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Official Publication of Istanbul University Faculty of Dentistry

Eur Oral Res 2024; 58(2): 83-87

Original research

Midface asymmetry in non-syndromic unilateral cleft lip-palate: A retrospective cbct analysis

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Purpose
The aim of this study was to determine the relationship between the zygomaticomaxillary complex (ZMC) and infraorbital foramen region (IFR) with facial symmetry in patients with unilateral cleft lip and palate (UCLP) using cone beam computed tomography (CBCT).

Materials and Methods
In this retrospective study, CBCT images of 30 non-syndromic UCLP patients were included, along with 30 age- and sex-matched control individuals. ZMC symmetry was evaluated in the axial section by comparing the right and left sides. Similarly, symmetry in the IFR was assessed in the coronal section. The significance level was set at $p<0.05$ for statistical analysis.

Results
The study group comprised 12 female and 18 male patients, with ages ranging from 10 to 18 years (mean age 14.1 years). Both ZMC and IFR measurements were significantly lower on the cleft sides of the study group compared to both the non-cleft sides of UCLP patients and the control group ($p<0.001$, $p=0.022$, and $p=0.036$, respectively). Furthermore, IFR measurements were significantly lower in the control group compared to the non-cleft sides of the study group ($p=0.04$).

Conclusion
This study demonstrated that individuals with UCLP exhibit asymmetry in both the ZMC and the IFR. These findings suggest a negative impact on facial aesthetics.

Keywords: *Facial asymmetry, cleft lip-palate, midface symmetry, esthetics, cone beam*

Introduction

Cleft lip and palate (CLP) is one of the most common craniofacial deformities. Although the exact etiology of CLP is not known, it is believed to be caused by a combination of genetic and environmental factors (1). Facial asymmetry, a common condition, can arise from various causes, including congenital malformations and hereditary and environmental factors (1). Among patient groups with facial asymmetry, those with CLP exhibit the most significant influence of heredity. Asymmetry can be observed in the middle and lower facial regions of these patients. Skeletal and dentoalveolar asymmetries have been documented on the cleft side of the maxilla in individuals with CLP (2). Studies have indicated that individuals with more symmetrical faces tend to have better emotional, psychological, and physiological health, and are often perceived as more attractive compared to those with asymmetrical faces (3, 4). The zygomatic complex plays a crucial role in determining the width and height of the lateral face and contributes significantly to overall facial shape (5).

The objective of this study is to investigate the relationship between the zygomaticomaxillary complex (ZMC) and the infraorbital foramen region

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Received: 1 September 2022
Revised: 3 January 2023
Accepted: 1 June 2023

DOI: 10.26650/eor.20241169632

How to cite: *Tumani Ustdal B, Evlice B, Duyan Yuksel H. Midface asymmetry in non-syndromic unilateral cleft lip-palate: a retrospective cbct analysis. Eur Oral Res 2024; 58(2): 83-87.* DOI: 10.26650/eor.20241169632

(IFR) in terms of midfacial symmetry in non-syndromic patients with unilateral cleft lip and palate (UCLP) using cone beam computed tomography (CBCT). Furthermore, the study aims to compare these findings with a control group. The null hypothesis tested in this project is that there are no differences in the measurements ZMC and IFR between individuals with or without UCLP.

Materials and Methods

Ethical approval

This retrospective study was conducted in accordance with the principles of the 1964 Declaration of Helsinki and it was approved by the Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (date: 01/10/2021, meeting no: 115, decision no: 32).

Sample size determination

To determine the sample size, power analysis was conducted using pilot study data (G*Power 3.1.9.4), which indicated that 30 patients were needed for each group based on an effect size of 0.88, significance level (α) of 0.05, and power (β) of 0.90.

Study design

In this retrospective study, CBCT images of 30 non-syndromic unilateral cleft lip and palate (UCLP) patients and 30 healthy individuals were evaluated. The study group consisted of 12 female and 18 male patients with a mean age of 14.1 years (ranging from 10 to 18 years). The control group was randomly selected from retrospective images of systemically healthy patients who were matched with the study group in terms of age and gender and had undergone CBCT for various reasons such as impacted teeth and implant planning. Radiographs were excluded from the study if they had artifacts, positioning errors, or insufficient image quality for detailed examination.

