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ORIGINAL RESEARCH

Dental and skeletal maturation of Chinese male children with unilateral cleft lip and palate

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Abstract

The aim of this study was to determine whether the relationship between dental age (DA), cervical stage (CS) and chronological age (CA) in Chinese male children with unilateral cleft lip and palate (UCLP) is similar to that of children without clefts. Panoramic and cephalometric radiographs of 105 male UCLP patients, aged from 8 to 16 years, were collected and compared to 210 age-matched healthy control males. The Demirjian and cervical vertebral maturation (CVM) methods were used to visually examine the radiographs and Spearman's correlation analysis was used to identify differences between the two groups with regards to CS, DA and CA. There was a significant positive correlation between DA and CA in both groups and the mean CA-DA difference was significantly higher in children with UCLP when compared to controls (0.319 *vs.* 0.003, $p < 0.05$). A significant delay in tooth development was detected in UCLP children from 10 to 12 years-of-age. Both the UCLP and control groups showed high correlations between CS and DA. Calcification stage D appeared only before CS3; however, from CS5 to 6, all teeth have almost completed their maturation phase. Chinese male UCLP patients are likely to experience delayed tooth development compared to healthy controls, especially during the fast-growing period. Evaluating the stages of tooth mineralization could represent a rapid method to assess growth potential.

Keywords

Cephalometric radiograph; Demirjian method; Cervical vertebral maturation method; Cleft lip and palate

1. Introduction

Cleft lip and palate (CL/P) is one of the most common maxillofacial birth deformities caused by congenital and/or environmental factors. The incidence of CL/P is reducing over time; a recent study stated that only 7.55 per 10,000 perinatal infants had CL/P in Guangdong, China [1]. Children with CL/P may experience a wide range of problems, depending on the severity of the illness, including issues with eating and breathing, speech difficulties, dental anomalies, hearing loss and psychological disorders [2]. These issues can ultimately lead to a negative long-term impact. Therefore, a multidisciplinary approach is needed if we are to address the morphological and functional disorders that accompany CL/P at various ages from birth to adulthood. During the puberty phase, orthopedic and orthodontic treatments are the key procedures used for the comprehensive treatment of CL/P. However, clinicians need to determine the best time to perform these treatments in order to achieve the best results. It is a widely held view that rapid growing jaws respond better to orthopedic treatment during the puberty growth spurt [3]. Thus, over recent years, there has been increasing levels of interest in predicting the growth spur during puberty.

Individual growth and development indicators predominantly include age, height, secondary sex characteristics, skeletal maturity and dental maturation [4]. Skeletal and dental maturity are frequently used to predict pubertal growth spurts and tooth eruption in children with CL/P in order to provide timely orthopedic and orthodontic treatment. In the past, skeletal maturity was commonly evaluated by radiographs of the wrist bones [5]. Subsequently, the cervical vertebral method (CVM) method was introduced as a more convenient, efficient and intuitive way to instantly determine the growth potential using the cephalometric radiograph that is included in routine pre-operative examinations. The CVM method suggested that the cervical morphological features of the second to fourth cervical vertebrae (C2–C4) on lateral cephalometric radiographs could be classified into six cervical stages (CS1–6) and then used to assess individual skeletal maturity [6]. Since it avoids additional exposure of the wrist to radiation, the CVM method has become a popular means of assessing skeletal maturity. Studies conducted in different countries and races have demonstrated the equivalent efficiency of using wrist bone analysis and CVM in predicting the growth peak of adolescents [7–9].

On the other hand, the most common method for determining tooth maturity is to assess the mineralization pattern of each tooth on panoramic films. In 1973, Demirjian *et al*. [10] developed a new dental age assessment method that enabled clinicians to visually estimate the age of children on panoramic radiographs. Because of its efficacy, the Demirjian method is widely used in orthodontics and forensics to estimate individual dental ages. However, children with CL/P are likely to possess dental and jaw deformities; this may lead to inaccurate estimation. The prevalence of dental anomalies has been shown to vary significantly depending on the type and severity of the cleft, including numeric abnormalities such as missing and supernumerary teeth, morphological abnormalities, such as microdontia and fusing teeth, and tooth replacement abnormalities [11, 12]. Furthermore, it has been reported that enamel defects are more common in CL/P patients than in non-CL/P individuals [13].

