±5.67	98.66	122.65	108.41±3.64	101.41	113.53	0.299
Columella Inclination NC	106.15±7.87	92.19	130.35	107.01±5.38	97.14	114.51	0.740
Upper Lip-Chin Angle	5.74±2.95	0.31	11.32	10.77±3.19	5.86	16.26	**0.0001*** **

(***) p <0.001, (**) p <0.01, (*) p <0.05

4.4.3. Proportional Measurements

The comparison of the proportional measurements between the UCLP and the control groups at T1 was given in Table 4.4.3..

At the labial region, there was no statistically significant difference in upper lip transverse length NC/C proportion between groups ($p>0.05$). Lateral lip height NC/C and medial lip height NC/C proportions were significantly greater ($p<0.01$, $p<0.001$, respectively), while cupid's bow arm width NC/C proportion was significantly smaller in the UCLP group compared with the control group ($p<0.05$).

At the nasal region, there was no statistically significant difference in lateral nasal length NC/C proportion between groups ($p>0.05$). Alar length NC/C, alar width NC/C, nasal base width NC/C, nostril long axis NC/C, nostril width NC/C proportions were smaller ($p<0.001$, $p<0.01$, $p<0.001$, $p<0.01$, $p<0.001$, respectively), whereas nostril height NC/C proportion was significantly greater in the UCLP group compared with the control group ($p<0.01$).

Table 4.4.3. Comparison of the proportional measurements at T1 between the UCLP and the control groups with independent t test

Proportional Measurements	T1						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Cupid's Bow Arm Width NC/C	1.00±0.21	0.58	1.36	1.16±0.15	0.88	1.35	**0.033***
Alar Length NC/C	0.85±0.08	0.69	1.05	1.01±0.05	0.94	1.11	**0.0001*****
Alar Width NC/C	0.91±0.10	0.70	1.10	1.03±0.06	1.00	1.10	**0.001****
Nasal Base Width NC/C	0.76±0.16	0.49	1.04	1.03±0.08	0.86	1.12	**0.0001*****
Nostril Long Axis NC/C	0.87±0.14	0.57	1.15	1.03±0.06	0.91	1.09	**0.001****
Nostril Width NC/C	0.74±0.15	0.43	0.92	1.00±0.09	0.86	1.21	**0.0001*****
Nostril Height NC/C	1.25±0.25	0.79	1.66	1.04±0.08	0.88	1.14	**0.009****
Lateral Nasal Length NC/C	1.00±0.07	0.86	1.12	1.01±0.06	0.90	1.14	0.656
Upper Lip Transverse Length NC/C	1.02±0.11	0.84	1.22	1.01±0.04	0.94	1.08	0.759
Lateral Lip Height NC/C	1.05±0.07	0.93	1.22	1.00±0.02	0.96	1.02	**0.009****
Medial Lip Height NC/C	1.17±0.12	1.02	1.53	0.99±0.04	0.90	1.06	**0.0001*****

(***) p <0.001, (**) p <0.01, (*) p <0.05

4.4.4. Perimetric Measurements

The comparison of the nostril perimetric measurements between the UCLP and the control groups at T1 was given in Table 4.4.4..

At the cleft side, nostril perimeter was significantly greater in the UCLP group compared with the control group ($p<0.001$). However, at the noncleft side, there was no statistically significant difference in nostril perimeter between groups ($p>0.05$).

Table 4.4.4. Comparison of the perimetric measurements at T1 between the UCLP and the control groups with independent t test

Perimetric Measurements (mm)	T1						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Nostril Perimeter C	29.97±3.43	22.85	36.09	24.79±3.08	20.58	29.73	**0.0001*** **
Nostril Perimeter NC	25.85±3.49	19.60	31.05	25.08±2.86	20.96	30.16	0.524

(***) p <0.001

4.5. Comparison of Linear, Angular, Proportional and Perimetric Measurements of the UCLP Group at T0 and T1

4.5.1. Linear Measurements

The comparison of the linear measurements of the UCLP group between T0 and T1 was given in Table 4.5.1..

At the labial region, upper lip vermilion height, upper lip transverse length NC, cupid's bow arm width NC, lateral lip height C, lateral lip height NC, medial lip height C, medial lip height NC measurements did not change significantly from T0 to T1 ($p>0.05$). However, upper lip length, philtrum height, mouth width, upper lip transverse length C, philtrum width, cupid's bow arm width C, crista philtri height C and crista philtri height NC measurements increased significantly in the UCLP group ($p<0.05$, $p<0.01$, $p<0.01$,$p<0.01$, $p<0.05$, $p<0.01$, $p<0.01$, $p<0.01$, respectively).

At the nasal region, alar length C, alar width NC, nasal tip protrusion, nasal base width NC, nostril long axis NC, nostril width NC, columellar width, columellar apex width, columellar base width, nostril height C, nostril height NC did not change significantly from T0 to T1 ($p>0.05$). Whereas, alar length NC, total alar width, alar width C, nasal dorsum length, nose height, total nasal base width, nasal base width C, nostril long axis C, nostril width C, nasal tip projection, lateral nasal length C and lateral nasal length NC increased significantly in the UCLP group ($p<0.05$, $p<0.05$, $p<0.01$, $p<0.001$, $p<0.001$, $p<0.05$, $p<0.05$, $p<0.05$, $p<0.05$, $p<0.001$, $p<0.01$, $p<0.05$, respectively).

Table 4.5.1. Comparison of the linear measurements of the UCLP group at T0 and T1 with paired t test

Linear Measurements (mm)	UCLP Group (n:20)							p
	T0			T1			T1-T0	
	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	
Upper Lip Length	14.73±1.44	11.82	17.46	15.63±1.89	12.89	19.29	0.91±1.7	**0.027***
Philtrum Height	11.64±1.46	8.90	14.40	12.41±1.65	9.43	15.39	0.77±1.16	**0.008****
Upper Lip Vermilion Height	3.81±1.17	1.50	5.31	3.91±1.47	1.30	6.10	0.11±1.38	0.738
Mouth Width	34.32±3.65	28.79	39.49	36.66±3.35	31.34	42.54	2.34±2.85	**0.002****
Upper Lip Transverse Length C	19.75±2.17	14.67	24.45	21.64±2.34	17.66	26.37	1.89±2.18	**0.001****
Upper Lip Transverse Length NC	21.24±2.43	16.72	25.19	21.86±2.43	16.77	26.97	0.61±2.23	0.234
Philtrum Width	8.58±1.48	6.26	11.30	9.35±1.84	5.94	11.88	0.77±1.63	**0.049***
Cupid's Bow Arm Width C	4.18±0.84	2.73	6.23	4.88±1.21	2.88	6.67	0.7±0.98	**0.005****
Cupid's Bow Arm Width NC	4.72±0.96	3.33	6.27	4.72±1.00	3.39	6.78	0±0.96	0.996
Crista Philtri Height C	11.79±1.53	8.60	14.64	12.64±1.48	9.65	15.29	0.85±1.24	**0.006****
Crista Philtri Height NC	11.29±1.39	8.97	14.05	12.15±1.45	10.26	15.00	0.86±1.25	**0.006****
Lateral Lip Height C	21.08±3.73	15.03	34.30	21.43±2.10	17.03	25.58	0.35±4.19	0.714
Lateral Lip Height NC	22.12±3.21	17.11	32.64	22.49±2.24	18.88	27.08	0.37±3.67	0.656
Medial Lip Height C	11.25±2.16	7.97	18.77	11.57±1.70	7.53	14.65	0.32±2.32	0.544
Medial Lip Height NC	12.79±1.91	10.48	18.91	13.40±1.30	11.47	15.82	0.6±1.88	0.168
Alar Length C	18.71±2.03	15.25	22.57	18.92±1.86	14.11	21.72	0.22±1.13	0.400
Alar Length NC	15.36±1.87	13.37	20.54	16.12±1.59	12.20	19.10	0.76±1.55	**0.041***
Total Alar Width	27.01±2.69	22.10	33.10	27.57±2.74	20.90	32.80	0.56±0.99	**0.02***
Alar Width C	15.44±1.98	12.01	19.27	16.01±1.92	11.93	19.51	0.57±0.85	**0.007****
Alar Width NC	14.45±1.76	12.14	18.54	14.52±1.50	11.22	17.11	0.08±1.47	0.815

Table 4.5.1. Comparison of the linear measurements of the UCLP group at T0 and T1 with paired t test (continued)

Linear Measurements (mm)	UCLP Group (n:20)							p
	T0			T1			T1-T0	
	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	
Nasal Dorsum Length	29.21±2.79	24.29	33.47	31.36±2.52	26.10	35.90	2.15±1.99	**0.0001*** **
Nasal Tip Protrusion	13.37±1.64	11.03	16.76	13.68±1.94	10.70	17.60	0.31±1.08	0.217
Nose Height	35.79±2.94	30.73	40.09	37.73±2.85	32.49	42.36	1.94±1.8	**0.0001*** **
Total Nasal Base Width	17.94±2.36	14.85	23.21	19.08±2.61	15.95	24.73	1.14±1.91	**0.015***
Nasal Base Width C	10.83±1.89	7.69	14.91	11.8±1.98	8.70	17.10	0.97±1.73	**0.022***
Nasal Base Width NC	8.29±1.36	6.08	11.43	8.82±1.53	6.03	11.69	0.53±1.17	0.058
Nostril Long Axis C	13.57±2.22	8.33	17.77	14.61±1.75	11.69	19.00	1.04±1.64	**0.011***
Nostril Long Axis NC	12.01±1.78	9.53	15.30	12.54±1.7	9.99	16.32	0.53±1.38	0.101
Nostril Width C	9.41±2.05	5.40	15.00	10.27±1.94	6.64	14.65	0.86±1.71	**0.037***
Nostril Width NC	7.31±1.46	5.20	11.49	7.41±1.57	5.03	11.02	0.1±0.9	0.627
Columellar Width	6.27±1.67	3.75	10.05	6.14±1.38	4.19	9.07	-0.13±2.13	0.785
Columellar Apex Width	15.43±2.72	11.15	20.97	15.20±3.12	9.53	21.23	-0.23±2.59	0.694
Columellar Base Width	12.84±2.17	9.85	17.51	12.88±1.64	9.86	15.89	0.05±1.8	0.912
Nostril Height C	6.35±1.48	4.06	9.81	6.88±1.78	3.55	9.27	0.53±1.2	0.065
Nostril Height NC	7.98±1.30	5.64	10.57	8.26±1.38	5.13	10.68	0.28±0.93	0.198
Nasal Tip Projection	15.82±1.7	13.46	19.43	16.62±1.98	13.30	21.50	0.79±0.73	**0.0001*** **
Lateral Nasal Length C	26.90±2.03	23.80	30.56	27.87±2.39	22.70	31.43	0.97±1.48	**0.009****
Lateral Nasal Length NC	26.62±3.17	15.93	31.15	27.92±2.59	22.58	32.63	1.3±2.71	**0.045***

(***) p <0.001, (**) p <0.01, (*) p <0.05

4.5.2. Angular Measurements

The comparison of the angular measurements of the UCLP group between T1 and T0 was given in Table 4.5.2..

When the facial angles were evaluated, it was found that there were no statistically significant changes in facial profile angle between T0 and T1 ($p>0.05$).

At the labial region, there were no statistically significant changes in eyes-mouth angle and upper lip-chin angle between T0 and T1 ($p>0.05$), while cupid's bow angle increased statistically in the UCLP group ($p<0.05$).

