

Scientific Article

Permanent Tooth Development in Children With Cleft Lip and Palate

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Abstract: **Purpose:** The purposes of this study were to: (1) quantify and compare permanent tooth development of cleft lip and palate (CLP) patients to age- and gender-matched controls; (2) relate these findings to cleft type and severity; and (3) examine delays in individual permanent maxillary teeth related to their proximity to the cleft. **Methods:** Standardized methods using panoramic radiographs were employed to stage dental development and dental age for 49 children with clefts and 49 matched controls. Data were analyzed with a mixed linear model. **Results:** Analyses indicated a correlation between delayed permanent tooth development and CLP with an overall delay of 0.52 years ($P=.02$) and with boys accounting for all the delay. No differences were found between subjects with unilateral or bilateral clefts. A nonsignificant trend was noted for greater delay in subjects with clefts of the primary and secondary palates vs primary palate alone. Teeth most often affected by the delay were maxillary first and second premolars and maxillary second molars. **Conclusions:** While permanent tooth development is delayed in cleft lip and palate patients, this delay is: found in boys only; is independent of the cleft type and severity; and is not correlated with proximity to the cleft. (*Pediatr Dent* 2008;30:408-13) Received July 24, 2007 | Last Revision October 29, 2007 | Revision Accepted November 24, 2007

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Cleft lip and palate is the most common craniofacial birth defect.¹ The presence of a cleft lip or palate has been associated with physical and psychological developmental anomalies.² Without therapeutic and surgical management, these children encounter significant barriers to proper speech, nutrition, and development. Numerous surgeries are required to repair oral clefts, and the timing for these surgeries depends on the child's stage of development. For this reason, there has been great interest in the dental development and possible differences in this development in the cleft population. It was demonstrated as far back as 1968 that children with clefts exhibit significant delays in permanent tooth development.³ Since then, several investigations of tooth development in the cleft population have reported important and sometimes conflicting results. In addition to a delay in development, asymmetric tooth development, anomalies in tooth size and shape, and hypodontia have been shown to occur more often in children with clefts.^{4,5}

The overall delay in tooth development has been quantified in various studies as ranging from 0.3 to 1.1 years.^{6,7}

Conflicting results exist regarding the differential effects of cleft severity and type.⁸ Some studies have shown different effects for females and males with clefts, with males exhibiting more significant tooth delays.^{7,9} The tooth's proximity to the cleft has been shown to play a role in its developmental delay. Some studies have demonstrated greater delays in teeth closest to the cleft, while others have shown that those further away experience significant delays.^{10,11} The effects of clefting on individual teeth, however, have rarely been tested and conflicting results have been found.

The purposes of this study were to: (1) quantify and compare permanent tooth development of cleft lip and palate patients to age- and gender-matched controls; (2) relate these findings to cleft type and severity; and (3) examine delays in individual maxillary teeth as related to their proximity to the cleft.

Methods

This was a retrospective chart review and radiographic analysis-based study. Panoramic radiographs for 6- to 13-year-old cleft lip and palate patients were chosen randomly from records meeting diagnostic criteria collected by the Cleft Palate and Craniofacial Anomalies Clinic at the School of Dentistry, University of Minnesota, Minneapolis, Minn, after approval by the Institutional Review Board. Excluded were patients with clefts presenting as part of a syndrome or with medical conditions suggestive of a syndrome. The control subjects were

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age- and gender-matched patients from the Pediatric Dentistry Clinic at the School of Dentistry, University of Minnesota, matched to within 60 days of age. Patients with any documented peri- or postnatal medical conditions were excluded. Only cases and controls with radiographs of sufficient clarity to score developing teeth were included in the study.

Eighty percent of radiographs were scored by 1 examiner. Additionally, 20% of radiographs were scored by a second examiner and results of both scorers were compared. Any disagreements were discussed and corrected. Identifying information, gender, and date of birth were masked on all radiographs. Every attempt was made to blind examiners regarding experimental or control status of subjects. The presence of a cleft on a panoramic radiograph, however, is apparent.