Similarly, maxilla dysplasia is common in CL/P patients, thus implying that the development of the jaws is abnormal. Furthermore, congenital cervical vertebrae anomalies have been reported in patients with CL/P [14], thus indicating that skeletal maturation is affected by the disease. Our previous research found that when boys with unilateral complete cleft lip and palate (UCLP) were 12 to 14 years-of-age, their skeletal maturity was significantly delayed when compared to controls [15]. However, there is no general agreement on whether CL/P patients and normal controls have different levels of skeletal maturity [16]. Furthermore, few researchers have focused on the dental maturation of CL/P patients, and the specific interactions between skeletal and dental maturation remains unknown. Therefore, the aim of this retrospective study was to investigate differences in dental age between CL/P patients and normal children, and to investigate the correlation between dental age and cervical stage. Our overall goal was to identify a more accurate method to evaluate the growth and development of CL/P patients.

2. Materials and methods

The study was designed as a retrospective, cross-sectional study. We collated a range of clinical information, including radiological records (panoramic and lateral cephalometric radiographs) and full medical records for 315 Chinese boys aged from 8 to 16 years attending the Department of Orthodontic Department of Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine for orthodontic treatment between 2014 and 2022.

There were 105 boys in the UCLP group; these boys were recruited according to the following inclusion criteria: (1) no additional congenital disorders, (2) cheiloplasty performed before 6 months and palatoplasty before 2 years-of-age, (3) good quality lateral cephalometric radiographs and panoramic radiographs available, and (4) no missing or abnormal teeth in the dentition.

The non-cleft group consisted of 210 boys who were age-matched to the cleft group at a ratio of 1:2; the following selection criteria were applied for this group: (1) no additional congenital disorders, (2) no trauma or other diseases that could affect skeletal and dental growth, (3) lateral cephalometric radiographs and panoramic radiographs available and clear, and (4) no missing or abnormal teeth in the dentition.

The Demirjian and cervical vertebral maturation methods [6, 10] were used to evaluate panoramic and lateral cephalometric radiographs, respectively. Only radiographs of the cervical vertebra and teeth were provided; the other personal information was blinded to the researchers.

2.1 Dental age estimation

All seven of the permanent mandibular teeth on the left side were analyzed using the Demirjian method; stages A to H were determined based on the mineralization pattern of the crowns and roots. Each stage was assigned a numerical score, and the total scores were added to calculate the dental maturity score (DMS). The DMS was then converted into dental age using a conversion table which was first introduced by Demirjian *et al*. [10]. Each panoramic radiograph was assessed twice by two different researchers to minimize evaluation bias. Following an 8-week wash-out period, a further 20% of the panoramic radiographs were randomly selected and re-analyzed for a second calibration.

2.2 Cervical stage evaluation

The CVM method introduced by Baccetti *et al*. [6] was used to determine the cervical stage (CS) from the cephalometric radiographs by visual inspection of the concavities of the lower border of the cervical vertebrae (Fig. 1). The definition of each CS was as follows: CS1, no concavities found in the 2nd to 4th cervical vertebrae (C2–C4); CS2, only C2 shows a concave lower border; CS3, concavities in C2 and C3; CS4, concavities in C2, C3 and C4, and all of the cervical vertebrae have a horizontal rectangular shape; CS5, concavities in C2, C3 and C4, and at least one cervical vertebra has a square shape, and CS6, concavities in C2, C3 and C4 and a vertical rectangular shape was evident on at least one cervical vertebra. To increase the reliability of measures, each lateral cephalometric radiograph was examined by two researchers; 20% of the radiographs were reassessed after an 8-week interval.