At the nasal region, there were no statistically significant changes in nasomental angle, nasal tip angle, nasal projection angle, alar wing angulation C, alar wing angulation NC, columella inclination C and columella inclination NC from T0 to T1 ($p>0.05$), whereas nasofrontal angle and lateral nasal tip angle increased significantly in the UCLP group ($p<0.01$, $p<0.001$, respectively).

At the nasolabial region, nasolabial angle did not change significantly from T0 to T1 in the UCLP group ($p>0.05$).

Table 4.5.2. Comparison of the angular measurements of the UCLP group at T0 and T1 with paired t test

Angular Measurements (º)	UCLP Group (n:20)							p
	T0			T1			T1-T0	
	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	
Facial Profile Angle	165.69±5.54	158.14	176.17	166.47±5.79	154.73	175.26	0.78±4.46	0.447
Nasofrontal Angle	147.93±4.64	138.68	156.12	149.86±4.73	138.49	158.95	1.93±2.17	**0.001****
Nasomental Angle	137.47±4.69	128.46	149.51	137.88±4.52	126.13	144.89	0.41±2.81	0.524
Nasal Tip Angle	104.84±7.80	83.75	117.07	103.67±6.66	89.67	117.46	-1.16±4.56	0.268
Lateral Nasal Tip Angle	86.74±7.19	75.50	99.26	89.40±6.91	77.02	100.64	2.66±2.71	**0.0001*****
Nasolabial Angle	131.64±9.8	114.44	145.96	131.76±10.49	113.60	149.10	0.12±7.83	0.945
Nasal Projection Angle	20.73±2.38	16.79	24.72	20.16±2.56	16.88	26.70	-0.56±1.81	0.182
Eyes-Mouth Angle	2.51±1.59	0.51	7.36	2.53±1.71	0.41	6.73	0.02±1.86	0.964
Cupid's Bow Angle	148.86±13.13	110.20	171.20	154.94±7.87	141.70	168.90	6.07±12.62	**0.044***
Alar Wing Angulation C	54.62±6.27	43.60	68.89	56.07±5.24	48.90	66.66	1.45±3.88	0.111
Alar Wing Angulation NC	58.74±4.15	51.95	65.22	57.43±4.77	47.90	64.27	-1.32±5.14	0.267
Columella Inclination C	105.92±8.36	90.52	120.32	106.47±5.67	98.66	122.65	0.55±6.39	0.707
Columella Inclination NC	102.46±6.32	88.53	115.28	106.15±7.87	92.19	130.35	3.69±7.99	0.053
Upper Lip-Chin Angle	6.18±2.68	0.72	11.55	5.74±2.95	0.31	11.32	-0.43±2.13	0.373

(***) p <0.001, (**) p <0.01, (*) p <0.05

4.5.3. Proportional Measurements

The comparison of the proportional measurements of the UCLP group between T0 and T1 was given in Table 4.5.3..

At the labial region, there were no statistically significant changes in lateral lip height NC/C and medial lip height NC/C proportions between T0 and T1 ($p>0.05$). On the other hand, cupid's bow arm width NC/C proportion decreased significantly and upper lip transverse length NC/C proportion increased significantly in the UCLP group ($p<0.01$, $p<0.05$, respectively).

At the nasal region, there were no statistically significant changes in alar length NC/C, alar width NC/C, nasal base width NC/C, nostril long axis NC/C, nostril width NC/C, nostril height NC/C and lateral nasal length NC/C proportions from T0 to T1 ($p>0.05$).

Table 4.5.3. Comparison of the proportional measurements of the UCLP group at T0 and T1 with paired t test

Proportional Measurements	UCLP Group (n:20)							p
	T0			T1			T1-T0	
	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	
Cupid's Bow Arm Width NC/C	1.15±0.25	0.73	1.59	1.00±0.21	0.58	1.36	-0.15±0.23	**0.007****
Alar Length NC/C	0.83±0.10	0.63	0.99	0.85±0.08	0.69	1.05	0.03±0.08	0.143
Alar Width NC/C	0.94±0.12	0.76	1.26	0.91±0.10	0.70	1.10	-0.03±0.12	0.273
Nasal Base Width NC/C	0.79±0.18	0.50	1.20	0.76±0.16	0.49	1.04	-0.02±0.15	0.481
Nostril Long Axis NC/C	0.90±0.18	0.71	1.48	0.87±0.14	0.57	1.15	-0.04±0.16	0.326
Nostril Width NC/C	0.80±0.19	0.51	1.29	0.74±0.15	0.43	0.92	-0.06±0.21	0.178
Nostril Height NC/C	1.29±0.22	0.91	1.65	1.25±0.25	0.79	1.66	-0.04±0.24	0.444
Lateral Nasal Length NC/C	0.99±0.10	0.60	1.10	1.00±0.07	0.86	1.12	0.01±0.08	0.449
Upper Lip Transverse Length NC/C	1.09±0.14	0.82	1.36	1.02±0.11	0.84	1.22	-0.07±0.12	**0.016***
Lateral Lip Height NC/C	1.06±0.09	0.90	1.30	1.05±0.07	0.93	1.22	0±0.09	0.824
Medial Lip Height NC/C	1.15±0.10	0.97	1.34	1.17±0.12	1.02	1.53	0.02±0.14	0.481

(**) p <0.01, (*) p <0.05

4.5.4. Perimetric Measurements

The comparison of the nostril perimeters of the UCLP group between T0 and T1 was given in Table 4.5.4..

At the cleft side, nostril perimeter increased significantly in the UCLP group ($p<0.01$). However, there was no statistically significant change in nostril perimeter at noncleft side between T0 and T1 ($p>0.05$).

Table 4.5.4. Comparison of the perimetric measurements of the UCLP group at T0 and T1 with paired t test

Perimetric Measurements (mm)	UCLP Group (n:20)							p
	T0			T1			T1-T0	
	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	
Nostril Perimeter C	28.20±2.96	23.17	32.55	29.97±3.43	22.85	36.09	1.77±2.56	**0.006****
Nostril Perimeter NC	25.23±3.24	19.38	29.79	25.85±3.49	19.60	31.05	0.62±1.85	0.149

(**) p <0.01

4.6. Comparison of Linear, Angular, Proportional and Perimetric Measurements of the Control Group at T0 and T1

4.6.1. Linear Measurements

The comparison of the linear measurements of the control group between T0 and T1 was given in Table 4.6.1..

At the labial region, there were no statistically significant changes in upper lip vermillion height, cupid's bow arm width L, medial lip height L and medial lip height R from T0 to T1 ($p>0.05$). Whereas, upper lip length, philtrum height, mouth width, upper lip transverse length L, upper lip transverse length R, philtrum width, cupid's bow arm width R, crista philtri height L, crista philtri height R, lateral lip height L and lateral lip height R measurements increased significantly in the control group ($p<0.01$, $p<0.05$, $p<0.001$, $p<0.01$, $p<0.01$, $p<0.01$, p<.,01, $p<0.01$, $p<0.05$, $p<0.05$, $p<0.05$, respectively).

At the nasal region, there were no statistically significant changes in alar width R, total nasal base width, nasal base width L, nasal base width R, nostril long axis L, nostril long axis R, nostril width R, columellar width, columellar apex width, columellar base width and nostril height L between T0 and T1 ($p>0.05$). On the other hand, alar length L, alar length R, total alar width, alar width L, nasal dorsum length, nasal tip protrusion, nose height, nostril width L, nostril height R and nasal tip projection measurements increased significantly in the control group ($p<0.05$, $p<0.05$, $p<0.05$, $p<0.01$, $p<0.01$, $p<0.05$, $p<0.01$, $p<0.05$, $p<0.01$, $p<0.01$, respectively).

Table 4.6.1. Comparison of the linear measurements of the control group at T0 and T1 with paired t test

Linear Measurements (mm)	Control Group (n:12)							p
	T0			T1			T1-T0	
	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	
Upper Lip Length	16.86±1.25	14.49	19.13	17.69±0.99	15.97	19.05	0.83±0.73	**0.002****
Philtrum Height	14.01±4.03	10.40	26.00	14.4±3.90	11.73	26.21	0.39±0.52	**0.024***
Upper Lip Vermilion Height	5.89±1.24	3.79	8.29	6.02±1.50	2.99	7.93	0.13±0.75	0.574
Mouth Width	33.70±3.03	29.55	38.08	35.80±3.23	32.12	42.23	2.1±1.28	**0.0001*****
Upper Lip Transverse Length L	21.42±2.39	17.49	24.43	22.09±2.29	18.49	25.72	0.67±0.62	**0.003****
Upper Lip Transverse Length R	21.25±2.83	16.48	25.29	22.24±2.31	17.42	24.71	0.99±0.79	**0.001****
Philtrum Width	7.81±1.55	5.34	10.64	8.76±1.84	5.92	11.67	0.95±0.76	**0.001****
Cupid's Bow Arm Width L	4.90±3.22	2.30	14.74	5.11±2.99	2.84	13.92	0.22±0.85	0.393
Cupid's Bow Arm Width R	5.09±2.92	2.98	13.89	5.67±2.78	3.80	14.05	0.59±0.31	**0.001****
Crista Philtri Height L	12.26±1.51	9.82	14.68	12.84±1.30	10.92	15.12	0.58±0.55	**0.004****
Crista Philtri Height R	12.41±1.47	9.85	14.93	12.87±1.35	10.75	15.30	0.46±0.58	**0.02***
Lateral Lip Height L	21.42±2.06	17.85	24.82	21.99±1.69	19.27	25.06	0.57±0.85	**0.042***
Lateral Lip Height R	21.05±2.23	16.40	23.82	21.89±1.94	18.42	24.82	0.85±1.04	**0.017***
Medial Lip Height L	13.26±1.02	11.90	15.89	13.70±1.48	11.04	17.15	0.43±0.81	0.092
Medial Lip Height R	13.29±1.18	11.73	15.90	13.47±1.24	11.72	16.52	0.18±0.54	0.270
Alar Length L	15.60±1.29	12.90	17.31	16.31±1.30	14.30	18.29	0.71±0.98	**0.03***
Alar Length R	15.72±1.12	13.25	17.28	16.46±1.21	14.40	19.20	0.74±0.99	**0.025***
Total Alar Width	25.92±1.74	23.10	28.60	26.54±1.84	23.90	30.30	0.62±0.84	**0.027***
Alar Width L	13.78±1.06	11.75	15.31	14.27±0.89	12.97	15.93	0.5±0.5	**0.006****
Alar Width R	14.33±1.22	12.65	16.48	14.78±1.41	12.74	18.06	0.45±0.77	0.07

Table 4.6.1. Comparison of the linear measurements of the control group at T0 and T1 with paired t test (continued)

