Mandibular Dysmorphology in Patients with Unilateral Cleft Lip and Cleft Palate

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Background: Conventional studies of the cleft lip/palate (CLP) dysmorphology have mainly focused on deformities of the lip, nose, and maxilla, while ignoring the mandible. Reasons for that were the lack of well-defined mandibular deformity and restriction from the research methodology.

Methods: This study used 3-dimensional computed tomography (CT) imaging data from 35 patients with unilateral CLP. The 3-dimensional images were rotated into a neutral position. Eight cephalometric landmarks were recorded: the pogonion (PG) and the infradentale (ID) from the frontal view; and the condylion (CO), the tip of coronoid process (CP), and the gonion (GO) from both sides of lateral views. The nasion was used as a reference point for the facial midline. Nine linear distances and four angular measurements were calculated from these landmarks. Each mandible was segmented into two hemi-mandibles for volume measurements. The image manipulation and measurements were performed using a personal computer running Analyze™ program. Landmark deviation from the facial midline was computed, and comparisons were made between the cleft and non-cleft sides.

Results: The results showed that the precision and accuracy of landmark localization was high with an average error of 0.4%. Deviation from the midline of the ID and PG points, and spatial distances between bilateral CP, CO, and GO points varied without a specific pattern. The average differences were within 2 mm. The volume of the cleft side hemi-mandible was consistently larger than that of the non-cleft side ($p < 0.0001$). Among linear and angular measurements, CP-GO-PG, CO-ID, CP-ID, and CP-GO showed significant difference between the two sides.

Conclusion: This study demonstrated that mandibular asymmetry and deformity existed and was measurable in patients with unilateral CLP. The influence of CLP to the mandibular development was expressed by the significant differences of hemi-mandible volume and some of the linear and angular measurements between the cleft and non-cleft sides.

(Chang Gung Med J 2002;25:502-8)

Key words: **cleft lip, cleft palate, mandibular deformity.**

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Received: Dec. 15, 2001; Accepted: Apr. 18, 2002
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While deformities of the cleft lip/palate (CLP) are typically located on the median facial area, i.e., the nose, palate, maxilla, and upper lip, mandibular deformities associated with CLP have been clinically observed as well. The mandible is the only mobile part in craniofacial area, which occludes the maxilla through the tempero-mandibular joints. It is therefore theorized that mandibular deformities exist in patients with CLP. Drahoradova and Mullerova found mandibular dysmorphology in a group of 5-year-old boys with unilateral CLP, characterized by shortened mandibular body, posterior rotation and retrusion.(1) Laspos et al, by means of posteroanterior cephalometric analysis, were able to document asymmetry of the mandible in patients with complete unilateral CLP.(2) They found that the asymmetry increased with growth and time, and developed in a parallel pattern with the affected maxilla. Capelozza et al studied unoperated adults complete unilateral CLP, and found well-defined differences in the mandibular body, ramus, gonial angle, and mandibular plane angle, compared with the healthy control group.(3) Because the development of the mandible is influenced by hereditary (intrinsic), developmental (growth), and environmental (extrinsic) factors, it is complicated to interpret the mandibular deformities by studying older children or adults. In a recent study, mandibular deformity was demonstrated in infants with complete unilateral CLP. Hermann et al found short mandibles and bimaxillary retrognathia in 2-month-old infants with unoperated unilateral CLP.(4) All the studies were performed using 2-dimensional cephalometric analysis. The disadvantages of using 2-dimensional images were the difficulties to control the ideal facial position at the time of X-ray taking for patients at younger ages or with asymmetrical face, and to locate landmarks out of the overlapping structures.(5) From our previous experience, 3-dimensional imaging study may help to solve the problems.(6-14) To the best of our knowledge, there has been no study of mandibular deformity in CLP using a 3-dimensional imaging method. In this report, we used 3-dimensional computed tomography (CT) data from 3-month-old unoperated cleft patients to evaluate the mandibular dysmorphology.