Zygomaticomaxillary complex (ZMC) symmetry was evaluated by measuring the distance between the most prominent point of the zygoma (malar eminence) and the vertical line drawn from the basion point on the right and left sides in the axial section, following the methodology of Khaqani et al. (6) (Figure 1). Infraorbital foramen region (IFR) symmetry was evaluated by measuring the distance between the widest point of the infraorbital foramen and the midsagittal reference line at the crista galli on the right and left sides in the coronal section (Figure 2). All measurements were conducted by two oral and maxillofacial radiologists (BE: 15 years of CBCT interpretation experience; BTU: 3 years of CBCT interpretation experience). To assess intra-observer agreement, the observers made the measurements twice, with a one-week interval.

Imaging protocols

Radiological evaluations were performed using a 22-inch LG Flatron monitor (LG, Seoul, Korea) with a screen resolution of 1440x900 pixels and a color depth of 32-bit. CBCT images were acquired using Planmeca Promax® 3D Mid (Planmeca, Helsinki, Finland) in standard resolution mode (90 Kv, 10 mA, 27 s scan time, voxel size: 0.4 mm3). The DICOM format data were transferred to Romexis 5.2.0 software (Planmeca Oy, Helsinki, Finland), and all images were evaluated in coronal and axial sections.

Statistical analysis

Statistical analysis was performed using IBM SPSS software version 20.0 (IBM SPSS, Armonk, NY, USA). The Shapiro-Wilk test was used to assess the normal distribution of the data. Paired samples t-test was employed to compare the cleft and non-cleft sides of CLP patients, while independent samples t-test was used to compare CLP patients with the control group. The significance level was set at $p<0.05$. The Pearson correlation coefficient was used to measure the reliability of the raters' repeated measurements, and the intra-class correlation coefficient was used to test inter-rater reliability.

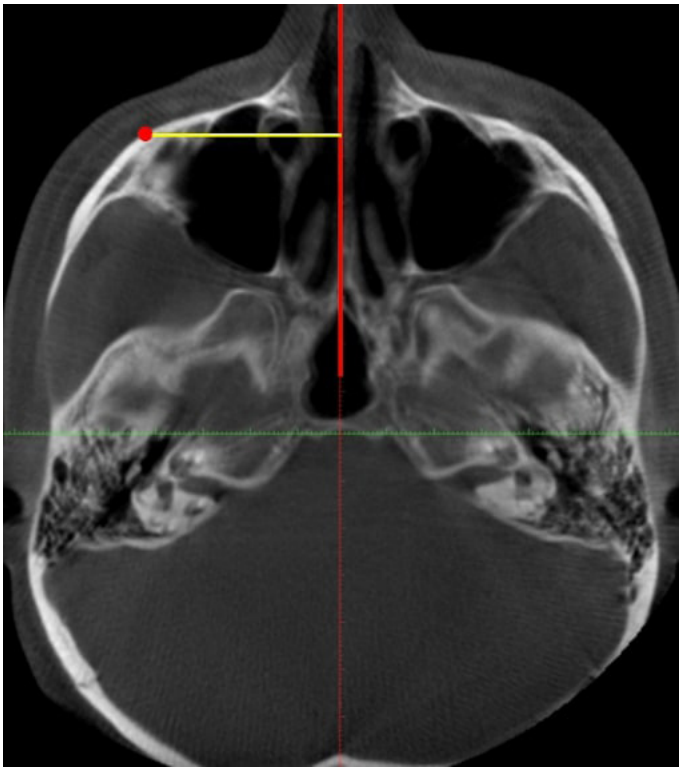

Figure 1. *Measurement of zygomaticomaxillary complex symmetry from the axial section.*

Results

In this retrospective study, ZMC and IFR measurements were performed on CBCT images from both the right and left sides of 60 patients. The measurements were calibrated by evaluating correlation coefficients. The minimum intra-rater reliability for the first and second observers was 0.83 ($p<0.001$) and 0.87 ($p<0.001$) respectively. The minimum inter-rater reliability was 0.81 ($p<0.001$) (Table 1).

Significant differences were observed in ZMC and IFR measurements between the cleft side and non-cleft side in the study group ($p<0.001$) (Table 2). Furthermore, the ZMC