2.3 Statistics

Statistical analysis was performed using SPSS software for Windows (version 23.0, SPSS, Inc, Chicago, IL, USA). Descriptive statistics (mean values and standard deviations) of the chronological age (CA) and differences in the dental age (DA) of patients were calculated. CA-DA was calculated and compared between groups; this represents the difference between chronological age and dental age. Spearman's rank correlation coefficient was applied to assess the relationship between the CS and dental calcification stages of all analyzed teeth. To test for significance, the t test was used.

3. Results

3.1 Reliability

With regards to the estimation of dental age, the agreement between researchers was good with an ICC (Intraclass Correlation Coefficient) of 0.97. Moreover, the intra-examiner reliability was excellent, with an ICC of 0.98. The kappa

FIGURE 1. Sagittal view of the second, third and fourth cervical bones from CS1–CS6.

coefficient value for cervical stage was 0.809, showing good agreement between researchers. The intra-examiner reliability was also satisfactory, with a kappa coefficient value of 0.884.

3.2 Descriptive statistics

In total, 105 boys were recruited for the UCLP group with a mean CA of 12.21 $\pm$ 2.16 years while the age-matched control group consisted of 210 boys with a mean CA of 12.31 $\pm$ 2.26 years (Table 1). Levene's test was used to test the equality of variance ($p > 0.05$). The t test showed that there was no significant difference in chronological age between the groups ($p = 0.718$).

3.3 Correlation between CA and DA

Fig. 2 depicts the mean CA-DA difference for the two groups. The mean CA-DA difference was greater in the UCLP group than in the control group, as shown by the descriptive statistics for both groups in Table 2. The mean CA-DA difference was 0.003 $\pm$ 0.971 years in the control group; this compared to 0.319 $\pm$ 1.207 years in the UCLP group; there was a significant difference between the two groups with regards to CA-DA difference ($p = 0.013$). Furthermore, when grouping by age, only the 10 to 12 group shows a significant CA-DA difference between UCLP patients and controls (-0.542 ± 0.783 years in the controls *vs.* 0.077 ± 0.239 years in the UCLP group).

3.4 Correlation between CS and DA

Table 3 shows the results of our correlational analysis. Both the UCLP and control groups showed high correlations between CS and DA ($p < 0.001$) and the control group showed a stronger correlation ($r = 0.831$) than the UCLP group. Further exploration revealed a correlation between tooth maturation stage and the CS for different tooth types (Table 4). The second molar ($r = 0.727$) in the UCLP group and the first premolar ($r = 0.758$) in the control group showed the strongest associations. Both incisor groups showed the weakest correlations, with a correlation coefficient of 0.285 in the UCLP group and a correlation coefficient of 0.262 in the control group. The lateral incisors of both groups showed a moderate association between maturation and CS. Dental maturation and CS are strongly correlated in the other types of teeth. The distribution of calcification phases in each tooth type, from CS1 to CS6, is shown in Fig. 3. It shows that as the cervical stage rises, the canines, premolars and second molars showed more variability. CS1 to CS3 had the most variable calcification stages ranging from D to H, whereas CS5 only featured stages G and H.

4. Discussion

To analyze the difference between skeletal and dental development in patients with UCLP and their normal peers, cervical stages and dental ages were measured and compared. We found that Chinese male UCLP patients showed delayed tooth development when compared to healthy controls, especially during the fast-growing period. The CVM method is normally used to assess skeletal maturity and represents a useful tool to predict a child's potential for growth. This technique has been employed commonly to compare the skeletal maturation of CL/P patients and normal youngsters. Most of the current research demonstrates a significant delay in the skeletal maturation of CL/P patients [17, 18]. However, some studies demonstrate the opposite outcomes [19, 20]. One possible explanation for this disparity is difference between ethnic groups. In a previous study, we discovered that Chinese male UCLP subjects aged 12 to 14 years-of-age were at a significantly higher risk of delayed skeletal maturity than normal controls. In the present study, we used the Demirjian method to measure dental age to evaluate the relationship between dental and skeletal maturation in UCLP patients.

