European Journal of Orthodontics, 2015, 544–549
doi:10.1093/ejo/cju082
Advance Access publication 29 December 2014

Original article

Effects of cleft lip and palate on the development of permanent upper central incisors: a cone-beam computed tomography study

Ahmet A. Celebi*, Faruk I. Ucar, Ahmet E. Sekerci***, Murat Caglaroglu**** and Enes Tan******

*Department of Orthodontics, Faculty of Dentistry, Ishik University, Erbil, Iraq, **Department of Orthodontics, Faculty of Dentistry, Selcuk University, Konya, ***Department of Oral and Maxillofacial Radiology, Faculty of Dentistry, Erciyes University, Kayseri, and ****Department of Orthodontics, Faculty of Dentistry, Kirikkale University, Turkey

Correspondence to: Enes Tan, Department of Orthodontics, Faculty of Dentistry, Kirikkale University, Kurtulus Mahallesi, 692. Sokak, No. 31, 71100 Merkez, Kirikkale, Turkey. E-mail: dentistan@yahoo.com

Summary

Objective: The aim of this study was to evaluate 1. the differences among the cleft sides of unilateral cleft lip and palate (UCLP) patients, non-cleft sides of the same UCLP patients and well matched control patients in the root development and position of permanent upper central incisors and 2. possible gender differences.

Materials and methods: The study sample consisted of 40 patient (20 males and 20 females; mean age: 14.84±3.2 years) with non-syndromic UCLP patients, and 40 control patients (20 males and 20 females; mean age: 13.38±1.6 years). Cone-beam computed tomography (CBCT) images were taken off from all patients. All tomographs were obtained in supine position by using CBCT (NewTom 5G, QR, Verona, Italy).

Results: Significant smaller root volume of central incisor was observed on the cleft side than on the non-cleft side of UCLP patients ($P < 0.05$). No significant difference in the root development and position of the central incisors was found between the non-cleft side of the UCLP and the control group ($P > 0.05$). There were no statistically significant gender differences in any linear, angular, or volumetric measurements ($P > 0.05$). Only the root volume of the cleft side was smaller in females than in males ($P < 0.05$).

Conclusions: In general, root volumes of central incisors on the cleft side were 12.15 per cent smaller than non-cleft side. Root development of the central incisor was much more influenced by the cleft in females than in males.

Introduction

Cleft lip and palate (CLP) are the most common congenital deformity of the head and neck (1). It is known that CLP influences the characteristics of the midface and anterior maxillary region, which may vary from slight alterations to extremely severe changes (2). Characteristically, children with these disorders require multidisciplinary care from birth to adulthood.

Clinically, clefts of the lip and palate are generally divided into two groups, isolated cleft palate and cleft lip with or without cleft palate, representing a heterogeneous group of disorders affecting the lips and oral cavity (3). Approximately 12 to 25 per cent of the genetic variations associated with non-syndromic CLP have been identified (4). Although genetic studies have identified a number of candidate genes and chromosomal regions associated

with CLP, findings from different studies have been inconsistent (5).

Patients with CLP usually present many dental anomalies such as hypodontia, supernumerary teeth, ectopic eruption, microdontia, fused teeth, posterior crossbites, and pseudoprognathism. These defects may be attributed to the cleft itself or to the early surgical correction of the defects (2).

In many studies, root lengths were measured to assess the root development in CLP patients (6,7). Al-Jamal *et al.* (8) measured the root lengths and crown-root ratios of permanent teeth of CLP patients by using panoramic radiography. Conventional radiographies, such as periapical and panoramic radiographs, have limitations such as magnifications and distortions. This can cause inaccuracy in the measurement of root length. Cone-beam computed tomography (CBCT) is a new radiographic method that has been applied in orthodontics and maxillofacial radiology for CLP patients. CBCT provides highly detailed three-dimensional imaging that can be obtained at any angle. This makes linear, angular, and volumetric measurement more accurate and reproducible.

