Association between maxillary lateral incisors’ root volume and palatally displaced canines: An instrumental variables approach to the guidance theory

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ABSTRACT
Objectives: To evaluate association and causation between maxillary lateral incisors’ (MxI2) apical root volume (ARV) and palatally displaced canines (PDC).
Materials and Methods: In a retrospective cross-sectional study, computed tomography scans of 179 patients with unilateral PDC were analyzed. MxI2 root length and volume on the impaction and eruption side were measured. A mixed logit model was used to infer the association between ARV and PDC and an instrumental variables approach to interpret causality.
Results: MxI2 root length on the impaction side was shorter in 42%, equal in 33% and longer in 25% of the patients. ARV amounted for 13.5% of total root volume on the impaction and 14.9% on the eruption side. Reduced ARV was significantly associated with the impaction side (P < .001). The causal effect of ARV on PDC in the instrumental variable approach amounted to less than half of the association in a standard noncausal approach.
Conclusions: An association between PDC and reduced MxI2 root length and volume was confirmed. However, the lack of causality did not allow the researchers to draw a conclusion as to whether a reduced ARV is causing PDC or resulting from it; this should be considered in etiologic theories. (Angle Orthod. 2018;88:719–725.)

KEY WORDS: Canine impaction; Palatal canine displacement; Guidance theory; Instrumental variables; Computed tomography

INTRODUCTION
Maxillary canine impaction occurs in up to 2.4% of the population, is more frequently seen palatally and unilaterally, and is more common in females than in males (ratio > 2:1).1 Risks associated with impacted canines include infections, cystic follicular lesions, and external root resorption of adjacent teeth, particularly the maxillary lateral incisors (MxI2).2

During regular eruption, the maxillary canine’s tooth bud begins its 22 mm descent into its final occlusal position just below the orbital floor.1,3 The eruption of the upper permanent dentition does not occur in a cascading manner, as the eruption of the lateral incisor and first bicuspid predates that of the canine by about 3 years and 1 year, respectively. These teeth are therefore inherently linked to the canine’s eruption pathway,2,4 and their respective size and shape anomalies have become the basis for one of the predominant theories for the etiology of palatally displaced canines (PDCs): the guidance theory.1,5,6 The guidance theory suggests that morphologic irregularities or agenesis of MxI2 can impede canine
eruption. In fact, the association between MxI2 size and PDC has been well established in the literature through observations on study casts (i.e. crown size), clinical examination, root length measurements in panoramic x-rays, and linear measurements from cone beam scans. Association, however, does not mean causation. In observational studies, a major challenge is the lack of random exposure, as confounders (preexisting variables that affect the outcome) differ in distribution between the observed groups. The instrumental variables method tries to account for such unmeasured confounders by introducing a variable (the instrument) that influences group allocation but is independent of (unmeasured) confounders and has no direct effect on the outcome besides its effect on group allocation. An instrument-derived group allocation can therefore be used to estimate a causal effect on the outcome.

If the regular eruption pathway is considered during the early to late mixed dentition, the unerupted maxillary canine is mesially inclined and positioned high on the distal side of the apical third of the MxI2 root. If the ensuing downward and uprighting movement of the erupting canine is then guided along the distal aspect of the MxI2 root, the apical third of its root has to be considered most critical at this stage. At the same time, however, it seems equally possible that root development of MxI2 is affected by the proximity of the canine’s crown and dental follicle. Since MxI2 root development would be close to completion at this point, the apical third would also be primarily affected. If MxI2 hypoplasia (presumably affecting all portions of the root) caused PDC, the apical portion of the root would be the actual culprit but might also be confounded by developmental impairment. The coronal portion of the root, however, would not be confounded and might serve as an instrument in such a causality model.

Under this premise, the aim of this study was twofold: (1) to evaluate the association between MxI2 apical root volume (ARV) and PDC and (2) to explore causality of this association; that is, is the ARV a priori smaller and therefore causes PDC or is a reduced MxI2 ARV in fact the result of PDC?

MATERIALS AND METHODS

Patient Recruitment

Institutional ethical committee approval was obtained to conduct this retrospective cross-sectional study (EK-Nr. 1093/2011). It included maxillary computed tomography (CT) scans of all patients referred to University Clinic of Dentistry (Medical University of Vienna, Austria) for the diagnosis of a unilateral PDC within a 5-year observational period. The following exclusion criteria were applied:

- Imaging artifacts due to patients’ movement or metal fillings in the region of interest
- Visible signs of root resorption (lacuna formation) at MxI2
- Cystic lesions in the region of interest
- Root fracture of MxI2
- Agenesis or hyperdontia of MxI2

Radiographic Examination

All CT scans were acquired with a conventional CT scanner (Tomoscan SR-6000, Philips, Eindhoven, Netherlands). A standard dental CT investigation protocol (1.50mm slice thickness, 1.0-mm table feed, 120 kV, 75 mA, 2 s scan time, 100–120 mm field of view, high-resolution bone filter) was applied.

Image Preparation

Multiplanar reformatting was applied to all CT scans with each MxI2’s long axis (center of the coronal pulp to center of the apex) as the vertical reference. Layers were then reconstructed at 1-mm intervals between the cementoenamel junction (CEJ) and MxI2’s apex (Dental Software Package 2.1, Philips Medical Systems, Best, Netherlands) (Figure 1a–b). The most apical layer with visible signs of enamel on the buccal side was chosen as the CEJ layer. The root’s circumference in each layer was then traced manually by a single examiner (Figure 1c–h) and the volume calculated by multiplying each layer’s area with its thickness of 1 mm. Root length was derived from the total number of reconstructed layers for each tooth. Circumferences of the five most apical layers of each tooth were retraced after 12 weeks by the same examiner.