Linear Measurements (mm)	Control Group (n:12)							p
	T0			T1			T1-T0	
	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	
Nasal Dorsum Length	28.97±3.66	22.08	33.33	30.78±3.69	23.70	36.50	1.8±1.68	**0.003****
Nasal Tip Protrusion	11.23±1.16	8.49	12.72	11.85±1.63	8.50	14.70	0.62±0.85	**0.027***
Nose Height	34.26±3.64	28.50	38.33	36.35±3.85	29.73	42.53	2.1±1.96	**0.003****
Total Nasal Base Width	18.59±1.75	15.68	20.64	18.98±1.94	16.15	21.97	0.39±1.21	0.288
Nasal Base Width L	9.84±0.93	8.56	11.35	10.19±1.06	8.40	11.60	0.35±0.89	0.198
Nasal Base Width R	10.33±1.04	8.41	11.61	10.46±1.02	9.00	11.73	0.12±0.71	0.563
Nostril Long Axis L	12.97±1.32	10.47	14.40	13.23±1.34	11.18	15.03	0.26±0.72	0.242
Nostril Long Axis R	13.28±1.16	10.97	14.60	13.56±0.94	11.79	14.53	0.28±0.58	0.123
Nostril Width L	7.71±1.47	6.00	9.70	8.30±1.48	5.86	10.47	0.59±0.76	**0.022***
Nostril Width R	8.07±1.50	5.57	9.61	8.31±1.60	5.64	10.42	0.25±0.75	0.281
Columellar Width	5.07±0.96	3.38	7.17	5.16±0.76	4.20	6.49	0.09±0.81	0.709
Columellar Apex Width	13.07±1.11	11.44	15.62	13.10±1.55	10.24	15.15	0.02±1.12	0.944
Columellar Base Width	12.00±2.45	7.25	16.16	12.73±1.55	10.47	15.81	0.72±1.46	0.115
Nostril Height L	6.54±0.97	4.40	8.30	6.98±0.79	5.47	8.43	0.44±0.84	0.097
Nostril Height R	6.69±0.72	5.34	7.76	7.26±0.71	6.04	8.36	0.56±0.47	**0.002****
Nasal Tip Projection	14.51±1.41	11.36	16.60	15.22±1.74	11.50	17.70	0.71±0.62	**0.002****
Lateral Nasal Length L	27.83±1.53	25.16	30.69	28.01±2.77	23.73	33.10	0.18±2.44	0.805
Lateral Nasal Length R	28.05±1.24	26.37	30.11	28.34±2.47	24.36	31.42	0.29±2.01	0.624

R: right, L: left, (***) p <0.001, (**) p <0.01, (*) p <0.05

4.6.2. Angular Measurements

The comparison of the angular measurements of the control group between T0 and T1 was given in Table 4.6.2..

When the facial angles were evaluated, it was found that facial profile angle increased statistically in the control group between T0 and T1 ($p<0.05$).

At the labial region, there were no statistically significant changes in eyes-mouth angle and cupid's bow angle between T0 and T1 ($p>0.05$), while upper lip-chin angle decreased statistically in the control group ($p<0.05$).

At the nasal region, there were no statistically significant changes in nasomental angle, lateral nasal tip angle, nasal projection angle, alar wing angulation L, alar wing angulation R, columella inclination L and columella inclination R between T0 and T1 ($p>0.05$). Nasofrontal angle increased significantly ($p<0.01$), while nasal tip angle decreased significantly in the control group ($p<0.05$).

At the nasolabial region, there was no statistically significant change in nasolabial angle between T0 and T1 ($p>0.05$).

Table 4.6.2. Comparison of the angular measurements of the control group at T0 and T1 with paired t test

Angular Measurements (º)	Control Group (n:12)							p
	T0			T1			T1-T0	
	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	
Facial Profile Angle	157.34±3.06	152.43	162.80	158.73±3.42	152.64	165.41	1.39±1.75	**0.018***
Nasofrontal Angle	144.46±6.27	131.38	153.56	146.03±5.90	137.47	156.14	1.57±1.69	**0.008****
Nasomental Angle	132.80±3.16	127.56	138.38	133.96±2.73	129.32	139.42	1.16±2.22	0.097
Nasal Tip Angle	112.35±8.26	101.91	129.63	108.71±7.99	94.38	119.80	-3.64±5.48	**0.042***
Lateral Nasal Tip Angle	81.38±4.39	75.19	89.46	81.59±5.06	74.32	92.65	0.21±3.44	0.833
Nasolabial Angle	128.00±8.53	110.55	139.43	128.78±9.62	111.40	141.00	0.78±4.56	0.567
Nasal Projection Angle	18.21±2.32	15.35	23.13	17.95±2.10	14.91	21.25	-0.26±1.39	0.525
Eyes-Mouth Angle	1.65±0.77	0.91	3.44	2.03±1.48	0.44	6.03	0.38±1.46	0.390
Cupid's Bow Angle	130.05±31.31	35.70	158.80	131.92±29.72	41.50	151.50	1.87±7.75	0.422
Alar Wing Angulation L	59.30±4.57	52.08	70.75	58.46±3.19	53.47	65.64	-0.84±3.15	0.378
Alar Wing Angulation R	61.80±5.35	55.09	71.25	60.38±4.66	52.01	66.63	-1.42±2.98	0.127
Columella Inclination L	109.74±3.96	102.87	117.39	108.41±3.64	101.41	113.53	-1.33±3.24	0.182
Columella Inclination R	106.45±4.93	98.72	115.09	107.01±5.38	97.14	114.51	0.56±4.97	0.704
Upper Lip-Chin Angle	11.82±2.35	6.75	15.73	10.77±3.19	5.86	16.26	-1.06±1.48	**0.031***

R: right, L: left, (**) p <0.01, (*) p <0.05

4.6.3. Proportional Measurements

The comparison of the proportional measurements of the control group between T0 and T1 were given in Table 4.6.3..

No statistically significant changes were observed in any of the proportional measurements of the control group between T0 and T1 ($p>0.05$).

Table 4.6.3. Comparison of the proportional measurements of the control group at T0 and T1 with paired t test

Proportional Measurements	Control Group (n:12)							p
	T0			T1			T1-T0	
	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	
Cupid's Bow Arm Width R/L	1.08±0.20	0.71	1.54	1.16±0.15	0.88	1.35	0.08±0.25	0.312
Alar Length R/L	1.01±0.06	0.94	1.13	1.01±0.05	0.94	1.11	0±0.03	0.927
Alar Width R/L	1.04±0.06	0.94	1.17	1.03±0.06	1.00	1.10	-0.01±0.06	0.654
Nasal Base Width R/L	1.05±0.08	0.90	1.20	1.03±0.08	0.86	1.12	-0.02±0.1	0.472
Nostril Long Axis R/L	1.03±0.05	0.94	1.11	1.03±0.06	0.91	1.09	0±0.06	0.844
Nostril Width R/L	1.05±0.11	0.92	1.30	1.00±0.09	0.86	1.21	-0.05±0.08	0.068
Nostril Height R/L	1.03±0.10	0.90	1.21	1.04±0.08	0.88	1.14	0.01±0.1	0.748
Lateral Nasal Length R/L	1.01±0.04	1.00	1.10	1.01±0.06	0.90	1.14	0.01±0.07	0.774
Upper Lip Transverse Length R/L	0.99±0.05	0.91	1.10	1.01±0.04	0.94	1.08	0.02±0.05	0.312
Lateral Lip Height R/L	0.98±0.03	0.90	1.00	1.00±0.02	0.96	1.02	0.01±0.03	0.155
Medial Lip Height R/L	1.00±0.04	0.92	1.08	0.99±0.04	0.90	1.06	-0.02±0.05	0.268

R: right, L: left

4.6.4. Perimetric Measurements

The comparison of the nostril perimeters of the control group between T0 and T1 was given in Table 4.6.4..

Both right and left nostril perimeters increased significantly in the control group ($p<0.01$).

Table 4.6.4. Comparison of the perimetric measurements of the control group at T0 and T1 with paired t test

Perimetric Measurements (mm)	Control Group (n:12)							p
	T0			T1			T1-T0	
	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	
Right Nostril Perimeter	23.10±3.20	18.32	27.77	24.79±3.08	20.58	29.73	1.69±1.24	**0.001****
Left Nostril Perimeter	23.46±2.68	18.99	26.97	25.08±2.86	20.96	30.16	1.63±1.52	**0.003****

(**) p <0.01

4.7. Comparison of Linear, Angular and Proportional Changes of the UCLP and the Control Group

4.7.1. Linear Measurements

The comparison of time dependent linear changes between the UCLP and the control groups was shown in Table 4.7.1.. No statistically significant differences were observed in any of the linear measurement changes from T0 to T1 between both groups ($p>0.05$).

Table 4.7.1. Comparison of the linear changes at T1-T0 between the UCLP and the control groups with Mann Whitney U test

Linear Measurements (mm)	T1-T0						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Upper Lip Length	0.91±1.70	-2.00	3.96	0.83±0.73	-0.16	2.68	0.892
Philtrum Height	0.77±1.16	-1.24	3.51	0.39±0.52	-0.49	1.30	0.251
Upper Lip Vermilion Height	0.11±1.38	-2.66	1.99	0.13±0.75	-1.45	1.42	0.861
Mouth Width	2.34±2.85	-2.06	9.11	2.10±1.28	-0.08	4.58	0.668
Upper Lip Transverse Length C	1.89±2.18	-0.77	6.85	0.67±0.62	-0.10	1.80	0.134
Upper Lip Transverse Length NC	0.61±2.23	-2.85	7.52	0.99±0.79	-0.58	2.01	0.150
Philtrum Width	0.77±1.63	-3.04	3.04	0.95±0.76	-0.37	2.10	0.876
Cupid's Bow Arm Width C	0.7±0.98	-1.30	2.41	0.22±0.85	-1.43	1.55	0.259
Cupid's Bow Arm Width NC	-0.01±0.96	-1.90	1.49	0.59±0.31	-0.01	1.00	0.134
Crista Philtri Height C	0.85±1.24	-0.69	3.69	0.58±0.55	-0.46	1.31	0.697
Crista Philtri Height NC	0.86±1.25	-2.30	3.12	0.46±0.58	-0.46	1.59	0.213
Lateral Lip Height C	0.35±4.19	-13.20	7.70	0.57±0.85	-0.40	2.70	0.969
Lateral Lip Height NC	0.37±3.67	-12.00	5.40	0.85±1.04	-0.90	2.80	0.785
Medial Lip Height C	0.32±2.32	-7.60	3.30	0.43±0.81	-0.90	1.80	0.559
Medial Lip Height NC	0.6±1.88	-5.68	2.81	0.18±0.54	-0.52	0.94	0.062
Alar Length C	0.22±1.13	-1.76	2.55	0.71±0.98	-0.84	1.90	0.213
Alar Length NC	0.76±1.55	-4.03	2.98	0.74±0.99	-1.07	2.32	0.815
Total Alar Width	0.56±0.99	-1.20	2.30	0.62±0.84	-0.70	1.90	0.846
Alar Width C	0.57±0.85	-0.85	2.57	0.50±0.50	-0.70	1.25	0.938
Alar Width NC	0.08±1.47	-3.40	2.30	0.45±0.77	-1.20	1.60	0.414

Table 4.7.1. Comparison of the linear changes at T1-T0 between the UCLP and the control groups with Mann Whitney U test (continued)

Linear Measurements (mm)	T1-T0						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Nasal Dorsum Length	2.15±1.99	-1.30	6.26	1.80±1.68	-1.01	5.55	0.572
Nasal Tip Protrusion	0.31±1.08	-1.16	3.28	0.62±0.85	-0.15	2.38	0.167
Nose Height	1.94±1.80	-0.83	5.20	2.10±1.96	-1.48	5.64	0.876
Total Nasal Base Width	1.14±1.91	-1.19	6.12	0.39±1.21	-1.91	2.25	0.392
Nasal Base Width C	0.97±1.73	-1.66	4.91	0.35±0.89	-1.08	1.87	0.259
Nasal Base Width NC	0.53±1.17	-2.12	3.32	0.12±0.71	-1.01	1.40	0.199
Nostril Long Axis C	1.04±1.64	-2.04	4.56	0.26±0.72	-1.21	1.65	0.179
Nostril Long Axis NC	0.53±1.38	-2.97	2.64	0.28±0.58	-1.01	1.02	0.340
Nostril Width C	0.86±1.71	-2.01	6.49	0.59±0.76	-1.34	1.21	0.907
Nostril Width NC	0.10±0.90	-1.27	2.32	0.25±0.75	-1.01	1.14	0.414
Columellar Width	-0.13±2.13	-5.82	3.39	0.09±0.81	-0.89	1.57	0.938
Columellar Apex Width	-0.23±2.59	-6.03	4.11	0.02±1.12	-1.95	1.43	0.815
Columellar Base Width	0.05±1.8	-4.41	3.56	0.72±1.46	-1.17	4.28	0.533
Nostril Height C	0.53±1.20	-1.26	2.81	0.44±0.84	-0.98	2.16	0.984
Nostril Height NC	0.28±0.93	-1.47	2.07	0.56±0.47	-0.49	1.17	0.235
Nasal Tip Projection	0.79±0.73	-0.18	2.42	0.71±0.62	-0.10	1.83	0.892
Lateral Nasal Length C	0.97±1.48	-2.34	3.15	0.18±2.44	-2.78	6.15	0.111
Lateral Nasal Length NC	1.30±2.71	-2.16	9.33	0.29±2.01	-2.53	3.43	0.330

4.7.2. Angular Measurements

The comparison of time dependent angular changes at T1-T0 between the UCLP and the control groups was shown in Table 4.7.2.. No statistically significant differences were observed in any of the linear measurement changes from T0 to T1 between both groups ($p>0.05$) except for lateral nasal tip angle. It was found that the change of lateral nasal tip angle was significantly smaller in the UCLP group compared with the control group ($p<0,01$).