The radiographs were scored and dental age analyzed using the method described by Demirjian et al, a highly reproducible method of evaluating and scoring dental maturity using panoramic radiographs to rate different stages of permanent tooth calcification.¹² According to written criteria, the stages of tooth formation of the 7 permanent mandibular left teeth (nos. 18-24) were assigned a stage (A-H).

Staging led to maturity scores by reference to gender tables. Total maturity scores were converted to a dental age based on percentile curves of a table of standards for boys or girls. The mandibular teeth were used in this system because they are reproduced with little distortion on panoramic radiographs. Dental age was then compared to chronological age to determine a dental age delay (chronological age minus dental age equals dental age delay). The dental age delay for each type of cleft was compared to determine whether cleft type or severity affects maturation delays.

A second comparison used weighted maturity scores for individual maxillary teeth comparing cleft and control subjects, allowing a determination of the role proximity to cleft plays in developmental delay.

The data were considered in 2 separate analyses. The first compared cases and controls according to dental age based on

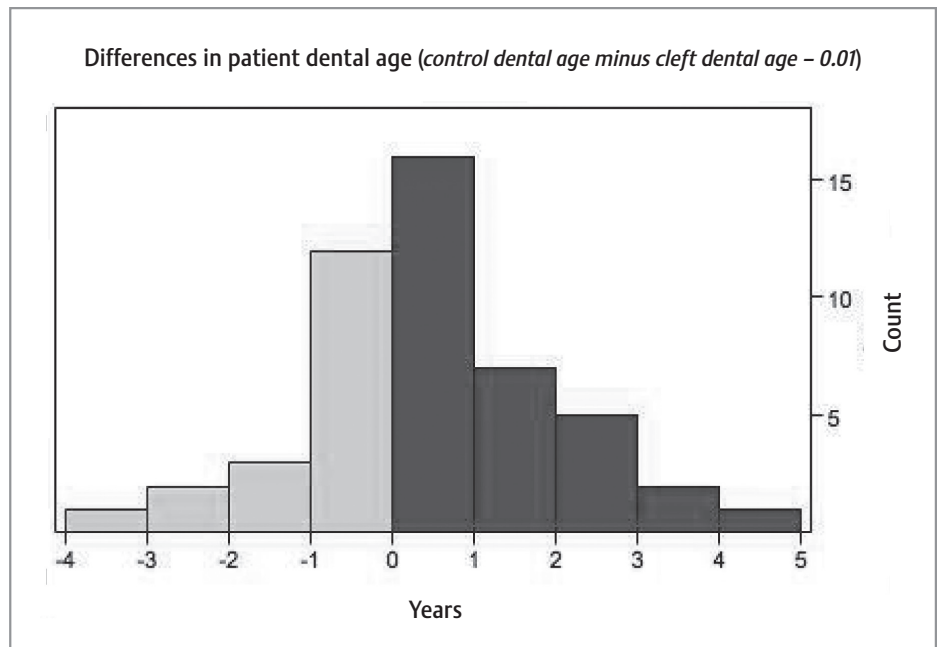


Figure 1. X axis: Differences in dental age (control minus cleft for each case/control pair) in years. Y axis: number of cases. Darker (positive values) demonstrate cases with cleft subject dental age delays (31 of 49 cases). Lighter portions (negative values) demonstrate cases with advanced cleft subject dental ages (15 of 49 cases). Cleft subjects showed an average dental age delay of 6 months.