Patients with UCLP had a significantly higher CA-DA difference than the controls; this was a key finding. The mean age of the UCLP subjects was underestimated by 0.319 years, thus indicating a possible delay in dental maturation; these results are consistent with previous research [21, 22]. Van Dyck *et al.* [23] systematically reviewed children with CL/P aged 5 to 13 years and noted that delayed dental development ranged from 0.2 to 0.9 years, with a mean delay of 0.56 years.

TABLE 1. Mean and standard deviation (SD) of chronological ages of the UCLP group and a control, as well as the effects of between-subjects tests for groups.

	UCLP group (n = 105)		Control group (n = 210)		*F*	*p*	*t*-value	*p*
	mean	SD	mean	SD				
CA	12.21	2.16	12.31	2.26	0.084	0.772	−0.362	0.718

Level of significance: $p < 0.05$. CA: chronological age; UCLP: unilateral cleft lip and palate.

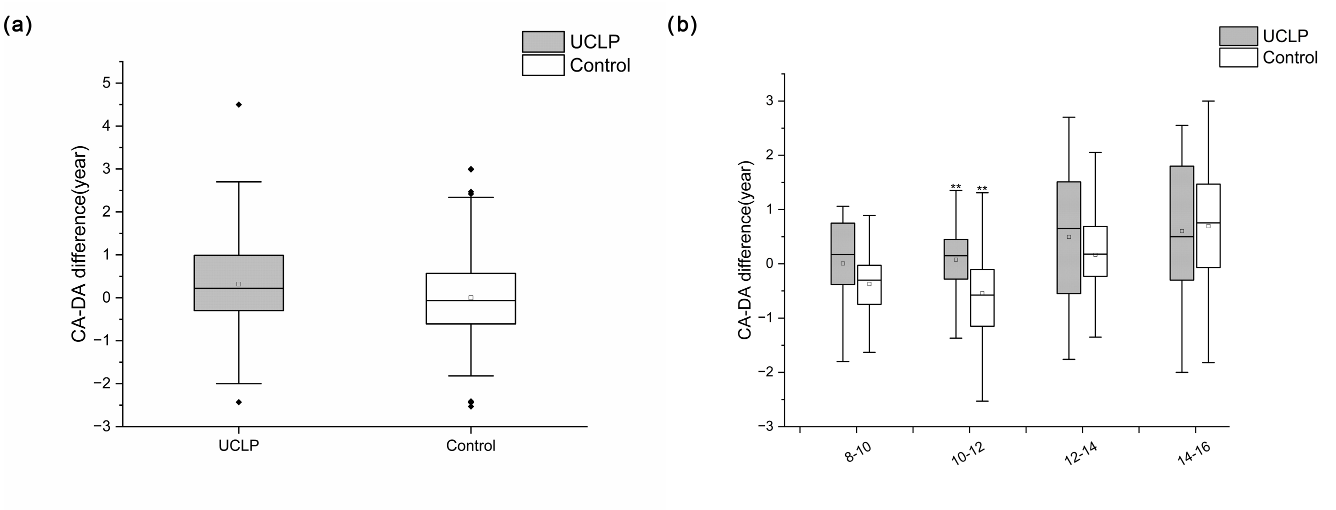

FIGURE 2. Mean CA-DA difference for UCLP and control groups. (a) CA-DA difference compared between UCLP and controls. (b) Difference between CA-DA differences (in years) as compared to the CA subgroups. CA: chronological age; DA: dental age; UCLP: unilateral cleft lip and palate.

TABLE 2. Mean and standard deviation of dental ages and CA-DA differences in all of the participants grouped by chronological ages.