Table 4.7.2. Comparison of the angular changes at T1-T0 between the UCLP and the control groups with Mann Whitney U test

Angular Measurements (º)	T1-T0						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Facial Profile Angle	0.78±4.46	-5.90	10.20	1.39±1.75	-0.38	5.66	0.371
Nasofrontal Angle	1.93±2.17	-1.88	6.11	1.57±1.69	0.07	6.09	0.371
Nasomental Angle	0.41±2.81	-4.62	6.21	1.16±2.22	-1.33	7.36	0.969
Nasal Tip Angle	-1.16±4.56	-7.66	10.20	-3.64±5.48	-10.12	4.64	0.243
Lateral Nasal Tip Angle	2.66±2.71	-4.93	8.24	0.21±3.44	-5.80	9.01	**0.002****
Nasolabial Angle	0.12±7.83	-15.53	17.73	0.78±4.56	-7.83	10.20	0.907
Nasal Projection Angle	-0.56±1.81	-3.28	3.06	-0.26±1.39	-3.10	2.02	0.697
Eyes-Mouth Angle	0.02±1.86	-2.98	4.86	0.38±1.46	-1.30	4.31	0.669
Cupid's Bow Angle	6.07±12.62	-11.70	36.30	1.87±7.75	-17.60	10.50	0.726
Alar Wing Angulation C	1.45±3.88	-6.37	6.93	-0.84±3.15	-5.11	3.61	0.073
Alar Wing Angulation NC	-1.32±5.14	-13.46	7.39	-1.42±2.98	-4.62	4.66	0.669
Columella Inclination C	0.55±6.39	-7.55	14.53	-1.33±3.24	-5.08	6.22	0.586
Columella Inclination NC	3.69±7.99	-8.92	20.84	0.56±4.97	-6.53	9.25	0.259
Upper Lip-Chin Angle	-0.43±2.13	-4.80	4.00	-1.06±1.48	-3.50	1.00	0.436

(**) p <0.01

4.7.3. Proportional Measurements

The comparison of time dependent proportional changes at T1-T0 between the UCLP and the control groups was shown in Table 4.7.3..

No statistically significant differences were observed in any of the proportional measurement changes from T0 to T1 between both groups (p>0.05) except for cupid's bow arm width NC/C and upper lip transverse NC/C proportions. The changes in cupid's bow arm width NC/C and upper lip transverse NC/C proportions were significantly smaller in the UCLP group compared with the control group (p<0,05).

Table 4.7.3. Comparison of the proportional changes between the UCLP and the control groups with Mann Whitney U test

Proportional Measurements	T1-T0						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Cupid's Bow Arm Width NC/C	-0.15±0.23	-0.56	0.28	0.08±0.25	-0.27	0.64	**0.016***
Alar Length NC/C	0.03±0.08	-0.19	0.17	-0.01±0.03	-0.04	0.06	0.191
Alar Width NC/C	-0.03±0.12	-0.30	0.17	-0.01±0.06	-0.11	0.08	0.654
Nasal Base Width NC/C	-0.02±0.15	-0.33	0.30	-0.02±0.10	-0.24	0.14	0.938
Nostril Long Axis NC/C	-0.04±0.16	-0.44	0.21	-0.01±0.06	-0.11	0.09	0.495
Nostril Width NC/C	-0.06±0.21	-0.81	0.30	-0.05±0.08	-0.20	0.10	0.953
Nostril Height NC/C	-0.04±0.24	-0.66	0.43	0.01±0.10	-0.17	0.21	0.599
Lateral Nasal Length NC/C	0.01±0.08	-0.07	0.33	0.01±0.07	-0.16	0.13	0.845
Upper Lip Transverse Length NC/C	-0.07±0.12	-0.34	0.12	0.02±0.05	-0.10	0.07	**0.023***
Lateral Lip Height NC/C	-0.01±0.09	-0.17	0.18	0.01±0.03	-0.04	0.06	0.292
Medial Lip Height NC/C	0.02±0.14	-0.20	0.40	-0.02±0.05	-0.10	0.10	0.545

(*) p <0.05

4.7.4. Perimetric Measurements

The comparison of time dependent perimetric changes at T1-T0 between the UCLP and the control groups was shown in Table 4.7.4..

When perimetric changes of the nostrils were evaluated, it was found that there were no statistically significant differences in both nostril perimeters between the UCLP and the control groups ($p>0.05$).

Table 4.7.4. Comparison of the perimetric changes at T1-T0 between the UCLP and the control groups with Mann Whitney U test

Perimetric Measurements (mm)	T1-T0						p
	UCLP Group (n:20)			Control Group (n:12)			
	Mean±SD	Min	Max	Mean±SD	Min	Max	
Nostril Perimeter C	1.77±2.56	-2.65	7.72	1.69±1.24	-0.30	3.97	0.907
Nostril Perimeter NC	0.62±1.85	-2.71	4.26	1.63±1.52	-1.37	3.62	0.087

5. DISCUSSION

5.1. Discussion of Purpose and Methods

The aim of this prospective study was to evaluate the short-term longitudinal nasolabial changes of patients with complete unilateral cleft lip and palate treated with NAM, primary cheiloplasty and palatoplasty and compare these changes with that of healthy subjects without CLP.

Nasolabial deformity in individuals with CLP is successfully corrected with various surgical techniques. The main objective of primary cleft surgeries is to achieve both esthetic and functional results in the affected maxillofacial unit which is expected to grow and develop comparable to normal individuals. For this purpose, some surgeons have adopted less invasive repair techniques when combined with preoperative infant orthopedics (5,90,210). In the 20th century, nasoalveolar molding, one of the preoperative orthopedic treatments, became widespread and positive results were shown. Grayson et al. (5) reported that with the advent of NAM, the primary surgeries have become much less extensive. Therefore, the combination of NAM and surgical treatment had been started to be used in various centers. Until today, many studies have been conducted examining the effectiveness of NAM (7,78,79,87,113,114,116–118). The proven benefits of NAM are reduction of the severity of the nasolabial deformity and increasing its symmetry before surgery (5,7,16,78,79,87). In this way, it is aimed to achieve more symmetrical nasolabial structures after surgery. But as mentioned by Grayson et al. (5), nasal molding is not sufficient to correct the nasal tip deformity. Although NAM stretches the columella skin into a more normal configuration and normalizes the shape and position of the lower lateral cartilages, coordinated primary nasal surgical correction is still required after NAM. The surgery with or without NAM manages to correct the nasolabial deformity to a great extent, however, some asymmetry is inevitable in the postoperative period. According to some studies, this asymmetry increases over time in the early postoperative period and secondary surgeries may be required at preschool age (14,15). Therefore, in our study, we aimed to examine the short-term nasolabial changes of individuals with UCLP who were treated with NAM - primary surgery combination.

One of the most important factors affecting treatment results is the surgical method. Different surgical methods have different aesthetic results on nasolabial structures (211,212). Therefore, all the individuals with UCLP included in our study were operated by the same surgeon (H.A.) at 3-4 months of age, using extended Mohler modification of rotation and advancement technique for primary lip repair. This is a modification of the technique initially described by Mohler, which, in turn, is based on the technique of Millard (105). Compared to the traditional Millard technique, this technique minimizes the alar base skin incisions and places the back-cut used to rotate the medial lip element at the base of the columella instead of the upper lip. With these modifications, the upper lip scar parallels the contralateral philtrum instead of curving across the philtral groove (90). During the primary lip repair, closure of the anterior nasal floor and primary tip rhinoplasty were also performed. Correction of the nasal deformity is coupled with the rotation-advancement repair. At the alveolar level, gingivoperiosteoplasty was not performed. At 9-10 months of age, the patients were operated by the same surgeon using Sommerlad modification Bardach's Two Flap palatoplasty with radical intravelar veloplasty for palatal repair.

The proper application of the NAM and surgical technique definitely affects the results. For this reason, the expert who applies the technique should be skilled and experienced (213). In cleft surgery, it has been demonstrated that skill improves with experience (214). Unquestionably, individual surgical skill and experience have an important bearing on outcomes, and Scandcleft showed that better results were achieved when surgeons were following protocols with which they were already familiar (215). The same circumstances no doubt apply to other disciplines involved in cleft care (216). Therefore, we only included patients treated by the same orthodontists and surgeon. Nasoalveolar molding of the subjects included in our study was performed by two experienced orthodontists (D.G.Ç. and B.N.Y.) who had the same training and used the same technique described by Grayson (5,78,79). Surgical treatments were performed by a single experienced surgeon (H.A.) using the same technique in every patient.

In addition, initiation time of NAM therapy is an important factor for the success of the treatment (217). It is recommended to start NAM treatment within a few weeks after birth, since high levels of maternal estrogen and hyaluronic acid of the neonate causes high degree of plasticity of the cartilage and the ability to shape the

nasal cartilage decreases over time after birth as the estrogen levels subside (5,100,218). For this purpose, NAM therapy starts as early as possible in newborns with CLP who are referred to our clinic. In our study, the onset of the NAM treatment was among the selection criteria of the subjects in the study group. The study group included cleft patients' whose presurgical treatment was initiated within the first weeks after birth and completed in the following three or four months.