The purpose of this study was to evaluate the root development, position anomalies of permanent upper incisors and possible gender differences in patients with UCLP and well matched control group by using CBCT.

Materials and methods

We examined the CBCT scans of 40 patients (20 males and 20 females; mean age: 14.84 ± 3.2 years) with non-syndromic unilateral cleft lip and palate (UCLP) (19 right and 21 left) and 40 control patients (20 males and 20 females; mean age: 13.38 ± 1.66 years) were selected from the archives of the Oral and Maxillofacial Radiology Department, Faculty of Dentistry, Erciyes University (Table 1). In this study, sample size calculation was based on Pandis' formula (9) a significance level of 0.05 and a power of 90 per cent to display a difference of 22.2 mm (±1.8 mm) for the central incisor root volume between UCLP and control groups. Thirty-five patients were required in each group according to the power analysis using the findings of Zhou *et al.* (7). The images used in the present study were part of the diagnostic records collected due to dental treatment needs. No patients were contacted and no CBCTs were taken for the objectiveness of the present study. The patients had signed an informed consent form allowing the use of their data for scientific purposes. The study was approved by the local ethics committee of Erciyes University.

Table 1. Mean and standard deviations of chronological age (years).

	Non-syndrome UCLP		Control group	
	Mean	SD	Mean	SD
Female (20)	13.73	4.13	13.3	2.17
Male (20)	15.08	3.11	13.97	1.17
Total (40)	14.84	3.2	13.38	1.66

SD, standard deviation; UCLP, unilateral cleft lip and palate.

We considered ALARA principle (as low as reasonably achievable) and the current European sedentex CT guidelines on the taking of CBCTs. All of the individuals of the control group had impacted canines so we took CBCTs from these patients for the localized assessment of the impacted canine including consideration of resorption of the adjacent teeth. Therefore, we could limit the area to upper canine region on the maxilla in the control group. However, we had to include all the face in CLP patients for the assessment of soft tissues including nose, lips, and velopharyngeal insufficiency. Control patients were matched by age and gender to the UCLP patients in the study. Selection criteria for UCLP and control patients are listed in Table 2.

All tomographs were obtained in supine position by using CBCT (NewTom 5G, QR, Verona, Italy). Scanning time was 18 seconds, collimation height was 13 cm, exposure time was 3.6 seconds, and the voxel size was 0.3 mm^3.

Primary reconstructions of the data were performed with the number needed to treat (NNT) software. Before Digital Imaging and Communications in Medicine (DICOM) data was obtained, the midsagital plane was constructed by NNT viewer software, and the sagital slice plane of incisors was established. Secondly, the exported DICOM files were viewed, and segmentation was carried out using SimPlant Pro 2011 (Materialise NV; Materialise; Figure 1).

Using Simplant software functions, Frankfurt horizontal plane was constructed by passing through right and left orbital points as well as midpoint of the right and left porion. Sagittal plane was constructed by passing through nasion and mid-orbital points, perpendicular to the Frankfurt horizontal plane (Figure 2 and Table 3). The angulations of the central incisors of the cleft and non-cleft sides were measured in relation to the Frankfurt horizontal and sagittal plane on 3D-reconstruction (Table 3).

Table 2. Criteria for sample selection.

Inclusion criteria for cleft lip palate patients	Exclusion criteria for cleft lip palate patients
Patients with complete/incomplete unilateral cleft lip and palate	Absence of upper permanent central incisors
Presence of upper permanent central incisors	Dilacerated root form of central incisor
Permanent or mixed dentition	Incompleted apexification of upper central incisors
Completed apexification of upper central incisors	Patients who had undergone orthodontic treatment
No history of trauma and systemic disease or neuromuscular deformities	History of trauma and systemic disease or neuromuscular deformities
Lack of orthodontic treatment and/or maxillary functional orthopedic treatment	
Patients had undergone lip and palate reconstruction surgery	
Inclusion criteria for control patients	**Exclusion criteria for control patients**
Presence of upper permanent central incisors	Dilacerated root form of central incisor
Permanent or mixed dentition	Incompleted apexification of upper central incisors
Completed apexification of upper central incisors	Patients who had undergone orthodontic treatment
Impacted canines which have no contact with central incisors	Impacted canines which have contact with central incisors
	History of trauma and systemic disease or neuromuscular deformities