	UCLP			Control			
CA	n	DA	CA-DA difference	n	DA	Mean CA-DA difference	*p*
8–10	18	9.358 ± 1.380	0.007 ± 0.227	36	9.200 ± 0.810	−0.372 ± 0.584	0.079
10–12	30	10.743 ± 1.066	0.077 ± 0.239	60	11.724 ± 0.964	−0.542 ± 0.783	0.005
12–14	31	12.289 ± 1.096	0.495 ± 0.217	62	12.782 ± 0.768	0.168 ± 0.740	0.174
14–16	26	14.504 ± 1.203	0.603 ± 0.251	52	14.533 ± 1.244	0.695 ± 1.139	0.748
	105	11.893 ± 2.137	0.319 ± 1.207	210	12.305 ± 2.260	0.003 ± 0.971	0.013

**Data are shown as mean ± standard deviation. Level of significance: $p < 0.05$. CA: chronological age; DA: dental age; UCLP: unilateral cleft lip and palate.*

TABLE 3. Correlation between CS and DA in the UCLP group and control group.

	n	*r*	*p*
UCLP	105	0.806	<0.001
Control	210	0.831	<0.001

r: Spearman's correlation coefficient. Level of significance: $p < 0.05$. UCLP: unilateral cleft lip and palate.

TABLE 4. Correlation between tooth maturation stage and CS of the UCLP and control group, grouped by different tooth types.

Tooth	UCLP		Control	
	r	*p*	*r*	*p*
I1	0.285	0.003	0.262	<0.001
I2	0.440	<0.001	0.510	<0.001
C	0.708	<0.001	0.711	<0.001
P1	0.713	<0.001	0.758	<0.001
P2	0.702	<0.001	0.756	<0.001
M1	0.692	<0.001	0.609	<0.001
M2	0.727	<0.001	0.750	<0.001

r: Spearman's correlation coefficient. Level of significance: $p < 0.05$. UCLP: unilateral cleft lip and palate.

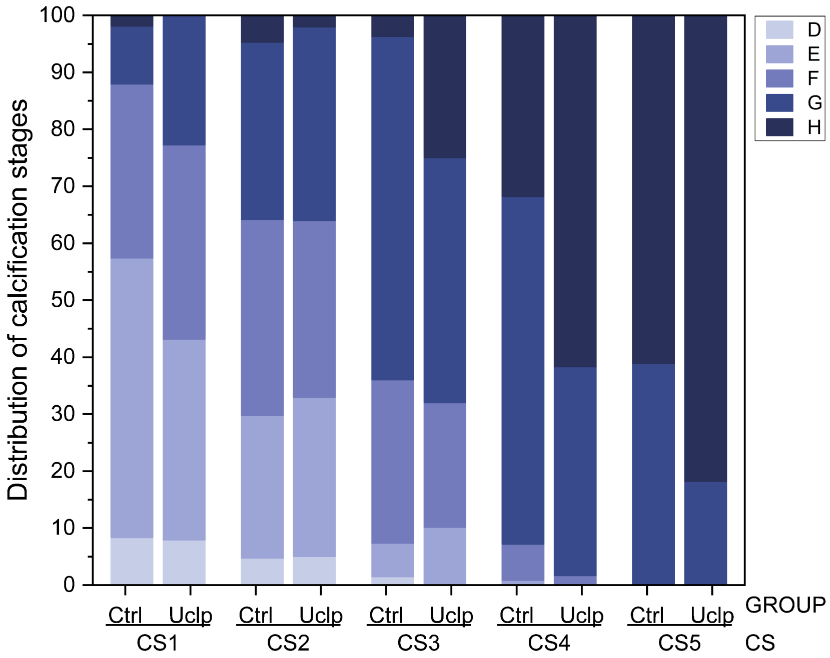

FIGURE 3. Distribution of teeth calcification stages from CS1–5, after excluding incisors and first molars which were least correlated. CS: cervical stage. Ctrl: Control. Uclp: Unilateral cleft lip and palate.

Similarly, Lai *et al*. [24] discovered a delay and asymmetry in tooth development in Chinese CL/P children. However, due to asymmetric development, it has been suggested that using the mean score of bilateral mandibular teeth for CL/P patients may improve accuracy; however, images of the right mandibular teeth were rejected using the Demirjian method in the present study. Further analysis may help to improve the methodology. Furthermore, Ranta *et al*. [25] reported that the delay in tooth development increased with the severity of the cleft, ranging from 0.3 to 0.7 years. Variable degrees of cleft have been shown to be associated with subsequent maxillary deficiencies in three dimensions, including length, height and protrusion [26]. Only unilateral CL/P patients were included in this study. More evidence relating to the impact of different severities and types of clefts on the results will be investigated in future research.