The absence of a control group consisting of healthy individuals causes deficiencies in the evaluation of treatment results. While examining treatment results, the growth and development of individuals with UCLP should be compared with healthy individuals. Thus, the anatomical regions deviating from normal can be revealed and a cause-and-effect relationship can be established between the outcomes and the treatments performed. In addition, the nasolabial asymmetry in individuals with UCLP can be evaluated more clearly. As a consequence, the treatment approach can be revised and the need for secondary surgeries can be determined when necessary. In previous studies, where the nasolabial changes were evaluated in individuals with UCLP, some of the researchers used noncleft side as a control group, while others used historic groups created in earlier studies (15,116,118,125). In 2017, Alazzawi et al. (13) evaluated the nasolabial growth of 24 newborns by using stereophotogrammetry and used the cleft side as the experimental group and the noncleft side as the control group. In their study, where the asymmetry was studied, due to the absence of control groups consisting of healthy individuals, the evaluation of nasolabial growth could not be specified exactly. Because the anatomic structures of the noncleft side may also be distorted even after surgical repair (123), using the noncleft side to compare the cleft side may reveal unrealistic results. In 2018, Mancini et al. (16) who assessed nasolabial growth by stereophotogrammetry, used as a control comparison the normal nasal anthropometric measurements of 13 noncleft infants aged 0 to 5 months which were previously published by Farkas (120). The use of historic groups was interpreted as confusing for reasons such as possible secular differences in craniofacial size or form, different examiners and measurement techniques. In order to eliminate aforementioned weaknesses of previous studies (14,15,123), our control group was composed of healthy caucasian individuals, matching the ages of the patients with UCLP at the beginning of the observation period (T0). At T0, the mean ages of the experimental and the control group were 20.6 and 20.8 months, respectively and did not differ between groups. The observation period was

approximately 1 year for both groups. Thus, the age factor which may significantly affect growth in the early years was eliminated.

In our prospective longitudinal study, we evaluated the short-term nasolabial changes after NAM and primary surgeries. In our team's protocol, preoperative orthopedic treatment and surgical treatments of patients with UCLP usually ends at 10-12 months of age. Revision surgeries are performed at preschool age (4-5 years old) when necessary. Orthodontic and orthopedic treatments start at 6-7 years old. Therefore we thought that the evaluation of these short-term changes in early childhood (1-4 years old) would give insight into pure nasolabial growth in UCLP patients without any surgical and/or orthodontic intervention at this particular time period. Thus, the findings obtained from this study would guide the team about the necessity of revision surgeries and auditing and revising the team's approach.

According to the results of the power analysis, there should be at least 20 subjects with UCLP in our study group. In order to be compatible with power analysis, 20 individuals, whose NAM and surgical treatments were completed between 2014-2019 were included and followed in our study group. The healthy infants whom the parents volunteered to participate in the study were included in the control group. Although 3D stereophotogrammetry is a noninvasive technique, it was not easy to convince the parents of healthy individuals. In addition, there were difficulties in ensuring the continuity of volunteer families' participation in the study and obtaining records at the right time. Therefore, although 20 healthy children were initially included in the control group, some subjects had to be removed. Consequently, the number of subjects of the control group was less than expected.

The number of studies examining the results of treatments on facial aesthetics is increasing day by day. In order to examine the growth and development of facial structures, many methods have been used in these studies such as direct anthropometric measurements, and indirect measurements on 2D photographs, or on 3D models obtained by laser scanning and stereophotogrammetry.

Stereophotogrammetry is accepted as the gold standard among the methods used today. This method has important advantages such as being noninvasive (not containing harmful x-rays, not hurting eyes), contact-free, reliable, highly accurate, and having ultrashort scanning process (147,148,151,157,180,192,203–206,219). Particularly, being able to capture 3D facial image in a short time facilitates recording in children where inactivity cannot be achieved easily. Furthermore, this method can identify soft

tissue surface texture better from laser scanning methods (164). This advantage allows the correct placement of landmarks, especially in individuals with cleft lip and palate. Therefore, it contributes to more reliable measurements. Although this method has many advantages, it also has disadvantages. Expensive equipment and a special room requirement are the major disadvantages of this system (148,192). For these reasons, this device is usually found in private centers and hospitals. In addition, a special software program is needed to evaluate the captured records. Moreover, this system is not portable, so individuals must come to the centers where the system is located. Despite these disadvantages of the stereophotogrammetry method, many researchers have used and suggested this method in the evaluation of facial features because it has very important advantages. The fact that this method is noninvasive enables recording from healthy individuals and enables the researcher to form a control group consisting of healthy individuals (162,199).

Facial expression should not be present in recordings taken using stereophotogrammetry. Expressions such as laughing, crying, and so on may create tension in the soft tissue, and this distortion impairs the quality of the recording obtained. Therefore, the individuals must be at the resting position while recording (196,220). The prospective nature of our study enabled us to obtain 3D facial images of the subjects in rest position. The 3D images were checked from the computer screen immediately after the recording and the records of poor quality were renewed. Thus, only high quality and non-distorted 3D images were evaluated in our study.

In our study, linear, angular, proportional and perimetric measurements were used to evaluate nasolabial growth. The correct identification of the landmarks that compose these measurements is crucial for providing reliable measurements. Therefore, the definition of these landmarks well depends on the correct determination of the anatomical points, the person making the evaluation and the quality of the recording (154,205). Since the experience and skill of the examiner is an important factor, all landmarks were marked by the same examiner who was trained in 3D image processing and data processing with the 3dMd camera and 3dMd Vultus software. When using 2D images, the landmark can be positioned correctly in one time, as it works on a single surface. However, when using 3D images, it is necessary to control the positions of the landmarks on the three planes. Thus, in our study, while positioning the landmarks, each landmark was first positioned on the frontal plane and then controlled on the sagittal and horizontal planes. The reproducibility of the landmarks and related

measurements were analyzed by the intraclass correlation coefficients which showed high reproducibility and reliability, in accordance with previous studies (147,157,205,219).

In our study, asymmetry between the cleft side and the noncleft side and right and left side was evaluated in individuals with and without UCLP, respectively. Similar to previous studies (7), facial symmetry was measured by proportioning bilateral linear measurements and these ratios were compared with the control group. Score 1 or closer to 1 indicated the presence of symmetry.

5.2. Discussion of Results

In our study, evaluation of the nasal region revealed that on the cleft side, alar length (18.71 mm, $p<0.001$), alar width (15.44 mm, $p<0.05$), nostril width (9.41 mm, $p<0.05$) were higher in the UCLP group compared with the control group at T0. Moreover, alar length NC/C (0.83 $p<0.001$), alar width NC/C (0.94 $p<0.05$), nasal base width NC/C (0.79 $p<0.001$), nostril long axis NC/C (0.90 $p<0.05$) and nostril width NC/C (0.80 $p<0.001$) ratios were lower in the UCLP group compared with the control group at T0, signifying an obvious asymmetry. This asymmetry may be mainly due to longer horizontal measurements on the cleft side (i.e. longer alar width, alar length and nostril width) and partly due to smaller horizontal measurements on the noncleft side (i.e. shorter nasal base width), or both (i.e. longer nostril long axis on the cleft side and shorter on the noncleft side) in individuals with UCLP. These results showed that although the nasal region on the cleft side has been tried to narrowed with NAM and primary surgery (7,15,16,87,113,115–118,221,222), it still remains large compared with healthy individuals. The larger nasal width on the cleft side in individuals with UCLP may be due to the persistent cleft deformity, scar tissue and surgical technique (125). Because of the relationship of the alar base with the deficient and retropositioned maxillary bone, septal deviation and the non-separation between the lower lateral cartilage and the piriform aperture during surgery, an opening on the alar region occurs towards the lateral direction postoperatively and alar webbing takes place in the lower lateral cartilage. The lateral drift of the alar base is well known after repair of unilateral cleft lip. Nowadays, as the surgeon observed these effects, he has modified his surgical technique in the piriform aperture with more radical intervention. Similar to our findings, previous studies have remarked that the nostril on the cleft side remains wider

compared to the noncleft side and to healthy individuals. In their study, Liou et al. (14) examined the nasal asymmetry on 2D photos and they also found asymmetry in terms of nostril width one year after primary surgery (modified rotation advancement cheiloplasty without nasal cartilage dissection) combined with NAM therapy. They showed that the nostril width on the cleft side was 2.3 mm longer and the nasal base width on the cleft side was 2.1 mm longer compared with the noncleft side one year after NAM-primary cheiloplasty in accordance with our findings revealing approximately 2 mm differences between cleft and noncleft sides. Similarly, Chang et al. (12) evaluated nasolabial asymmetry of the individuals with UCLP at the age of 5, who were treated with 4 different methods, including NAM and primary rhinoplasty. According to the result of this study, asymmetry in nostril width was observed at all groups and it was stated that nostril width on the cleft side was longer compared with noncleft side. Funayama et al. (128) evaluated nasal asymmetry of the individuals with UCLP who were treated with different methods, including the use of PNAM or postsurgical nostril retainer in combination with primary lip repair. They stated that nostril width ratio was high in all groups either treated with PNAM, postsurgical retainer or not, as nostril width on the cleft side was wider than that on the noncleft side at 4 years of age. They also mentioned that this horizontal parameter is the most difficult to improve using only these nonsurgical methods and seems to widen over time. The difficulty of improving and maintaining nostril width after surgeries was commonly reported in the literature and different solutions are still being developed (12,125). Chang et al. (12) proposed 20% surgical overcorrection of the nostril width to a more narrow form where they used NAM in combination with modified Mohler technique, primary rhinoplasty with Tajima incision, and active postsurgical retainer. Sharing a similar point of view, Knight et al. (125) stated that the heminasal width (sn-al) measurement was 0.7 mm narrower on the cleft side compared with the noncleft side before and at the age of 6.6. They attributed this situation to the surgical technique where a suture from muscle or periosteum was used to secure the alar base medially controlling the lateral drift and larger nostril width. On the other hand, medial overcorrection of the alar position could indicate nostril stenosis, which is far more difficult to correct than a wide nostril (125).

When the change of the nasal measurements were examined over time in our study, on the cleft side, alar length (18.92 mm, $p<0.001$), alar width (16.01 mm, $p<0.01$)

and nostril width (10.27 mm, $p<0.01$) were found higher in the UCLP group compared with the control group at T1, and the differences were higher at T1. These results showed that growth in both groups continues, so the wider alar region on the cleft side persists in individuals with UCLP (Figure 5.2.1). This alar deformation and asymmetry is generally corrected by additional surgery at preschool age in individuals with UCLP. Besides these measurements, although no statistically significant differences were found between the UCLP group and the control group in nasal base width on cleft side and nostril long axis on cleft side at T0, these values became significantly higher in the UCLP group compared with the control group at T1. Moreover, alar length NC/C (0.85, $p<0.001$), alar width NC/C (0.91, $p<0.01$), nasal base width NC/C (0.76, $p<0.001$), nostril long axis NC/C (0.87, $p<0.01$) and nostril width NC/C (0.74, $p<0.001$) ratios were found lower in the UCLP group compared with the control group at T1. Furthermore, when we particularly examined alar length NC/C, nasal base width NC/C and nostril width NC/C, we observed that these regions were significantly asymmetric at the beginning and at the end of the observation period, without any improvement or deterioration in the symmetry index during growth. Liou et al. (14) also found a significant asymmetry in the nasal area two years after primary cheiloplasty and stated that nostril width on the cleft side was 2.2 mm longer and nasal base width on the cleft side was 2.3 mm longer compared with the noncleft side. Moreover, they showed that nostril width on the cleft side was 2.0 mm longer and nasal base width on the cleft side was 1.8 mm longer compared with the noncleft side three years after primary cheiloplasty, indicating no significant change. They indicated that although the nasal asymmetry in the horizontal dimension deteriorated in the first year postoperatively, which was attributed to the relapse and differential growth between the cleft and noncleft side, the relapse stopped and the nasal growth was the same between both sides in the second and the third years. Therefore, similar to our findings, they concluded that the asymmetry of nasal width and nasal base width did not change with growth and remained stable. In our study, when the T1-T0 difference of horizontal nasal measurements were examined, no statistically significant difference was observed between groups. Based on these results, we can say that nasal growth of individuals with UCLP is similar to the healthy subjects. Neither NAM nor surgical technique did not yield to a nasal growth disturbance of the patients with UCLP.