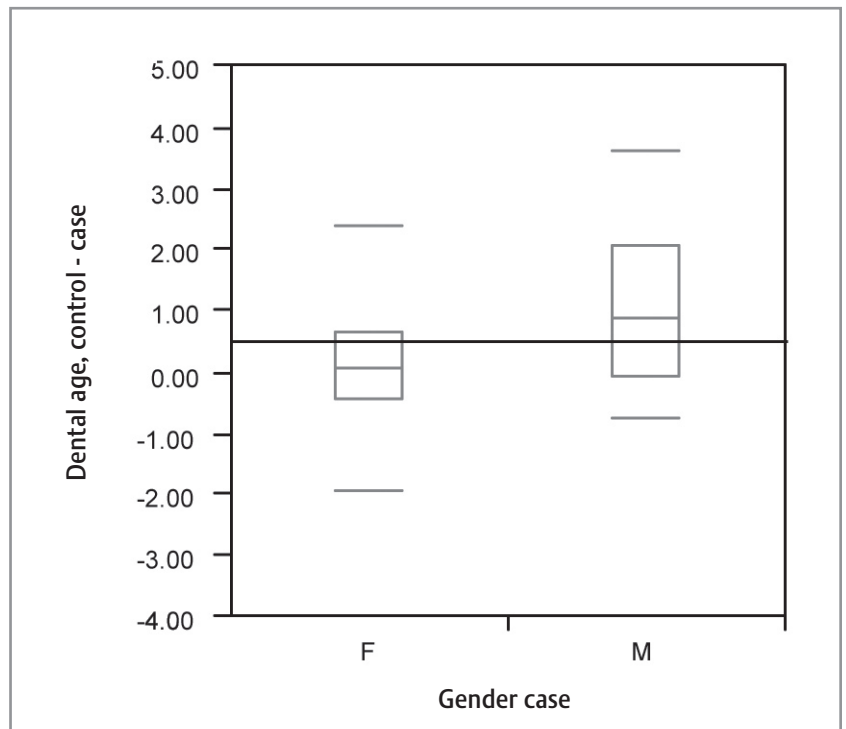


Figure 2. Dental age (control minus cleft) by gender

mandibular tooth development, as per Demirjian. The second compared cases and controls according to the development of the individual maxillary teeth, asking whether the distance

from the cleft is associated with the developmental deficit. For the comparison of dental age, a simple case vs control comparison was done using a paired *t* test checked by the Wilcoxon signed rank test. For each pair, the dental-age discrepancy “control dental age minus cleft dental age” was computed. To compare groups of patient pairs (eg, male vs female) according to dental-age deficit, 2-sample *t* tests were used. These analyses were used to determine whether the difference of dental age, control minus case, depended on cleft characteristics or gender. The second part of data analysis involved determining delays in individual teeth and testing whether they were associated with the tooth’s proximity to the cleft. These analyses were done using permutation tests.^{13,14}

Results

Overall dental age. Fifty children with clefts of the primary and secondary palates were staged, and their dental ages were assessed. One pair was removed from the sample because the control subject was missing 1 of the 7 mandibular left teeth required to assign a dental age. No racial/ethnic data were recorded for cases or controls in this study, but both clinics in the School of Dentistry see a mix of patients with a preponderance of Caucasian and Hispanic backgrounds. In 31 out of 49 pairs analyzed, the control subject’s dental age exceeded that of the cleft subject. In 15 out of 49 cases, the cleft subject’s dental age exceeded that of the control. In 3 cases, the dental ages for cleft and control subjects were the same. Overall, a mean delay in tooth development of 0.52±0.22 (SD) years

was found for the cleft subjects (Figure 1; *P*=.02) by both the paired *t* test and the Wilcoxon signed rank test, indicating that patients with cleft lip and palate experience an average delay in tooth development of 6 months.

Males and females differed in dental-age discrepancy (Figure 2; *P*=.03). Males had an average difference of 1.07±0.32 years. Females had an average difference of 0.11±0.28 years.

Figure 3 shows a box plot and averages of the dental age difference (control minus cleft) for 2 groups differing according to the cleft type (primary palate vs primary and secondary palate). These results show a trend toward subjects with clefts of the primary and secondary palate experiencing more significant dental delays than those with clefts of the primary palate only. This difference, however, did not reach statistical significance (*P*=.11). Only 6 subject pairs had clefts of the primary palate alone, resulting in decreased power with which to find a significant difference. The observed average difference in dental-age discrepancy of over a year (0.65-(-0.42)=1.07), however, is large enough to be of clinical interest and merits further study.