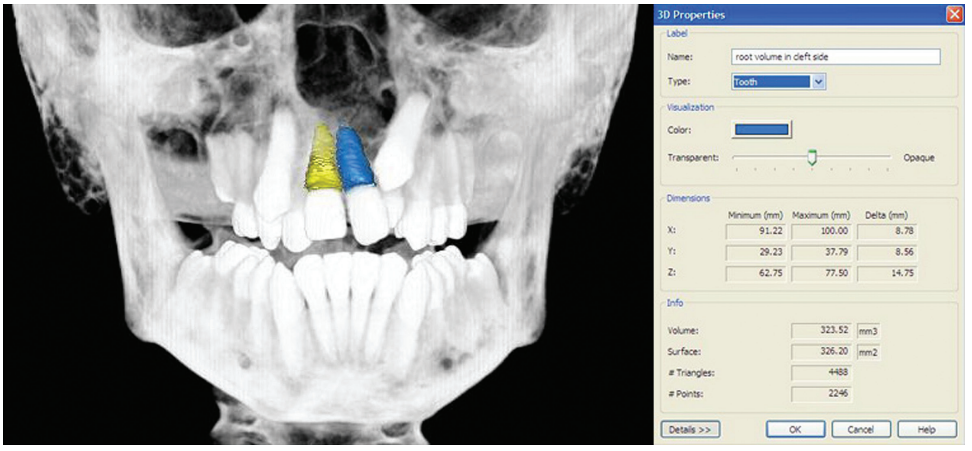

Figure 1. Volumetric measurements of the maxillary central roots.

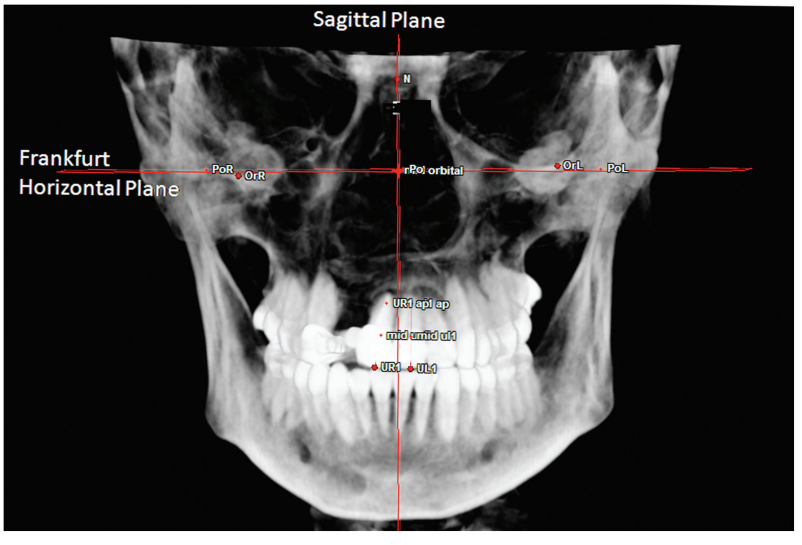

Figure 2. Landmarks and references planes used in this study.

Table 3. Description of the measurements.

Measurements	Definition
Frankfurt horizontal plane	Plane defined by point PoL, point PoR, and midpoint of the right and left porion
Sagital plane	Plane through point N and point mid orbital and perpendicular to Frankfurt horizontal plane
U1 to Frankfurt horizontal plane (mm)	Distance between midpoint of U1 and Frankfurt horizontal plane
U1 to Frankfurt horizontal plane angle	Angle between U1 axis and Frankfurt horizontal plane
U1 to sagital plane (mm)	Distance between mid point of U1 and sagital plane
U1 to sagital angle angle	Angle between U1 axis and sagital plane

The distance of the center point of the teeth to sagittal and Frankfurt horizontal plane was measured in order to determine the position of teeth according to the sagittal and Frankfurt horizontal plane.