Figure 5.2.1. Nasolabial view of a patient with UCLP at (A) T0 and (B) T1

When we examined nostril height on the cleft side, no statistically significant difference was found at T0 and T1 between groups. Moreover, there was no statistically significant difference between groups in terms of change of this measurement from T0 to T1. The cleft nostril height reaching the normal values at the first years postoperatively may be explained by the treatment effects of both NAM and primary rhinoplasty. One of the main purposes of NAM therapy is to increase the nostril height for reshaping the depressed alar cartilage and the nose (223). The nasal stent attached to the alveolar molding plate serves as a custom tissue expander for the columella on the cleft side (5). The upper lobe of the nasal stent enters the nose and gently lifts the dome and the lower lobe of the nasal stent lifts the nostril apex and defines the top of the columella (90). The increase in the cleft nostril height with the use of NAM plate is well documented in the literature (7,14,87,116,118). Furthermore, Birli (7) who evaluated the effects of NAM therapy in infants with UCLP compared to healthy infants found that the nostril height reached the normal values after NAM and this increase (approximately 3 mm) exceeded the changes due to growth, showing a positive effect of the NAM. Some authors also suggested slight orthopedic vertical overcorrection of the alar dome on the cleft side to compensate for the vertical relapse potential after surgery (114). Overtreatment of patients to compensate for relapse and possible differential growth is a controversial aspect of PNAM treatment (118). Reexamination of the findings of the previous studies conducted in our clinic revealed that our NAM technique does not involve overcorrection of the nostril height on the cleft side (7,87). During NAM, overexpansion of the nasal tissues may create meganostril and it is advised to eliminate this risk (90,118).

NAM is an adjuntive treatment to the primary surgeries in patients with clefts to reshape the alar cartilages and facilitate the surgery. Besides NAM induced effects, we think that the surgical technique further improved the nostril height. The surgeon

technically prefers overcorrection of the nostril, particularly the nostril height, compared to the normal side to prevent vertical relapse in the postoperative period as suggested by some authors (14). Membranous incision up to the caudal septum superior and intermedial middle crus dissections and upward release and lifting resulted in the increase of the vertical dimensions of the nose. This overcorrection helps reaching and maintaining the normal nostril height on the cleft side.

In general, an asymmetry in the nostril height was shown although the vertical dimensions of the nostrils were less asymmetric in the individuals treated with nasal stent before primary surgery. Similar to Funayama et al. (128), Chang et al. (12) also stated that NAM contributed to nostril height symmetry, however postoperative stent application was indicated to preserve it. In our study, nostril height NC/C ratio was found higher compared to the control group at T0 and T1, indicating an asymmetry in the subjects with UCLP. Although the cleft nostril height was normal, we encountered these results due to the longer nostril height on the noncleft side. The nostril heights on the noncleft side at T0 and T1 (7.98 mm, $p<0.001$ and 8.26 mm, $p<0.05$, respectively) were longer compared to the control group. It appears that the surgical overcorrection resulted in longer nostril height on the contralateral side as well. Because the nostril height on the cleft side generally tends to be shorter in individuals with UCLP in later ages, the columella is overcorrected with the surgical technique. Therefore, overcorrection is likely to affect the nostril height on both sides. This causes normalization of the nostril height on the cleft side, while the nostril height on the noncleft side is higher compared with the healthy individuals. In addition, these results show that nasal measurements on the noncleft side may be different from healthy individuals and therefore, when the deformity on the cleft side is evaluated, the noncleft side should not be considered normal. During the observation period of our study, despite this asymmetry, nostril heights in UCLP group changed in line with the growth of the normal subjects, showing no relapse or improvement. Liou et al. (14) also did not observe any change in the asymmetry of the nostril height in the 2nd and 3rd years following primary cheiloplasty.

When the noncleft side dimensions were evaluated in our study, the nasal base width (8.29 mm, $p <0.001$) and nostril long axis (12.01, mm $p <0.05$) were significantly smaller in the UCLP group than in the control group at T0. Whereas, at T1, nasal base width on noncleft side (8.82, mm $p <0.05$) was still smaller in the UCLP group compared to the control group, the difference decreased over time. Furthermore, no

statistically significant difference was found between the UCLP and the control group in the nostril long axis on the noncleft side at T1. The smaller measurements on the noncleft side may be due to the initial deformity of the UCLP group. Birli. (7) who evaluated the development of individuals with UCLP before and after NAM treatment and compared them with the healthy individuals in his study, revealed that nostril diameter on the noncleft side was significantly smaller in the UCLP group than in the control group before NAM treatment. He attributed this finding to the initial columellar deviation toward the noncleft side at the beginning of treatment.

When we examined nostril sizes from a different aspect, nostril perimeter on the cleft side was higher in the UCLP group compared with the control group whereas there was no difference on the noncleft side between groups at T0 and T1. On the cleft side, this supports that although the nostril height was similar for both groups, the nostril width was higher in the UCLP group compared with normal individuals. Therefore, the nostril perimeter on the cleft side was significantly larger in individuals with UCLP. Keçik et al. (117) and Gomez et al. (118) stated that the nostril area on the cleft side was larger than the noncleft side before PNAM. In addition, after PNAM treatment, there was no statistically significant change in the nostril area on the noncleft side, while they observed a significant increase in the nostril area on the cleft side. It is believed that this may be associated with increasing the nostril height while trying to reduce the nostril width and establishing the alar cartilage convexity on the cleft side. As seen in these previous studies, overcorrection of nostril height on the cleft side may cause meganostril. Therefore, caution should be exercised during PNAM not to increase the circumference of the nostril and to not extremely thin the nasal cartilages as a result of the PNAM pressure that could lead to an unstable nasal outcome (118). In our clinical practice, every effort was made to prevent creating meganostril during NAM. On the other hand, Chang et al. (12) who examined nostril area in individuals with UCLP at 5 years of age, stated that the nostril area symmetry was better in individuals who were treated with NAM before primary rhinoplasty. Since no cleft subjects treated without NAM was evaluated in our study, a comparison couldn’t have been made. Other possible explanations of the greater nostril perimeter on the affected side may be the surgical technique which did not attempt to overcorrect the alar position and its lateral drift and cleft anatomy with the retropositioning of the maxillary bone and the alar base on the cleft side.

In our study, nasal tip protrusion (13.37 mm, $p<0.001$) and nasal tip projection (15.82 mm, $p<0.05$) measurements were higher in the UCLP group compared with the control group at T0. In addition to these linear measurements, at T0, nasal projection angle (20.73º, $p<0.01$) was higher in the UCLP group compared with the control group. This finding can be partly explained by our surgical technique aiming to increase the columella length by overcorrection to overcome the postoperative potential relapse and partly by the fact that Sn and Sbal points might be posteriorly located depending on the position of maxilla. Similar to our findings, Mancini et al. (16) found approximately 3 mm improvement in nasal projection measurements after NAM combined primary cheilorhinoplasty and stated that this represented an overcorrection when compared to noncleft controls, which may be of benefit due to the possibility of impaired growth in this patient population. They attributed the significant improvement of the nasal tip projection to their primary rhinoplasty technique involving overcorrection of the nasal tip position. On the other hand, when the nasofrontal angle was examined in our study, although the angle was slightly increased in the UCLP group, no statistically significant difference was found between both groups at T0 and T1. It appeared that the pronasale was in comparable position in both groups according to the forehead but probably not in an overcorrected position in UCLP group. Although the projection of the nasal tip was overcorrected by the surgery, the underlying maxillary hypolplasia or retrognathia might compensate its over projection relative to the frontal area. Ayoub et al. (127) also stated that the anteroposterior position of Sn was significantly different between individuals with UCLP and healthy individuals. However, in our study, it was not possible to clearly state that the maxillary position remained retrognathic, since a cephalometric analysis was not performed. It is not ethical and possible to conduct a cephalometric study in our age group (2-3 years old) due to radiation exposure. On the other hand, in previous cephalometric studies, it was reported that the maxilla is hypoplastic and remains retrognathic in individuals with UCLP (224–226). The underdevelopment of the maxilla may be caused by the type and timing of primary and secondary surgical interventions or intrinsic factors and morphogenetic pattern of the individuals with cleft (227–230). Although nasal tip protrusion (13.68 mm, $p<0.05$) is higher in the UCLP group than in the control group at T1, the difference is observed at T0 decreased. On the other hand, when nasal tip projection was evaluated at T1, no statistically significant difference was observed between the UCLP group and the control group. When we evaluated angular measurements at T1, nasal projection angle

(20.16º, p<0.05) was higher in the UCLP group than in the control group at T1, but the differences decreased at T0. These results indicate that the columellar length and nasal projection are greater in individuals with UCLP a while after surgery. In addition, when the T0-T1 difference was examined, it was observed that both groups grow similarly. Similar to the results of our study, Kim et al. (231) did not observe any difference in growth of nasal tip projection and columellar length from postoperative 6th month to 3rd year between normal individuals and individuals with UCLP who underwent primary nose repair.

In our study, at the beginning and at the end of the observation period, facial profile angle (T0:165.69º, p<0.001, and T1:166.47º, p<0.001) was found greater in the UCLP group compared with the control group, whereas upper lip-chin angle (T0:6.18º, p<0.001, and T1:5.74º, p<0.001) was found lower in the UCLP group compared with the control group. The fact that these angles were different in individuals with UCLP than in normal individuals indicated that the facial profiles of individuals with UCLP were flatter or concave (Fig.5.2.2.). This may be due the retrognathic position of the maxilla in the sagittal direction in individuals with UCLP. However, this assumption should be justified by cephalometric studies as mentioned earlier. Several different reasons for the flat profile seen in individuals with UCLP were documented. It was concluded that the growth of the midface is affected by three primary factors, such as intrinsic tissue deficiency of the bone, teeth, and soft tissue, intrinsic genetic growth pattern characterized by inherited midface deficiency distinct from the cleft, and surgical and orthodontic treatments (232). So, in individuals with UCLP, the maxilla may be genetically retrognathic. Hypoplasia of the cleft side may also cause a flat profile. In some previous studies, it has been stated that maxilla in individuals with unilateral cleft lip and palate remained retrognathic due to its hypoplasia on the cleft side, inadequate fusion and subnormal growth (22,23).