Figure 4 describes the delay in tooth development according to the severity of cleft present (unilateral vs bilateral). According to these results, children with unilateral and bilateral clefts do not differ in their dental delays (*P*=.77).

Delays in individual teeth. The maxillary teeth were scored using the staging described by Demirjian et.al.¹² This method resulted in a letter stage assignment for each tooth, rather than an overall patient dental age. This was then used to compare cleft and control patients within each case/control pair. For each tooth, we calculated the frequency in which the tooth for cleft subjects was more developed, equally developed, or delayed compared to the same tooth in the control group. Figure 5 shows that simple proximity to the cleft did not determine the developmental delay of individual teeth. Teeth demonstrating delays most often were the first and second premolars, followed by the second molars. Figure 5 illustrates that some teeth were delayed in the majority of cleft subjects (eg, teeth nos. 4 and 5), while others showed no differences among case and control groups at all (eg, teeth nos. 3 and 6).

Our data also demonstrated that the cleft vs control comparison is the same for antimere teeth (eg, teeth nos. 6 and 11, 3 and 14). In other words, asymmetric dental development was not exhibited by this cleft population.

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Discussion

Several studies exist on the dental development of children with clefts. Previous studies compared cleft populations to unmatched groups

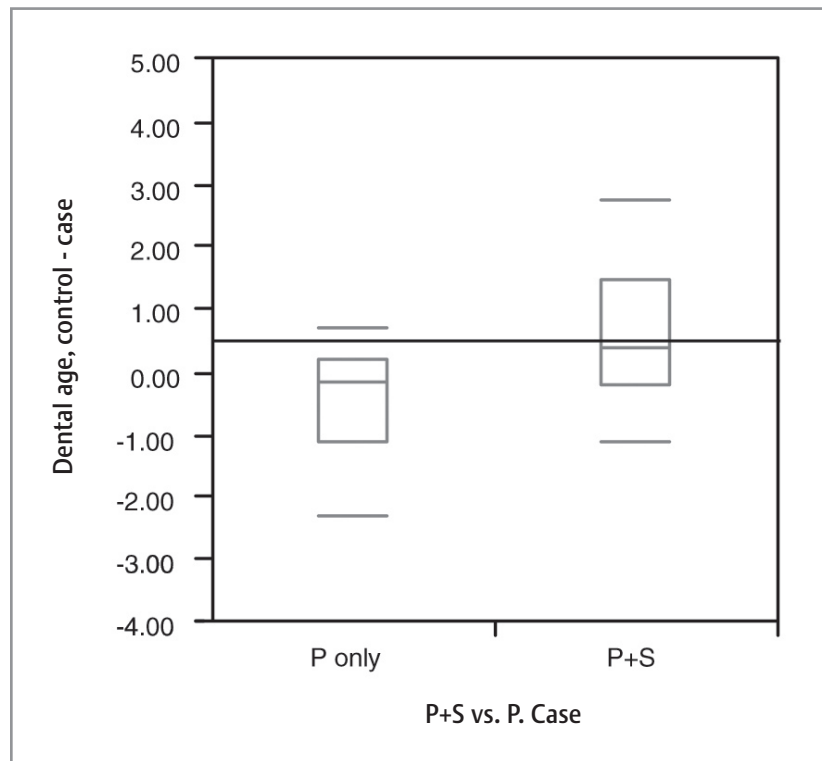


Figure 3. Dental age (control minus cleft), primary and secondary (P+S) palate vs primary palate only (P only).