METHODS

In this study, 3-dimensional CT imaging data were used to evaluate mandibular deformity. Thirty-five patients with unilateral complete cleft lip, alveolus, and palate were included. Twenty-six patients had left CLP, and nine had right CLP. These patients were non-syndromic and had no other major congenital anomalies that may otherwise be associated with facial bone problems. The average age of the patients was 3.2 months (range, 2.7 to 4.0 months) and the cleft was unrepaired at the time of CT scanning. The CT scanning was performed according to a standard protocol (i.e., spiral scanning for the whole head). The data were reconstructed to create continuous slices at 1.5 mm thickness before being transferred to the imaging laboratory. Data processing was carried out using a personal computer running Analyze™ program (Mayo Clinic Rochester, Minn, USA).(15-18) The data were reformatted and the voxel size was set between 0.4 and 0.6 mm for these scans. A thresholding technique with fixed ranges of CT intensities was applied to display the osseous tissues.

The 3-dimensional images were rotated into a neutral position (Frankfort horizontal, true antero-posterior, and vertical midline).(13) The axes were reconfigured to the rotation of the image in the standard position (Fig. 1). Using the object definition

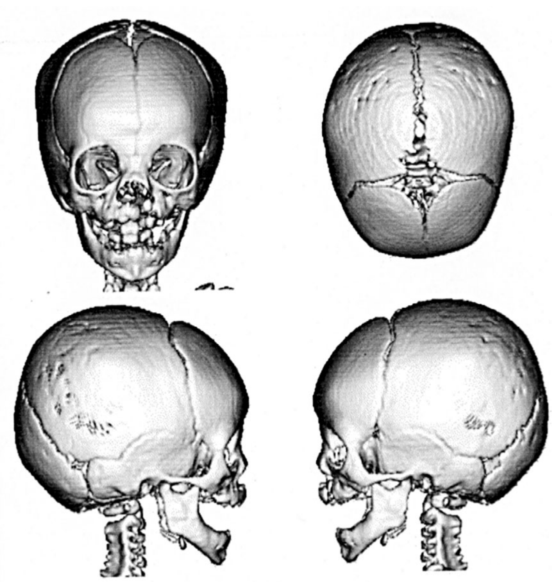

Fig. 1 The 3-dimensional images were rotated into a neutral position (Frankfort horizontal, true antero-posterior, and vertical midline). The axes were reconfigured to the rotation of the image in standard position.

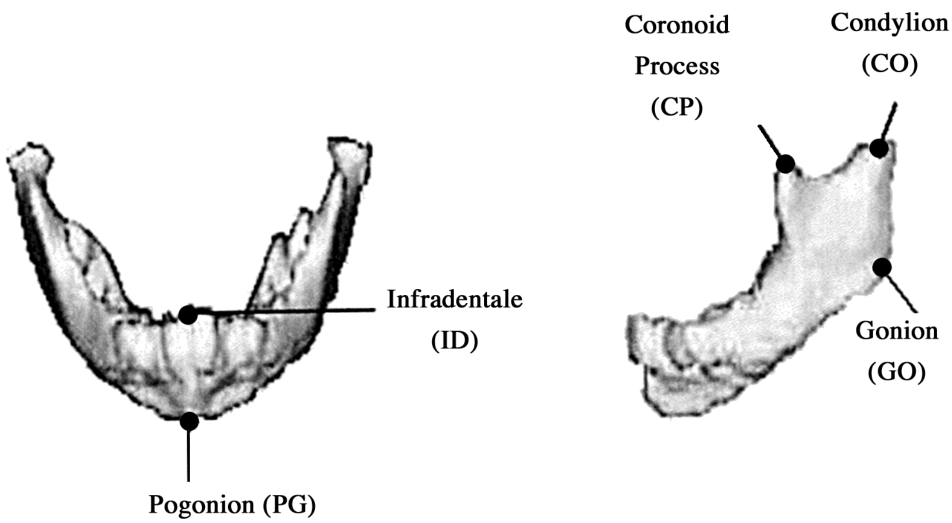

Fig. 2 The mandible was extracted from a 3-dimensional skull image after rotation into a standard position. The landmarks were identified from the frontal and lateral views.