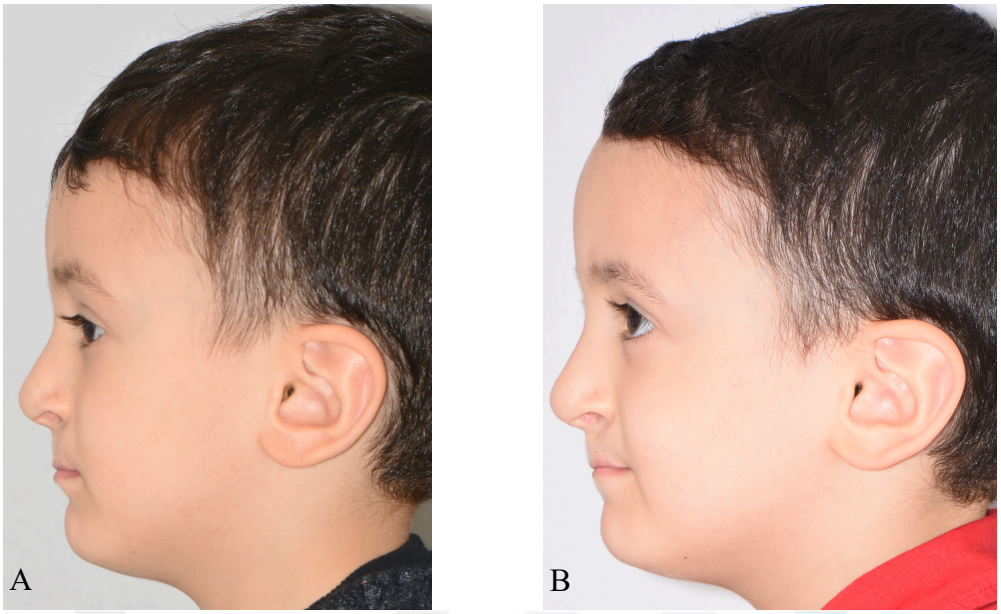


Figure 5.2.2. Facial profile of a patient with UCLP at (A) T0 and (B) T1

As a component of the early treatment of patients with UCLP, presurgical infant orthopedics was criticized or evaluated as a factor causing impairment in the normal maxillary growth and development (232–235). Several studies assessing the effects of passive plates on maxillary growth revealed no negative or positive effects (232,233). NAM is an active treatment which approximates the cleft segments to reduce the gap and the soft tissue tension. This fact raised the following question: Does NAM lead to maxillary growth disturbance? Akarsu-Guven et al. (234) examined the effect of NAM on maxillary growth in 5 years old individuals with UCLP using lateral cephalometric films. In those patients, lip repair was performed with the modified Millard procedure, and the palate repair was performed with the 2-flap palatoplasty technique. As a result of this cephalometric study, no difference in maxillary growth was observed between individuals who were treated with NAM and those who were treated without NAM. Similarly, in a recent study where the patients treated with NAM and primary cheilorhinoplasty (with extended Mohler modification rotation advancement) in New York Team were compared to nonPSIO treated patients from European Centers, it was revealed that NAM did not impact the midfacial growth in school aged children (236). So one can conclude that NAM alone do not cause any maxillary retrusion in operated UCLP patients. On the other hand, Naqvi et al. (237) examined the effect of surgery on maxillary growth in three different age groups (3-5 years, 8-10 years, 20-25 years) and assessed the individuals with complete unilateral cleft lip and palate using lateral cephalometric films. In operated group, all individuals were treated with Millard's

technique and Bardach two-flap palatoplasty. They stated that cleft lip and palate operations affected the growth of the maxilla in the sagittal direction, so the maxilla remained in the retrognathic position. In addition, it was also reported that maxillary growth was normal in unoperated individuals in this study. In 2013, Xu et al. (238) used facial impressions to examine nasolabial structures. In their study, 63 individuals with UCLP and 96 individuals with isolated cleft palate were included and all individuals' facial casts were taken before and after primary cheiloplasty and before palatoplasty. They repaired cleft lip with the geometrically justified rotation advancement technique and cleft palate with Sommerlad's method. And they stated that nasolabial structures were in normal sagittal position immediately after primary cheiloplasty but sagittal projection decreased approximately 10 months after the operation. However, in this study, preoperative orthodontic treatment was not applied to individuals and individuals with incomplete cleft were used as control group. There are many studies stating that lip pressure that increases after primary cheiloplasty has a negative effect on maxillary growth (239,240). In their study, Bardach et al. (102) included 44 individuals with UCLP and 148 healthy individuals and they examined lip pressure at 3 months (before primary cheiloplasty), 4 months, 6 months, 8 months, 11 months, 14 months, 18 months and 24 months of age. They stated that lip pressure increased significantly after primary cheiloplasty compared to healthy individuals. In our study, over a period of 1 year, between the ages of 2 to 3 years, we observed similar growth changes in UCLP and control groups regarding the facial profile. However, long term follow-up studies are required to evaluate the effects of primary treatments on the facial profile.

Columella deviation is an important stigmata of the cleft deformity and an indicator of nasolabial symmetry. When individuals with UCLP were compared with healthy individuals, no significant difference was found at T0 and T1 in terms of columellar deviation in our study. Previous studies that examined the nasal region before and after PNAM treatment reported that the columella deviation improved with PNAM, by repositioning of the nasal cartilage and the correction of the greater alveolar segment's displacement which led to improvement of the overlying soft tissue as well (2,5–7,114,116–118). The residual deviation is corrected with surgeries. The studies examining the effects of the primary cheiloplasty performed after NAM showed a significant correction of the columellar deviation (15,16). Furthermore, NAM treated patients were found to be more symmetrical regarding columellar deviation in the long-term. Barillas et al. (8) stated that individuals who received NAM treatment had more

symmetrical columellar inclination between the ages of 7-11. When Funayama et al. (128) examined the individuals at the age of 4, they reported that the individuals who were treated with POT had better esthetics in terms of columellar deviation. On the other hand, a slight relapse tendency following primary treatments was also reported. The follow-up of the results in the study by Pai et al. (15) revealed that the columellar deviation relapsed at rate of 4.7% within one year after primary cheiloplasty. The relapse mentioned in this study was not observed in the age group in which our study took place. The columella inclination did not change between the postoperative first and second years.

In our study, we found that columellar width (6.27 mm, $p<0.05$) and columellar apex width (15.43 mm, $p<0.01$) were greater in the UCLP group than in the control group at T0. This difference decreased over time. On the other hand, when we evaluated columellar base width, we found that there was no statistically significant difference between the UCLP group and the control group at T0 and T1. Moreover, there was no statistically significant difference between groups from T0 to T1 in terms of columellar width at any level. Due to the fact that nostril apices on the cleft and noncleft sides were not at the same level, these lines were more oblique in individuals with UCLP compared with the control group. Therefore, we found that the columellar width is greater towards columellar apex in the UCLP group. In their study, Bennun et al. (241) compared individuals treated with PNAM (44 children), individuals not treated with PNAM (47 children) and healthy individuals (48 children) when these individuals were six years old. In this study, Millard II procedure with a musculature dissection and reposition according to Delaire (242) was performed by a single surgeon. However, they did not use any surgical technic to correct the nose. Similar to the results of our study, they found that the columellar width of treated individuals had a greater thickness comparing with healthy individuals.

When the vertical measurements at the labial region were examined in our study, upper lip length (14.73 mm, $p<0.001$), philtrum height (11.64 mm, $p<0.05$), upper lip vermilion height (3.81mm, $p<0.001$) and medial lip height on the cleft side (11.25 mm, $p<0.01$) were found shorter in the UCLP group compared with control group at T0. It was observed that these vertical linear lip measurements (except medial lip height on the cleft side) in the UCLP group approached healthy individuals' measurements at T1, and even there was no statistically significant difference between the control group and the UCLP group in terms of philtrum height at T1. Meanwhile the lateral lip height of

the UCLP group was comparable to that of the control group at the beginning and end of the observation period, indicating a normalization after NAM and primary repair. When the vertical symmetry of the labial region was evaluated, it appeared that the medial lip height was significantly asymmetric in UCLP group compared to the control group at T0 and T1 (medial lip height NC/C ratios were 1.15 and 1.17, $p<0.001$, respectively). The vertical shortness of the medial labial region may be to the vertical incision technique and the resulting scar tissue, underlying osseous misalignment, and soft tissue deficiency. The medial lip height was measured as the distance between the crista philtri (Cph) and subalar (Sbal) points. The positions of these points could be affected by the scar tissue and surgery, which in turn may lead to shortness of the medial lip height because the Mohler repair is a straight line repair. Knight et al. (125), who did direct antropometric measurements, also observed that the lateral oblique height (Sbal-Cph) was shorter on the cleft side than on the noncleft side, and the growth of both sides was similar, so the asymmetry did not change with growth after the primary repair including rotation-advancement and primary nasal repair. In accordance with their findings, we also found that the vertical asymmetry in the medial region of the lip remained without any relapse or improvement (Fig.5.2.3). However, a normal vertical growth of the lip in UCLP patients was observed following the primary repair. The literature is conflicting regarding the postoperative changes in the lip height. Some authors showed that lip height symmetry was maintained during long-term follow-up, whereas others stated that the lip height either decreased or increased following surgery (243–247). It seems that one of the main factor is the type of surgical intervention besides other factors (i.e. host factors). Cutting and Dayan (110) who evaluated both NAM and nonNAM cases treated with Extended Mohler surgical technique found that the lip height was very symmetrical at the second postoperative year. Although they used the same surgical techniques as we did, this inconsistency between the findings may be explained by using different landmarks. To measure the labial height, they used the base of the columella instead of subalar point. Therefore our measurements may be affected by alar base asymmetry. On the other hand, when another vertical measurement, crista philtri height (from subnasale to crista philtri) was evaluated, we also observed that the vertical labial dimension was nearly symmetrical with an asymmetry index of 0.96.

When evaluated horizontally, the upper lip transverse length on the cleft side (19.75mm, $p<0.05$) was found shorter in the UCLP group than in the control group at

T0, while no statistically significant difference was found between the control group and the UCLP group at T1. Moreover, upper lip transverse NC/C ratio (1.09, $p<0.05$) was higher in the UCLP group at T0, whereas no statistically significant difference was found between groups at T1 in this ratio (1.02 in UCLP group). On the other hand, no statistically significant difference was found between groups in cupid's bow arm width NC/C ratio at T0, whereas it was lower in the UCLP group compared to the control group at T1. However, cupid's bow arm width NC/C and upper lip transverse length NC/C ratios decrease with growth in individuals with UCLP and these ratios approached the value of "1" even more. Therefore, we can say that the lip area became more symmetrical transversally with growth in individuals with UCLP at T1 (Fig.5.2.3.). The postoperative improvement of the transversal dimensions of the upper lip was also reported by other authors (110,125). Cutting and Dayan (110) found that lip width deficiencies significantly normalize as the patients grow. They attributed this positive change to careful repair of the muscle during lip closure. They explained the surgical key points as dividing the medial muscle under the columella and rotate it downward as it is to perform the same maneuver on the skin. The tip of the lateral muscle flap should be interposed into the medial defect. As the patient functions normally after repair, the lateral lip skin elongates to accommodate the change with time. Similarly, Knight et al. (125) reported that the labial width (Cph-Ch) measurement on the cleft side was 1 mm shorter at the age of 6.6 compared to the noncleft side and 0.7 mm shorter at the age of 11.5 years. Therefore, they observed an improvement in the symmetry of the labial region with growth. Ayoub et al. (126), who examined 3D stereophotogrammetric records of 3 years old patients with UCLP (treated by modified Millard cheiloplasty and McComb primary rhinoplasty) and healthy individuals, did not observe a difference between the control group and the UCLP groups in the upper lip transvers length (Ls-Ch) measurement on the cleft and noncleft sides. In our study, while no difference was observed in cupid's bow arm width (Cph-Ls) between groups on the cleft and noncleft sides, they observed that the philtrum width (Cph-Ls) was longer in the UCLP group on the cleft and noncleft side. Different results observed in the study conducted by Ayoub et al. (126) may be attributed to not applying PNAM and using different surgical techniques. In addition to carefully designed and applied surgical technique, performing NAM may also have played a role in achieving normal labial width. During NAM, with the help of the molding plate and adhesive tapes, the approximation of the alveolar segments and overlying lip tissues to each other enables

the surgeon to repair the upper lip under less tension, which may lead to development of minimal scar tissue and normal labial widths (12,121,128,248).