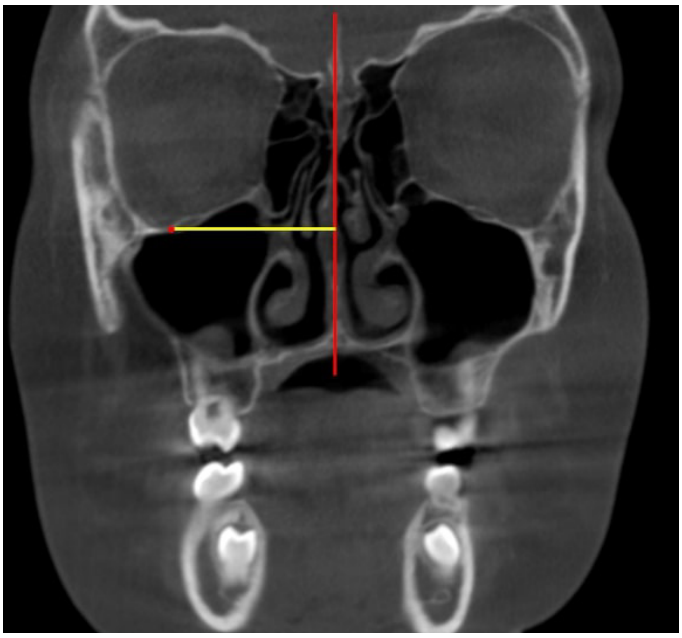

Figure 2. *Measurement of infraorbital foramen region symmetry from the coronal section.*

and IFR measurements were significantly lower on the cleft side of the study group compared to the control group, with p-values of 0.022 and 0.036 respectively (Table 3). Additionally, the IFR measurements were significantly lower in the control group compared to the non-cleft sides of the study group (p=0.04) (Table 3).

Table 1: *Correlation coefficients for intra-rater and inter-rater measures.*

Side	PCC for 1st observer	PCC for 2nd observer	ICC for inter-observer
IFR	0.832	0.871	0.825
ZMC	0.858	0.898	0.811
	p<0.001 (for all measurements)		

ICC: Intra-class correlation coefficient, PCC: Pearson correlation coefficient

Table 2: *Comparison of the cleft and non-cleft sides of the study group according to ZMC and IFR measurements.*

Side	N	Mean± Std. Dev.	*p*
IFR-Non Cleft	30	33.08±2.59	<**0.001***
IFR-Cleft	30	29.79±2.11	
ZMC-Non Cleft	30	43.59±4.66	<**0.001***
ZMC-Cleft	30	40.54±5.23	

ZMC: zygomaticomaxillary complex, IFR: infraorbital foramen region

Table 3: *Comparison of the study and control groups according to ZMC and IFR measurements.*

Side	N	Mean± Std. Dev.	*p*
IFR-Non Cleft	30	33.08±2.59	**0.004***
IFR-Control	30	31.16±2.39	
IFR-Cleft	30	29.79±2.11	**0.022***
IFR-Control	30	31.16±2.39	
ZMC-Non Cleft	30	43.59±4.66	0.600
ZMC-Control	30	43.03±3.59	
ZMC-Cleft	30	40.54±5.23	**0.036***
ZMC-Control	30	43.03±3.59	

ZMC: zygomaticomaxillary complex, IFR: infraorbital foramen region

Discussion

Children born with cleft lip and palate often exhibit significant facial asymmetry resulting from the congenital deformity. Asymmetrical facial features have been extensively documented in the literature (2,7,8). The objective of this study was to investigate the relationship between the zygomaticomaxillary complex (ZMC) and infraorbital foramen region (IFR) with midface symmetry in patients with non-syndromic unilateral cleft lip and palate (UCLP).

Various methods have been employed to assess facial asymmetry, including direct measurements of anthropometric landmarks, measurements from photographs or video frames, and 3D scans (9,10,11,12-14). Similarly, various methods have been used to evaluate ZMC symmetry (5,15-18). However, the increasing availability of low-dose cone beam computed tomography (CBCT) has provided researchers with a quantitative and three-dimensional tool to assess cleft deformities and asymmetry (14). In this study, the CBCT technique was selected due to its significantly lower radiation dose and high reliability in length measurements (19-21).

Although numerous studies have examined asymmetry in UCLP patients, the evaluation of midface asymmetry remains limited (14). Our study revealed a significantly higher rate of asymmetry in the midface region of UCLP patients. Harikrishnan and Balakumaran (19) developed a 3D model of an UCLP patient's skull using CBCT and observed asymmetry not only in the maxilla but also in the orbital, zygomatic, and frontal bones, consistent with our findings. Agarwal *et al.* (22) described the maxilla and its associated bones as hypoplastic, deformed, and volumetrically reduced in UCLP patients. Since the maxillary bone is interconnected with the orbital region, the hypoplastic and defective maxillary bone may also contribute to insufficiency in the orbital region.