tool, the mandible was extracted from the 3-dimensional osseous volume image. The skull was rotated to allow accurate cutting (for extraction) of the mandible. Eight cephalometric landmarks were recorded from each 3-dimensional osseous image: the pogonion (PG), and the infradentale (ID) from frontal view; and the condylion (CO), the tip of coronoid process (CP), and the gonion (GO) from two lateral views (Fig. 2). Intra-rater errors for localization of the landmarks were calculated from the differences between repeated landmark definitions. The nasion was picked to serve as the reference point for face midline. The x, y, z coordinates of the landmarks were compared with the face midline, and between both sides. Nine linear distances (CP-CO, CP-GO, CP-PG, CP-ID, CO-GO, CO-PG, CO-ID, GO-PG, GO-ID) and four angular measurements (CP-CO-GO, CO-GO-PG, GO-PG-ID, CP-GO-PG) were calculated from these landmarks. The mandible was segmented into two hemi-mandibles from symphysis junction. The heminandibles were divided into cleft side and non-cleft side. Computing the hemimandible volume was performed by the measure function within the Analyze™ program that automatically counted the numbers of voxels within the segmented objects and multiplied this number by the volume of a unit voxel. The linear and angular measurements were also achieved using built-in tools in the Analyze™ program. The accuracy of the measurements has been validated.[19] These measurements were compared between the cleft and non-cleft sides using the formula: (cleft side - non-cleft side)/non-cleft side. Statistical analysis was performed using the paired *t*-test. To keep the overall alpha level at 0.05, the Bonferroni adjustment was used when multiple testings were performed.

RESULTS

Intra-rater accuracy for landmark localization was high, with a mean error of 0.4% and a range from 0 to 5.6% between the repeated tests. Deviation of ID and PG from the face midline (x coordinate of nasion) ranged from 1.8 mm on the non-cleft side to 3.6 mm on the cleft side, with a mean deviation of 0.6 mm for both ID and PG to the midline (Table 1). The spatial differences between bilateral CP, CO, and GO in the x, y, and z axes were irregular and varied from -6.6 mm to 10.2 mm without a specific pattern. The mandibular deformities could be grossly observed on computer displays of patients with wide spatial differences of the landmarks. However, the average differences were within 2 mm between the two sides (Table 1). The volume on the cleft side hemi-mandible was consistently larger than that on non-cleft side, with statistical significance (Table 2). Among the linear and angular measurements, CP-GO-PG, CO-ID, CP-ID, and CP-GO showed significant differences between the cleft and non-cleft sides, while others did not. Wide ranges of the differences were observed (Table 3). Although not fully supported by statistical analyses, the cleft side hemimandible seemed to be relatively longer, as shown in the linear distances from CO-ID, CO-PG, CP-ID, and CP-PG measurements (Table 2).

Table 1. Deviation of ID and PG from Face Midline (as Compared with the X Coordinate of the Nasion), and the Spatial Differences between Both Sides of CP, CO, GO

	X	Y	Z
CP	0.0 (-3.0~4.2)	0.6 (-6.0~ 4.8)	-0.6 (-3.0~3.0)
CO	0.5 (-4.8~5.4)	0.1 (-6.6~ 4.2)	-0.7 (-4.8~3.0)
GO	0.8 (-5.4~7.2)	0.9 (-3.0~10.2)	1.6 (-4.2~1.2)
ID	0.6 (-1.8~3.6)		
PG	0.6 (-2.5~3.6)		

Positive data means toward the cleft side, and negative data means toward the non-cleft side. The data are shown by mean (minimum, maximum) in mm.