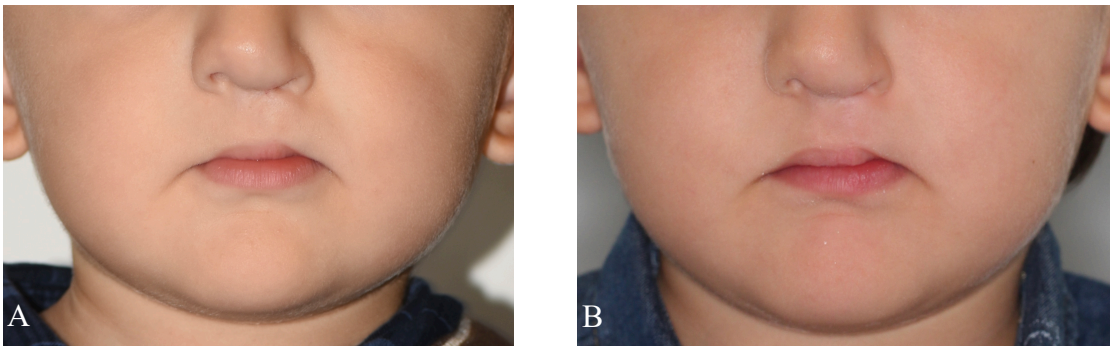


Figure 5.2.3. Labial view of a patient with UCLP at (A) T0 and (B) T1.

Nasolabial asymmetries are seen between the cleft side and the noncleft side in individuals with UCLP (241). Although NAM and primary surgeries greatly correct the asymmetries, some asymmetry of the nose and the lip still remains (110,241). According to the findings of our study, when the symmetry of the nasal region was examined, it was observed that individuals with UCLP had more asymmetrical features comparing with the control group at T0 and T1. A significant asymmetry in terms of nostril width was seen in individuals with UCLP (alar length NC/C, nasal base width NC/C, nostril width NC/C). No statistically significant changes in the nasal region were observed between groups from T0 to T1. Similar to our results, Liou et al. (14) observed asymmetry in the nasal area in individuals with UCLP in the postoperatively 1st, 2nd and 3rd year. They stated that this asymmetry remained stable from the postoperative 1st year to the 3rd year. Brons et al. (199) also stated that there was residual nasal asymmetry in individuals with UCLP at 12 months of age. Al-Rudainy et al. (123) stated that tip of nose deviated to noncleft side at 4 years following surgery in individuals with UCLP but the residual asymmetries of nares and paranasal area increased towards 4 years following surgery. Unlike the results of our study, we can attribute this increase in the asymmetry observed by Al-Rudainy (123) to the fact that the individuals were not initially treated with NAM. Kimura et al. (249) also stated that although the symmetry is quite corrected, the nasal area remains asymmetrical at 4-6 years of age. Moslerova et al. (250) also reported that individuals with UCLP showed significant asymmetry in the nasolabial region (the alae nasi on the cleft side, the philtrum and the upper lip on the cleft side) compared to healthy individuals. They showed underlying skeleton and muscular diastasis as the reason for this asymmetry

seen in individuals with UCLP. When the asymmetry in the upper lip was examined, it was observed that the cupid's bow angle NC/C and upper lip transverse length NC/C ratios improved in individuals with UCLP from T0 to T1. We can say that lip transversal asymmetry improves with growth. On the other hand, when lip asymmetry was examined vertically, statistically significant asymmetry was observed in individuals with UCLP in lateral lip height NC/C and medial lip height NC/C ratios. No statistically significant change was observed in these ratios with growth from T0 to T1 between individuals with UCLP and healthy individuals. The reason for this situation may be the deficiency in the soft tissue due to the initial deformity in the cleft region. Similar to the results of our study, Al-Rudainy et al. (123) also observed vertical deficiencies at upper lip region at the age of 4 in individuals with UCLP in their study. Most significant asymmetries were observed in the alar cartilage and nostril area. We think that the persistent lower lateral cartilage deformity with alar webbing and flaring led to the nasal asymmetry. It seems that the labial asymmetry was less significant.

Overall, did we achieve our treatment objectives in children with UCLP treated by NAM and primary cheilorhinoplasty in the postoperative first years? We can say that although cleft stigmata was still evident to a certain degree as also reported by previous studies, normalization and maintenance of the columellar inclination, nostril height, philtrum width, Cupid’s bow arm, lateral nasal width, upper lip width and lateral length and nasofrontal angle supported the success of the treatment. For the unattained objectives, the treatment techniques were revised for the refinement of the outcomes. As mentioned before, the surgeon has started modifying his surgical technique in the piriform aperture with more radical intervention to control the lateral drift of the alar tissues and alar webbing. From the orthodontic standpoint, the orthopedic correction of alar base on the cleft side which might improve the transversal nasal symmetry, may also be achieved using different POT techniques such as Latham’s Dentomaxillary Advancement (DMA) treatment (251–253). With the use of DMA, besides of correcting the lateral rotation of the greater segment, approximately 4 mm of anterior displacement of the lesser segment can be achieved in the sagittal direction, which enables the establishment of the proper cleft-side ala base support before cleft lip and nasal reconstruction. Achieving anteroposterior alar base symmetry by resetting the cleft side piriform rim and aligning the cleft site tissue margins may help the surgeon to optimize the surgical outcomes in terms of alar symmetry. However, as orthodontists who have already experienced DMA appliance, we think that Latham approach is a more invasive

technique compared to NAM, requiring anesthesia and application of retention pins to the palate of the infant to fix the appliance.

An important clinical implication of our study is the fact that we might not need to use postoperative nasal stents to reach and preserve the normal nostril heights in patients with UCLP. Although we did not use any nasal stents in our study group after the surgery, the nostril heights on the cleft side were normal in the short-term. Some authors advocated the use of nostril retainers to prevent collapse of the nostrils and obtain better nasal outcomes (12,254). On the other hand, it was also reported that the use of postsurgical silicone nasal retainer is demanding in children because they resist the placement of the device (128). Furthermore, the authors suggested presurgical NAM instead of postsurgical nasal retainers because of the ease of use and since they couldn't find any difference between both approaches in terms of postoperative nasal symmetry outcome at age of 4 years (128). However, we still think that before reaching a decision, we need to evaluate long-term results of patients treated with and without postsurgical nostril retainers.

It is worth to consider some of the limitations of our study. Firstly, it can be said that individuals with CUCLP who had not received NAM treatment were not included and only one type of surgical intervention was evaluated. In order to include individuals who have not been treated with NAM, this study should be converted into a multicentric study. Because, if the general health status of individuals with CUCLP referred to our clinic does not constitute an obstacle to the treatment and the parents accept this treatment modality, it is recommended to apply NAM to all the patients with CUCLP. Despite the fact that some individuals do not have general health problems, their parents may refuse the treatment due to various reasons such as living away from the institution center providing the treatment, the treatment costs, being a challenging treatment, and psychological conditions. Apart from these individuals, treatment is recommended to all individuals with CULCP who applied to our craniofacial clinic. Therefore, it is unethical to include untreated individuals in our study. In addition to NAM treatment, many studies have shown that the pressure after primary cheiloplasty and secondary operations also affect nasolabial growth (255,256). However, primary cheiloplasty and secondary operations both contribute positively to development of the proper functions of the individual with UCLP, increase their comfort and support the psychology of the parents. Since it is not possible to not to repair a cleft deformity, one can only use historical untreated groups for comparisons and evaluation of the surgical effects on the

nasolabial growth. In addition, since different surgical techniques may have different effects on nasolabial growth. a multicenter study may help to reveal these differences.

Secondly, while evaluating the development of individuals with UCLP, severity of the initial cleft deformity before NAM may affect the results. The correction of nasolabial deformity with NAM can be limited in individuals with severe deformity. Moreover, scar tissue formation can be more due to tension created during surgery in individuals with severe deformity. Moreover, severity of osseous misalignment and columellar deficiency may also affect the treatment results. Therefore, in future studies, the correlation between these factors and the treatment outcomes should be examined.

Thirdly, only the development of short-term nasolabial growth was followed in our study after NAM and surgical treatments. When the results of our study were examined, the nasolabial region of UCLP patients showed similar growth pattern to that of normal subjects. It is not known how nasolabial growth will be affected in the following years. More studies with longer follow-up period are needed to examine how nasolabial growth is affected in individuals with UCLP at later ages. In order to examine how relapses and improvements observed in some regions will be affected in later ages, there is a need for 3-dimensional studies in which control group consisting of older healthy individuals is included.

6. CONCLUSION

In our prospective longitudinal controlled study conducted on children with UCLP following the first years after NAM and primary cheilorhinoplasty evaluating 3D nasolabial changes, the following conclusions were reached:

At the nasal region of the patients with UCLP;

- Nostril width on the cleft side was higher at T0 and T1 compared with healthy individuals,
- Nostril height on the cleft side was found similar between groups at T0 and T1,
- The nostril perimeter on the cleft side was found greater compared with healthy individuals at the beginning and the end of the observation period.
- Nasal tip protrusion was higher compared with healthy individuals at T0 and T1.
- No columellar deviation was noted during observation period compared to the healthy individuals.

At the labial region;

- Some of the vertical labial measurements were shorter compared to the control group whereas labial transversal measurements were generally normal or getting normal and more symmetrical over time.

At profile;

- Facial profile evaluation revealed a flatter profile compared to control group.

When the asymmetry was further evaluated;

- An explicit transversal nasal asymmetry was observed especially in alar length, nasal base width and nostril width whereas a less significant labial asymmetry was noted.
- In individuals with UCLP, an improvement in the transversal lip symmetry was observed with growth. However, vertical asymmetry remained especially in medial lip height.

The null hypothesis was accepted. In general, there was a similar growth tendency of the nasolabial area both in children with and without UCLP. Moreover, no

adverse effect of NAM-surgical technique combination was observed on the nasolabial growth of children with UCLP.

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27/09/2018

İlgili Makama (Begüm Dikmetaş)

Yeditepe Üniversitesi Diş Hekimliği Fakültesi Ortodonti Bölümü Prof. Dr. Derya Çakan'ın koordinatör olduğu **"Nazoalveoler Şekillendirme ile Tedavi Edilmiş Dudak Damak Yarıklı Bireylerde Nazolabial Büyümenin Kısa Süreli Takibi"** isimli araştırma projesine ait Klinik Araştırmalar Etik Kurulu (KAEK) Başvuru Dosyası (**1515** kayıt Numaralı KAEK Başvuru Dosyası), Yeditepe Üniversitesi Klinik Araştırmalar Etik Kurulu tarafından **26.09.2018** tarihli toplantıda incelenmiştir.

Kurul tarafından yapılan inceleme sonucu, yukarıdaki isimi belirtilen çalışmanın yapılmasının etik ve bilimsel açıdan uygun olduğuna karar verilmiştir (**KAEK Karar No: 895**).

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9. CURRICULUM VITAE

Personal Information

Name	Begüm	**Surname**	Dikmetaş
Place of Birth		**Date of Birth**	
Nationality		**TR ID Number**	
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Education Status

Degree	Department	The Name of Institution Graduated From	Graduation Year
Doctorate	Orthodontics	Yeditepe University	2021
Master	Faculty of Dentistry	Yeditepe University	2014
University	Faculty of Dentistry	Yeditepe University	2014
High School		Tuzla Behiye – Dr. Nevhiz Işıl Anatolian Highschool	2009

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Program	Level
MS Office	Good