Patel *et al.* (23) reported significant midface asymmetry in the majority of cleft patients, including expansion to the mandible and upper midface (zygoma) in some cases. Choi *et al.* (14) utilized CBCT to compare asymmetries in the midface and dentoalveolar areas and found significant differences only in the nasolabial and dentoalveolar regions when comparing the cleft and non-cleft sides of UCLP patients. Similarly, Bugaighis *et al.* (24) discovered statistically significant differences in the symmetry of all 3D landmarks between UCLP patients and the control group, with the most significant differences observed in the nasolabial region. Another study by Yang *et al.* (25) reported significant differences between the cleft and non-cleft sides primarily around the cleft and nasal chamber, with no significant differences extending to deeper regions of the maxillary complex.

In contrast to these studies, our findings revealed asymmetry extending beyond the nasolabial region. The facial asymmetry observed in UCLP patients is believed to arise from hypoplastic and deformed bones and associated muscles, which not only impact aesthetics but also diminish the patients' quality of life. In addition to addressing functional concerns, enhancing aesthetics can improve the quality of life for individuals with UCLP, who are already disadvantaged due to the deformity.

This study had certain limitations. Firstly, the study did not encompass soft tissues, which may play a crucial role in determining aesthetic facial symmetry. Additionally, the sample size was relatively small. Future studies with larger sample sizes, including soft tissue analysis, should be conducted to provide more comprehensive insights.

Conclusion

This study demonstrates that individuals with UCLP exhibit greater asymmetry in the midface region when compared to the control group. This condition adversely affects facial aesthetics, emphasizing the importance for physicians to address both functional improvement and enhancement of facial aesthetics throughout the stages of treatment for UCLP patients.

Türkçe özet: *Non-Sendromik Unilateral Dudak-Damak Yarığında Orta Yüz Asimetrisi: Retrospektif Bir KIBT Analizi. Amaç: Bu çalışmanın amacı, unilateral dudak damak yarığı (UDDY) olan hastalarda konik ışınlı bilgisayarlı tomografi (KIBT) kullanarak zigomatikomaksiller kompleks (ZMK) ve infraorbital foramen bölgesinin (IFB) yüz simetrisi ile ilişkisini belirlemektir. Gereç ve Yöntem: Bu retrospektif çalışmaya yaş ve cinsiyet açısından uyumlu 30 non-sendromik UDDY'li ve 30 sağlıklı bireyin KIBT görüntüleri dahil edildi. ZMK simetrisi aksiyal kesitte sağ-sol taraflardan değerlendirildi. IFB'deki simetriyi belirlemek için ölçümler koronal kesitte sağ-sol taraflardan yapıldı. İstatistiksel analizde anlamlılık düzeyi p<0,05 olarak belirlendi. Bulgular: Çalışma grupları 12 kadın ve 18 erkek hastadan (yaş aralığı:10-18, ortalama yaş:14.1) oluşmaktadır. ZMK ve IFB ölçümleri çalışma grubunun yarık olan tarafında, hem UDDY'nin yarık olmayan tarafına kıyasla hem de kontrol grubuna kıyasla anlamlı derecede düşüktü [sırasıyla (p<0.001), (p=0.022) ve (p=0.036)]. Ayrıca kontrol grubunun IFB ölçümleri çalışma grubunun yarık olmayan tarafına kıyasla anlamlı derecede düşüktü (p=0,04). Sonuç: Bu çalışma, UDDY'li bireylerin hem ZMK'te hem de IFB'de asimetriye sahip olduğunu göstermektedir. Bu durum yüz estetiği açısından olumsuz bir etki yaratır. Anahtar kelimeler: Yüz asimetrisi; Dudak damak yarığı; Orta yüz simetrisi, estetik, konik ışın*

Ethics Committee Approval: The study protocol was reviewed and was approved by the Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (date: 01/10/2021, meeting no:115, decision no:32).

Informed Consent: Participants provided informed constent.

Peer-review: Externally peer-reviewed.

Author contributions: BTU, BE participated in designing the study. BTU, BE participated in generating the data for the study. BTU, BE participated in gathering the data for the study. HDY participated in the analysis of the data. BTU wrote the majority of the original draft of the paper. BTU, BE participated in writing the paper. BTU, BE, HDY has had access to all of the raw data of the study. BTU, BE, HDY has reviewed the pertinent raw data on which the results and conclusions of this study are based. BTU, BE, HDY have approved the final version of this paper. BTU, BE, HDY guarantees that all individuals who meet the Journal's authorship criteria are included as authors of this paper.

Conflict of Interest: The authors declared that they have no conflict of interest.

Financial Disclosure: The authors declared that they have received no financial support.

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