The patient-specific Hounsfield values (min: 1500, max: 3071) were set to include the largest amount of voxels in the tooth volume calculation. CBCT data were reconstructed with surface and volume rendering, and the volumetric image was manipulated to display the root surfaces from various orientations. Central incisors were cropped and separated from the maxilla. To obtain pure 3D mask of central incisors, redundant voxels and surrounding alveolar bone were extracted by using 'edit mask in 3D' feature of the software. The tooth was rotated and moved to be perpendicular to Frankfurt horizontal plane. On the axial plane, the tooth was cut on the tip of the cementoenamel junction parallel to the Frankfurt horizontal plane. Thus, the root and crown were separated from each other. Finally, the root volume was calculated by the software.

All data were measured in angle, mm or mm^3 and all landmark identifications and measurements were made by the same author to prevent inter observer variability. The percentage of root volume difference was calculated as:

$$\frac{(\text{Root volume in non cleft side - Root volume in cleft side}) \times 100}{\text{Root volume in cleft side}}$$

Statistical analysis

To determine the random error, 15 images were selected randomly and then all linear and root volume measurements were repeated 3 weeks after the first examination by the same orthodontist with no knowledge of the first measurements. The coefficients of reliability according to the Houston method (10) for volumetric measurements confirm reliability. Intraclass correlation coefficients (ICC) were performed to assess the reliability of the measurements, and the difference between the two examinations was tested by means of a paired *t*-test.

All statistical analyses were performed using the statistical package for social sciences, 13.0 (SPSS for Windows; SPSS Inc., Chicago, Illinois, USA). Normality of the data was tested using Kolmogorov–Smirnov test. All UCLP data was normally distributed with homogeneous variance. Therefore, we used parametric tests to evaluate the volumetric, angular, and linear data. Independent sample *t*-test was used to compare genders. To compare the gender differences between the cleft and non-cleft sides in UCLP patients, and between the right and left sides in control patients, independent sample *t*-test was used. We performed paired sample *t*-tests to evaluate side differences, and differences between UCLP and control patients. The right and left sides of the control group were compared with the non-cleft side of UCLP patients to evaluate the differences in root development between UCLP and control patients. *P* values less than 0.05 were considered as significant.

Results

The ICC values were 0.992, confirming the reliability of the measurements. In addition, results of the paired *t*-test showed that the measurements were free of the systemic error ($P > 0.05$). No statistically significant sex differences were found in either cleft or non-cleft sides in all parameters ($P > 0.05$), except the upper central root volume was found significantly smaller in females than in males on the cleft side of UCLP patients ($P < 0.05$; Table 4).

Descriptive statistics, comparisons of the upper central incisor root volume, angulations and position measurements between the cleft and non-cleft sides of UCLP patients and both sides of the control group are presented in Table 5. In UCLP patients, upper central incisor root volume was smaller on the cleft side than on the non-cleft side ($P < 0.01$). Root volume was $194.92 \pm 62.53\ mm^3$ on the cleft side and $237.25 \pm 63.22\ mm^3$ on the non-cleft side. Approximately 12.15 per cent decrease was calculated in the root volume compared to non-cleft side. In control group patients, upper central incisor root volume was $251.08 \pm 44.61\ mm^3$ on the right side and $242.90 \pm 45.96\ mm^3$ on the left side. No statistically significant difference was found on the right and left side of the control group ($P > 0.05$; Table 5).

There were no significant differences in angular, linear, and volumetric measurements of the central incisors between the non-cleft side of UCLP patients and the control group ($P > .05$; Table 6).

Table 4. Sex differences in linear, angular, and volumetric measurements between the cleft and non-cleft sides in UCLP patients sides in UCLP.