Table 3. Quantitative Measurements from 3D CT Images and the Differences between the Cleft and Non-Cleft Sides by Formula as (Cleft Side - Noncleft Side)/Noncleft Side in Percent

	Average Difference	Range of Differences
Volume	5.21% (335.48 mm^3)	0.3%~10.3%
Angle		
CO-GO-PG	1.2% (1.31 degrees)	-7.6%~16.5%
CP-GO-PG	6.1% (5.07 degrees)	-17.1%~23.3%
GO-PG-ID	2.9% (1.98 degrees)	-20.3%~19.6%
CP-CO-GO	-1.1% (-1.01 degrees)	-27.3%~20.2%
Line		
CO-ID	2.1% (1.06 mm)	-10.9%~10.4%
CO-PG	1.8% (1.01 mm)	-15.8%~12.1%
CO-GO	3.9% (0.77 mm)	-16.1%~18.3%
CP-ID	4.6% (1.80 mm)	-5.9%~19.9%
CP-PG	2.0% (0.95 mm)	-19.4%~14.5%
CP-GO	1.2% (0.16 mm)	-15.0%~19.7%
CP-CO	-4.7% (-0.90 mm)	-19.9%~17.7%
GO-ID	-0.5% (-0.28 mm)	-14.4%~14.4%
GO-PG	1.8% (0.63 mm)	-10.4%~18.5%

The actual difference, cleft side - non-cleft side, is shown in the parenthesis.

Table 2. Quantitative Measurements from 3D CT Images and Comparisons between the Cleft and Non-Cleft Sides

	Cleft Side	Non-Cleft Side	*p**
Volume	6963.4 ¡ 1151.6 mm^3	6627.9 ¡ 1146.3 mm^3	< 0.0001#
Angle			
CO-GO-PG	130.9 ¡ 5.2 degrees	129.6 ¡ 6.3 degrees	NS
CP-GO-PG	95.5 ¡ 7.7 degrees	90.4 ¡ 8.2 degrees	0.0017#
GO-PG-ID	82.3 ¡ 19.3 degrees	81.4 ¡ 7.8 degrees	NS
CP-CO-GO	68.2 ¡ 9.2 degrees	69.2 ¡ 7.0 degrees	NS
Line			
CO-ID	55.7 ¡ 2.9 mm	54.7 ¡ 3.5 mm	0.0451
CO-PG	62.3 ¡ 3.3 mm	61.2 ¡ 3.1 mm	NS
CO-GO	26.1 ¡ 2.8 mm	25.3 ¡ 3.3 mm	NS
CP-ID	43.6 ¡ 2.6 mm	41.8 ¡ 3.4 mm	0.0001#
CP-PG	52.4 ¡ 4.1 mm	51.4 ¡ 3.7 mm	NS
CP-GO	26.2 ¡ 1.9 mm	26.0 ¡ 2.4 mm	NS
CP-CO	15.9 ¡ 1.4 mm	16.8 ¡ 1.7 mm	0.0041#
GO-ID	41.7 ¡ 2.7 mm	42.0 ¡ 2.3 mm	NS
GO-PG	42.0 ¡ 3.3 mm	41.4 ¡ 3.0 mm	NS

Data presented are mean ¡ SD
NS: not significant
*: calculated using paired t-test
#: still significant after Bonferroni adjustment

DISCUSSION

The development of unilateral CLP occurs at the embryonal stage when the maxillary process fails to fuse with the frontonasal process on one side, resulting in the separation of the lip, alveolus, and palate on this side.[20] The separation gradually becomes wide and asymmetric during fetal development, possibly due to the tongue movement and asymmetric pulls from the attached facial muscles. After birth, the major facial deformities for a patient with unilateral CLP include twisted and depressed nose, and cleft lip with wide alveolar and palatal cleft. The premaxilla is deviated toward the non-cleft side, and the cleft side maxillary segment is more posteriorly displaced.[13] It is to be noted that the spatial position of the non-cleft side maxilla is not normal, instead the dysmorphology of the non-cleft side maxilla, together with its overlying nose, has been observed and measured. Because the mandible occludes with the maxilla, it is therefore theorized that mandibular dysmorphology exists in patients with unilateral cleft lip and palate.