In the present research, we divided the subjects into four subgroups based on their chronological age. Only the 10- to 12-year-old showed a significant difference in CA-DA when compared between the UCLP and control groups. For subjects aged 10 to 12 years, the methodology underestimated the ages of UCLP patients but overestimated the ages of patients in the control group. This implies that tooth development in UCLP patients is likely to be slower than in their normal peers between the ages of 10 and 12 years. Patients with CL/P are more likely to have dental abnormalities during the mixed dentition phase. Because this usually coincides with tooth replacement and occurs around the time of the puberty growth spurt, this period is critical for growth and development. Our findings suggest that permanent tooth development may be delayed in UCLP patients; therefore, orthodontists should be aware of changes in tooth replacement and eruption in their treatment planning.

The observed difference in other age subgroups, however, was not significant. This could imply that dental maturation differs only during the fast-growing period. Although tooth development begins later for UCLP patients, when growth becomes stable and slow, this delayed tooth development may catch up with the normal situation. This finding needs to be validated further to identify whether this reduces the time available for dental maturation in UCLP patients.

Another intriguing discovery suggested that assessing teeth mineralization stages could be a simple way to estimate growth potential. After excluding the incisors and the first molars, which showed weaker correlations, analysis showed that stage D existed only in subjects classified as CS1 to CS3. If, on the other hand, the mineralization stage reaches G or H, our analysis indicates that the puberty growth spurt has passed, and that dental and skeletal maturation is nearing completion. The phase before the growth peak is known as CS1 to 3; this is the best time for orthopedic treatment and early orthodontic treatment because it has the highest potential for growth. The interpretation of tooth mineralization stages on panoramic radiographs may represent a rapid tool for determining treatment time. Further research should be performed to investigate the reliability of this method.

This research has some limitations that need to be considered. For example, the sample population only included UCLP patients with mild dental deformities; the inadequate number of UCLP samples may have led to imprecise results. The Demirjian method is a useful but somewhat limited approach which necessitates counting all seven teeth in the left mandibular region; however, results can be influenced greatly by both ethnicity and gender. As a result, many patients were recruited because they had missing teeth, extra teeth or other dental abnormalities. Further improvements could involve carrying out the study in different genders and in populations with a larger sample size with long follow-up periods to further validate our findings. Future studies can also be optimized with more advanced technologies such as fully automated assessing methods [27].

5. Conclusions

Our analysis showed that dental maturation differed between CL/P patients and healthy controls. Chinese male UCLP patients had a significantly higher CA-DA difference than healthy controls. Furthermore, tooth maturation in UCLP children aged 10 to 12 years may be delayed in comparison to their normal peers. Our findings suggest that permanent tooth replacement may be delayed in UCLP patients; orthodontists should take this finding into consideration when planning treatment. Assessing the stages of tooth mineralization could be a novel way to estimate growth potential. However, more data is needed to confirm the reliability of this method. Furthermore, samples of different genders and severity levels could be added for further investigation.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

YG—conceptualization, methodology, software, investigation, formal analysis, writing original draft; HQY—software, investigation, data curation; writing original draft; JP—data curation, software, validation; QHR—resources, supervision; CJY—conceptualization, supervision, writing review & editing. FJ—conceptualization, funding acquisition, resources, supervision, writing review & editing.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The authors are responsible for all parts of the work. The study and included experimental procedures were approved by the ethical review committee at Shanghai Ninth People's Hospital (SH9H-2021-T415-2) which is affiliated with Shanghai Jiao Tong University's School of Medicine. The study was performed in accordance with the ethical requirements of the institutional and/or national research committee(s) and the Helsinki Declaration (as revised in 2013). The patient's parents gave permission for radiographs and participation in the study. Informed consent was obtained from the participant with a detailed description of the purpose and advantages of the study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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