Measurements	UCLP patients										Control group									
	Cleft side					Non-cleft side					Right side					Left side				
	Female		Male			Female		Male			female		male			Female		Male		
	Mean	SD	Mean	SD	*P*	Mean	SD	Mean	SD	*P*	Mean	SD	Mean	SD	*P*	Mean	SD	Mean	SD	*P*
Upper central root volume (mm^3)	160.84	50.93	214.64	61.14	0.02	217.66	49.35	248.60	68.66	NS	236.63	42.07	269.48	42.54	NS	229.09	47.93	260.48	38.44	NS
U1 to Frankfurt horizontal plane (mm)	34.61	4.50	37.19	4.69	NS	34.10	5.27	36.30	5.54	NS	34.05	7.90	36.85	3.92	NS	37.60	3.91	37.09	4.13	NS
U1 to Frankfurt horizontal plane angle	71.59	7.60	70.14	6.68	NS	66.05	9.70	71.68	7.29	NS	58.51	27.24	69.15	7.41	NS	72.44	6.09	69.08	7.90	NS
U1 to sagital (mm)	3.31	2.26	3.43	2.05	NS	4.59	2.00	3.99	1.99	NS	3.39	2.47	4.39	1.78	NS	4.46	2.05	3.15	2.28	NS
U1 to sagital plane angle	11.97	10.89	13.46	8.07	NS	12.70	8.66	8.83	7.34	NS	10.8	8.56	9.56	8.00	NS	11.40	8.26	10.58	9.07	NS

NS, non-significant; SD, standard deviation; UCLP, unilateral cleft lip and palate.

Table 5. Side-to-side comparison of the linear, angular, and volumetric measurements between the cleft and non-cleft sides in UCLP patients and right and left sides of control group.

	UCLP					Control				
	Cleft side		Non-cleft side			Right side		Left side		
	Mean	SD	Mean	SD	*P*	Mean	SD	Mean	SD	*P*
Upper central root volume (mm^3)	194.92	62.53	237.25	63.22	0.001	251.08	44.61	242.90	45.96	NS
U1 to Frankfurt horizontal plane (mm)	36.44	4.63	35.76	5.52	NS	35.98	5.36	37.25	3.94	NS
U1 to Frankfurt horizontal plane angle	68.99	6.14	71.70	8.50	NS	66.31	15.76	70.08	7.12	NS
U1 to sagital (mm)	3.65	2.25	3.90	1.83	NS	4.08	1.99	3.56	2.24	NS
U1 to sagital plane angle	12.74	8.50	10.18	8.08	NS	13.82	16.14	11.13	7.35	NS

NS, non-significant; SD, standard deviation; UCLP, unilateral cleft lip and palate.

Table 6. Comparison of the linear, angular, and volumetric measurements between non-cleft side of UCLP and control group

	Non-cleft side of UCLP		Control group		
	Mean	SD	Mean	SD	*P*
Upper central root volume (mm^3)	237.25	63.22	244.99	45.30	NS
U1 to Frankfurt horizontal plane (mm)	35.76	5.52	36.61	4.67	NS
U1 to Frankfurt horizontal plane angle	71.70	8.50	67.98	12.53	NS
U1 to sagital (mm)	3.90	1.83	3.82	2.10	NS
U1 to sagital plane angle	10.18	8.08	7.99	3.68	NS

NS, non-significant; SD, standard deviation; UCLP, unilateral cleft lip and palate.

Discussion

The present study stated that the root development of permanent upper incisors was affected by the cleft. Approximately 12.15 per cent decrease was calculated in the root volume compared to non-cleft side. There were no significant differences in the volume of the central incisors between the non-cleft side in UCLP patients and the control group which shows that environmental factors play a key role in determining root volume rather than genetics.

In previous studies, periapical (11) and panoramic radiographs (12) were used for the evaluation of root development quantitatively and qualitatively. However, radiographs may appear blurred and distorted, which causes inaccuracy in marking and measurements. Besides, the precision and reliability of conventional radiographs are affected by the angulation and rotation of the tooth and also by the patient's position (13, 14). Therefore, it is difficult to determine root development of the upper central incisors particularly with the use of conventional radiographs. CBCT provides highly detailed 3D imaging, which can offer favourable view and no superposition. Furthermore, the complex anatomical structures like roots of teeth can be performed in three dimensions by using Simplant 13.01.