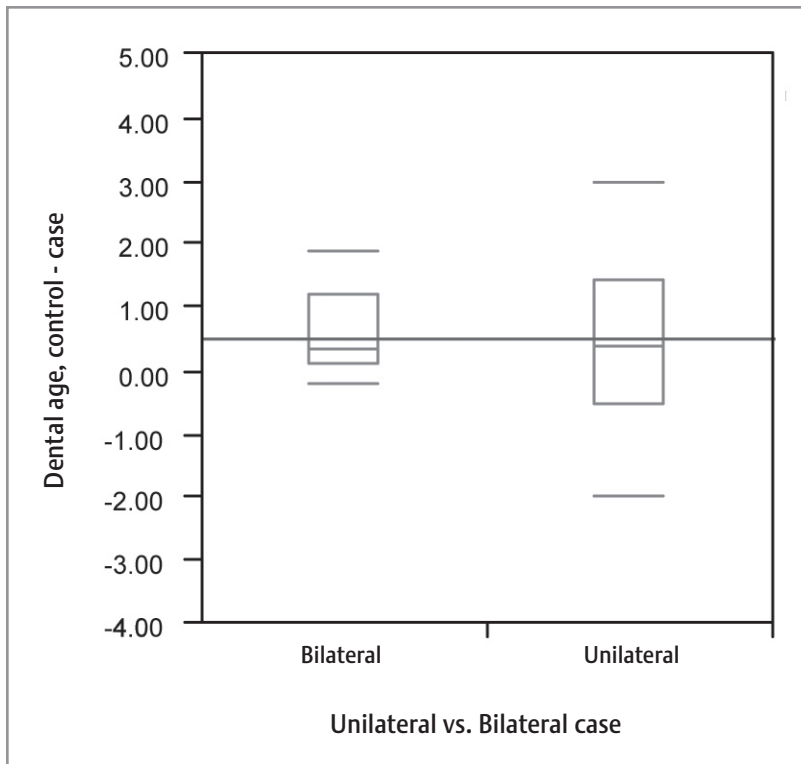


Figure 4. Dental age difference (control minus cleft), unilateral vs bilateral.

of control subjects whose data were collected at a separate time and place. Our study aimed to closely match the cleft subjects with contemporary age- and gender-matched controls from the same clinic. Another goal was to answer questions regarding gender and cleft type and severity. Additionally, there have been few attempts to score development of permanent maxillary teeth.⁷ This study attempted such scoring as a way to assess tooth delay as a function of cleft proximity.

We found a delay in dental age of 0.52 years, consistent with previous studies reporting delays ranging from 0.3 to 0.7 years.^{6,7,10} The proportion of subjects experiencing delays in this study (31 of 49, or 63%) was less than that reported by another study (48 of 54, or 89%).¹⁰ In our study, the male cleft subjects showed a statistically significant delay while female cleft subjects did not. Previous studies have reported similar gender specific results,^{7,9} while others have reported opposing results.^{6,15} Females are known to develop dentally at a slightly faster rate than males overall,¹⁶ which could help female cleft subjects “catch up” before a significant delay is noted.

When comparing dental delays found among subjects with different types of clefts (unilateral vs bilateral), no differences were found. Other investigators have shown that the more structures involved in the cleft, the more exaggerated the delay.¹⁷ This study demonstrates, however, that the presence of any cleft causes a delay, whether one or both sides of the face are affected. In addition, we found no greater delay in teeth on the side closest to the cleft, since individual tooth delays appeared to be symmetrical.

Cleft palate only subjects only were excluded from this study because they have a separate genetic diagnosis. For this group, however, most investigators have reported an increased delay in development as well as a higher occurrence of dental anomalies.^{6,18} This study compared tooth development among subjects with clefts of the primary palate only and subjects with clefts of the primary and secondary palate. Our data suggest a trend toward less dental delay in subjects with only primary palate clefts compared to those subjects with involvement of both palates. This result did not reach statistical significance, possibly due to the small number of subjects with primary palate clefts only (N=6). If this trend holds up in subsequent studies, it suggests that the fewer structures involved in the defect, the less the effect on the dentition's development.

Cleft malformations occur between the seventh and 10th prenatal week. It is not surprising that an adverse event occurring so early might create a lasting effect on the oral cavity's proximal structures. The difficulty lies in speculating exactly why oral structures are affected. Some investigators have linked the affects to adverse early postnatal environment, during which children with clefts have difficulty eating and growing.¹¹ Others link alterations to the

prenatal environment, stressing that the early insult interacts with and affects the development of concurrently forming structures.³ Several growth factors are of major importance during craniofacial development, and these factors may be overexpressed or underexpressed when a cleft defect occurs. This aberrant expression can modify odontogenesis and cause abnormalities of the dental lamina.¹⁹ Growth factors such as transcription growth factor alpha have been linked to the occurrence of clefts, and these factors are also involved in tooth development.