It is rational to use unoperated cleft patients to study mandibular deformities, since the influence from surgery is eliminated. Conventional cephalometry is difficult to perform on such young children, and the landmark localization is complicated as well. Three-dimensional CT obviates these problems, and allows for accurate measurement.[19,21,22] Accuracy and precision of landmark localization was confirmed in this study, as well as in another study.[23]

The mandibles in this group of 3-month unilateral CLP patients were more likely to be deviated to the cleft side, as shown in the mean deviation from 0.5 to 0.8 mm of CO, GO, ID, and PG. This is similar to the observation of patients with hemifacial microsomia, in which the mandible deviates toward the lesion side. Comparatively, the deviation was of smaller magnitude in the cleft patients. Larger volumes of cleft side hemimandible were observed in all 35 patients, which is in contrast to those with hemifacial microsomia. This result is difficult to explain, but its relation to the effect of the maxillary cleft is clear. Longer linear distances from the CO-ID, CO-PG, CP-ID, and CP-PG on the cleft side may explain the consistent volume differences. Although wide ranges of differences on the linear and angular measurements were noted (Table 2), the influence of the unilateral CLP to the mandibular asymmetry and deformities was demonstrated by the significantly different hemimandible volume along with some of the linear and angular measurements. Because dental and surgical management corrects the cleft deformity and improves the maxillary as well as dentoalveolar symmetry, it will be interesting to follow up the cleft patients and evaluate the corresponding changes of the mandibular dysmorphology over time. The findings may help to refine our CLP treatment protocol.[24]

In conclusion, although most of the comparisons between the cleft and non-cleft sides did not show statistical significance, wide ranges of differences were observed (Tables 1, 2 and 3). This study showed that mandibular asymmetry and deformity existed and was measurable in patients with unilateral CLP. The influence of CLP on mandibular development was demonstrated by the significant differences of hemi-mandible volume and some linear and angular measurements between the cleft and non-cleft sides.

Acknowledgments

We would like to thank Dr. Richard A Robb, PhD, Biomedical Imaging Resource, Mayo Foundation, Rochester, Minnesota, USA, for providing the Analyz™ program, and Miss Meng-Chen Wu for technical support. The study was supported by a grant from the National Science Council, NSC 89-2314-B-182A-152.

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單側唇顎裂病人的下顎骨異常

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背 景：唇顎裂會造成功能上和外觀上問題，過去的和傳統的研究焦點大多在唇、鼻，以及上顎，而忽略下顎的研究，一方面是下顎外觀無明顯異常，部分原因也是因爲研究方法和工具的限制。

方 法：這項研究利用35位單側唇顎裂的病人，三度電腦斷層影像爲3個月年齡的手術前影像。首先調整三度影像X、Y、Z軸水平，垂直與正前的標準位置，以比較目標點的相關位置，記錄的8個測顱術使用座標點分別是正面pogonion (PG)和infradentale (ID)，以及兩側的condylion (CO)，coronoid process (CP)，和gonion (GO)，以nasion當作中線的標準點。吾人計算9個線性距離：CP-CO，CP-GO，CP-PG，CP-ID，CO-GO，CO-PG，CO-ID，GO-PG，GO-ID，4個角度：CP-CO-GO，CO-GO-PG，GO-PG-ID，CP-GO-PG，以及半側下顎骨的體積作對稱性的比較。

結 果：研究結果顯示，座標點取得的準確度相當高，其平均誤差爲0.4%。對於ID、PG中線偏離或CP、CO、GO的兩側對稱性，則有裂側與非裂側不同程度的差異出現，然而其平均差皆在2mm以下。裂側的半側下顎骨體積比起非裂側顯著較大 ($p<0.0001$)，平均角度在CP-GO-PG有顯著差異，而平均線性距離在CO-ID、CP-ID和CP-CO有顯著差異外其餘沒有差異。

結 論：這項研究顯示唇顎裂病人的下顎骨異常是的確存在的，此下顎骨異常受唇顎裂的影響可以在較大的裂側下顎骨體積以及部分線性距離和角度測量表現出來。
(長庚醫誌 2002;25:502-8)

關鍵字：唇顎裂，下顎骨異常。

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