UCLP patients were included in the present investigation instead of patients having bilateral CLP. This allowed us to use the measurements of the contralateral non-cleft side of each individual as an internal control. Maxillary central teeth were used to evaluate the effects of CLP on the root development because the central teeth are the earliest erupted teeth around the cleft. Lateral incisors are commonly congenitally missing or have root malformations (7). Maxillary canines are the last of the permanent dentition to erupt and to complete root development. For these reasons, maxillary central incisors were used in this study.

Zhou *et al.* (7) indicated that root lengths of the central incisor were reduced by 15.8 per cent and found 1.1 mm shorter root length on cleft side of UCLP patients compared to non-cleft side. In the present study, volumes of central incisors on the cleft side were 12.15 per cent smaller compared to non-cleft side. Authors also evaluated the effects of cleft side on genders, but did not find a significant difference. In our study root development of upper central incisors on non-cleft side were not affected by the gender. On the contrary, root volume of the upper central incisors on the cleft side was found smaller in females. This finding could be the result of longer roots in males or shorter roots in females.

The relationship between genetic and environmental factors in the human tooth root formation is not well understood. Some types of environmental factors such as chemotherapy (15) and radiotherapy (16) during tooth development were reported to result in short-rooted teeth. Several studies investigating the effects of sex chromosome abnormalities on the growth of the root concluded that promoting effect of Y chromosome on the root length was found greater than the effect of X chromosome (17). This could have been the cause of longer roots in males.

In a previous study, on the panoramic radiographs, it was reported that the maxillary incisors of cleft patients had significantly shorter roots than non-cleft patients (8). In one study about the lateral incisors, root development was compared in maxillary lateral incisors using cleft and non-cleft sides (6). It was found that the root development was delayed on the cleft side, which was in agreement with the findings of previous studies (18, 19). Similarly, Demirjian *et al.* (20) concluded that mechanisms controlling dental development are independent of somatic and sexual maturity and are highly influenced by the same etiologic factor as the cleft. Because some types of environmental determinants during tooth development and genetic factors may result in short-rooted teeth (21). CLP patients should be considered as potentially having short roots.

It is interesting to note that cleft and non-cleft side difference in central root volume was found significant in the UCLP group in this

study. However, no statistically significant differences were found in any of the other central position measurements. These differences may be related to genetic factors or to functional matrix around the cleft side particularly in the masticatory apparatus. But, there was no significant difference in the root volume and position of the central incisors between the right and left sides of the control group.

Some researchers suggest that a deficient blood supply near the cleft side, either congenital or as a result of surgery, may negatively affect incisor root formation (18). The less vascularization of the CLP patients may decrease the differentiation and proliferation of the cells in the developing roots, which could cause deficiencies in the organization of the root dentine during tooth development (7). Similarly, the root formation of the central incisors was affected by CLP in our study.

Eruption pattern of the central incisor was not affected in the cleft side compared to the normal side. Our results, consistent with the observations of Peterka *et al*. (22), showed that angulations of the upper central incisors on the cleft side were not different from the normal side. Previous studies (2, 6, 7) used CBCT or panoramic radiographs. They concluded that root of upper incisors in non-syndromic CLP patients are underdeveloped and that incisors which are closer to the cleft show more developmental deficiency. They measured root length from the cementoenemal junction to the root apex. Nevertheless, not only the root apex but also the whole root was affected by the cleft. In our study, we revealed how much the cleft affects the total volume of root.

Conclusion

Root development of the central incisor was more influenced by the cleft side in females than in males. Root volumes of central incisors on the cleft side were 12.15 per cent smaller compared to the non-cleft side. Root volumes of central incisors were not different between the non-cleft side of UCLP and the control group.

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