It is also feasible that events occurring during infancy and young childhood could have an influence on concurrently forming structures. For instance, children with clefts undergo many surgeries beginning at a young age. With each surgery, the child undergoes general anesthesia and manipulation of the oral cavity's tissues. It is possible that these events cause immediate changes in orofacial structures forming around the same time or shortly after the surgeries, and subsequently show the effects in eventual growth and maturation. Finally, one may also hypothesize that children with clefts possess a systemic restriction in growth potential—one not limited to the orofacial area.⁴

Harris and Hullings found that teeth formed early during postnatal development (permanent first molars) were most affected by delays, while those formed later (premolars, second molars) were least affected.¹⁰ Solis et al found that teeth on the cleft side were delayed, with the degree of delay corresponding

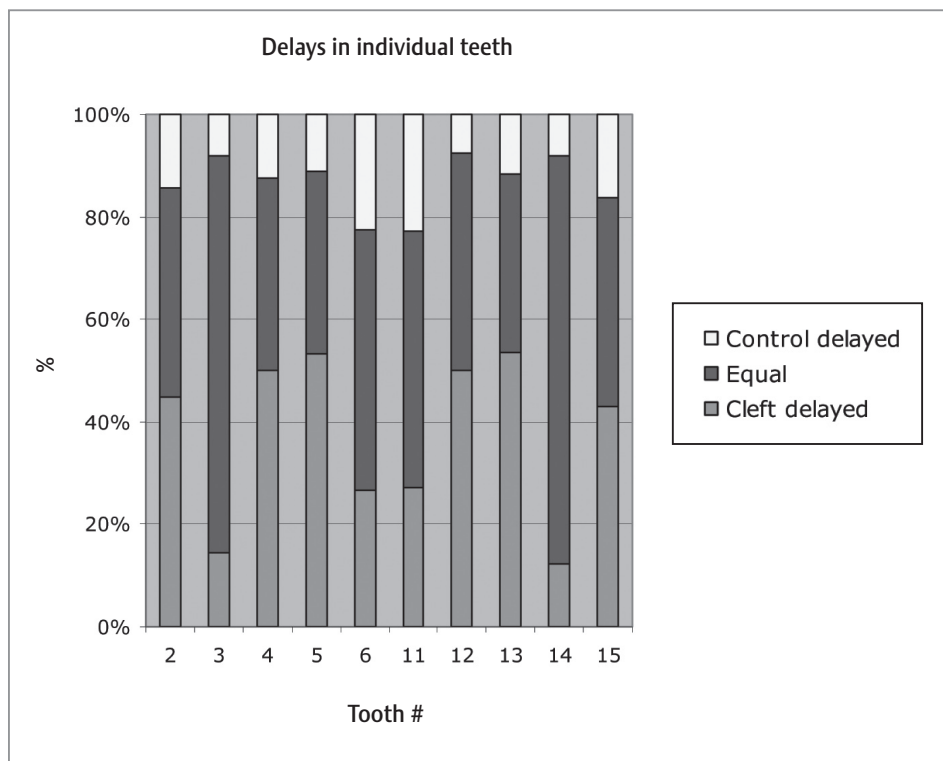


Figure 5. Percent of total cleft to control pairings (Y axis) for each tooth number scored (X axis). White bars indicate measured delays in control patients; light grey bars indicate measured delays in cleft patients; dark grey bars indicate equal cleft and control scores. Teeth #4, 5, 12, and 13 exhibit delays in the cleft group most often, followed by #2 and 15.

to proximity to the cleft.¹¹ The lateral incisors were most delayed, followed by the canines and premolars. Our study demonstrated that the teeth most often delayed in cleft subjects were the first and second premolars, followed by the second molars. The initiation times for the permanent dentition are after the fifth month in utero; hence, their formation does not coincide with formation of the cleft defect.

It is possible that the teeth are affected as a result of the earlier cleft malformation, but it's difficult to explain the variation in delay with some teeth experiencing delays more frequently than others. The answer may lie in the chronology of the human dentition by focusing on the initiation and calcification times for the premolars and second molars. Most interdisciplinary cleft teams recommend that the palate be surgically repaired at 1 year of age.² Note that the second premolars and second molars are beginning to form around the time that most subjects undergo palatal repairs. Additionally, the calcification times for all of the second premolars and second molars occur shortly after the palatal repair surgery. We speculate that one explanation for the findings in second molars and premolars relates to adverse events associated with surgery being "archived" by the teeth in early, susceptible growth stages, resulting in developmental delays in these specific teeth.

Many previous studies have reported asymmetric development in patients with clefts.^{5,6,10} Interestingly, this phenomenon was not observed in our sample of cleft subjects. This study's

results agree with a 2001 study of Greek children.¹⁹ Mitsea et al found a delay in premolar development in children with unilateral and bilateral clefts. No asymmetric development was observed in this group, but unlike the present study, tooth delays were noted in both males and females.

A concern of this study design involves possible systematic bias of the scorers because of the inability to fully mask the radiographs' cleft status. All other aspects of the patient information, such as gender, chronological age, and demographics, were fully masked, but not cleft status. No systematic bias appears in the data analyses. The fact that males showed a difference in dental development related to cleft status and females did not argue against a bias of the scorers, since the gender of the subject whose radiograph was being read was not known. A systematic bias toward cleft subjects differing in some way from noncleft subjects would have appeared in subjects of both genders. In addition, the

findings that proximity of the forming permanent tooth to the cleft was not directly related to developmental delay and that the delay was not asymmetric again argues against a bias of the scorer toward any preconceived expectation of the findings. In this study, the investigators were unable to clearly define the effect of cleft type on dental delay due to the small number of subjects with clefts of the primary palate only. Future studies to investigate this question will require a population with more subjects showing primary palate clefting only.

Previous studies have reported that children with clefts experience a "catch up" in development in the preteenage years.¹¹ Still, other studies have refuted this, stating that the dental delay is more exaggerated in 8- to 12-year-old subjects.^{6,7} This study included children ranging from 6 to 13 years old. It did not provide enough children at each age to provide conclusions about delays and different chronological ages.

The Demirjian method was employed in this study as a method for assessing dental age. This method uses the 7 permanent mandibular left teeth to determine dental age. The mandible's lower left quadrant does not reflect the full effect of clefting in the maxilla. Effective use of the Demirjian method requires clear radiographic quality. This is often difficult to achieve for maxillary teeth on a panoramic radiograph. For this study, the investigator was able to select panoramic radiographs on which maxillary teeth were clearly captured so that the Demirjian method could be expanded to stage

maxillary teeth. Expanding upon this method allowed the investigator to examine individual maxillary teeth and their relation to cleft proximity.

Surgical timing for cleft repair and revision depends on dental age, not chronological age. It is important that clinicians have an understanding of how children with clefts develop so they may accurately assess dental age and stage of development, with the goal of limiting the number of required surgeries. Treatment protocols for procedures such as orthodontics and graft placement must be modified to account for differences in dental development in this population. Also important are the aforementioned potential negative effects of surgeries on odontogenesis and tooth maturation. The dental impact of timing for cleft repair must be considered.

Conclusions

Based on this study's results, the following conclusions can be made:

1. Cleft lip and palate patients exhibit a delay in tooth development of 6 months, which should be considered when planning treatment and surgeries.
2. This delay is independent of cleft severity, with an equal delay seen in both unilateral and bilateral cleft lip and palate.
3. Cleft type may affect the dental delay; a nonsignificant trend was observed in subjects with primary palate clefts only, who exhibited less dental delay.
4. Boys exhibited a statistically significant delay, while girls did not.
5. The permanent teeth most often delayed were maxillary first and second premolars and maxillary second molars, demonstrating that the effects of a cleft reach beyond the cleft area.

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