Root length was then sectioned in an apical third and coronal two-thirds as follows: the length of the longer root (i.e. either the eruption or impaction side) was determined and two-thirds of this length starting from the CEJ was used to calculate the coronal root volume (CRV) for both sides. The remaining root length on both sides was then used to calculate the respective apical root volume (ARV; Figure 1a–b and Figure 2). Since volume (and length) was measured discretely in 1-mm layers, in some cases one layer could not be completely assigned to either part. In these cases, the volume of this layer was divided proportionally to both, the ARV and the CRV. This approach of root-length sectioning was chosen to better reflect ARV differences resulting from variances in length and circumference on the impaction side.

Statistical Analysis

Data were described with frequencies, means, medians, standard deviations (SDs), and interquartile ranges. For inference on the association between ARV...
and PDC a mixed logit model was fitted, predicting, by the ARV as percentage of the total root volume, whether the side would be the impaction or eruption side, including patient identification (ID) as a random effect; 95% profile confidence intervals (CIs) for the effects were calculated.16

Subsequently, an attempt to establish causality of this association was made through an instrumental variables approach.14 Figure 3 shows the graphical model as a directed acyclic graph. The arrows denote the assumed causal relationships between the variables, encircled variables denote observed measurements, and variables in squares are unobserved. For the model to be valid and causally interpretable, the (unobserved) squares posed no problem. Potential (as of yet unknown) variables “X” could bias the results though. CRV was then used as an instrument for ARV. Absolute ARV was used, since the percentage of the total volume used in the previous analysis did not provide enough information to use CRV as an instrument (coronal \(= 100 – \text{apical}\)). To define the instrumental variable, ARV was used as the dependent variable and CRV as the independent variable in a linear mixed model, including patient ID as the random effect. For the second stage of the approach, a logit mixed model was used to predict PDC, again using patient ID as a random effect; 95% CIs were calculated using a bootstrap approach. Reproducibility was tested with the intraclass correlation coefficient.

All computations were done using R version 3.3.1.17 Statistical graphs were created using ggplot2.18

RESULTS

Patient Characteristics

In total, 227 patients were originally referred for CT imaging of unilateral PDC within the observational period. After screening the scans, 48 were excluded and 179 included in the analysis (Figure 4). Age and sex distributions are described in Table 1.

### Root Length

MxI2 root length on the impaction side was shorter in 42% \((n = 75)\), equal in 33% \((n = 59)\), and longer in 25% \((n = 45)\) of the cases compared with the eruption side.
The differences in root length (eruption minus impaction side) are displayed in Table 2.

**Apical Root Volume**

MxI2 ARV amounted to 13.5% (SD = 3.7%) of the total root volume on the impaction side and 14.9% (SD = 2.7%) on the eruption side. Root volumes are described in Table 3 and Figure 5. Figure 6 shows a clear distinction between the impaction and eruption sides in terms of the apical to coronal root volume relationship.

**Inductives**

In the mixed logit model, a decrease of 1% of the ARV percentage was associated with an increase in the odds of being the impaction side of about 15% ($P < .001$, a multiplicative effect of about 1.15), with a 95% CI of 4 to 8%.

**Instrumental Variables Approach**

The causal effect of ARV on PDC in the instrumental variable approach was 1.017 (CI, 0.982 to 1.050; $P = .318$) and therefore amounted to less than half of the association of ARV and PDC (1.043; CI, 1.020 to 1.066) that would have been found in a standard non-causal approach.

**Reliability**

Evaluation of the reliability of tracing the circumferences showed a high degree of intraexaminer repeatability with an intraclass correlation coefficient of 0.983 of the most apical layer and 0.990, 0.995, 0.996, and 0.998 for the subsequent ones.
DISCUSSION

This study showed an association between the MxI2 ARV and PDC. However, the applied instrumental variables approach suggested that only a fraction of this association could be explained by a causal effect of ARV on the occurrence of PDC. Associations of reduced MxI2 root dimensions and PDC have been widely reported in the literature,¹ but few authors have addressed causality (or lack thereof) in such findings.⁸ The presented data suggest that reduced MxI2 ARV is not necessarily the cause for PDC but possibly also a result thereof. In part, the association may, therefore, be due to impeded MxI2 root development in the apical third caused by PDC.

Most previous studies compared MxI2 dimensions with a matched control group. In those studies, a reduced root length of MxI2s adjacent to PDCs has been found in two-dimensional¹¹ and three-dimensional radiographs.¹² Root volume has also been investigated and was found to differ mostly furthest (8 mm) from the CEJ (i.e. in the apical third),¹² which is in agreement with the current findings. However, as overall tooth-size discrepancies have been reported between PDC and non-PDC patients,¹⁹ a split-mouth design, as chosen herein, might be superior due to the within-subject comparison between the impaction and eruption side. Particularly, MxI2 size anomalies appear to occur more commonly bilaterally (but not necessarily to the same extent), despite PDC occurring far more commonly (60% to 75%) unilaterally.¹ The only other study applying a split-mouth design and comparing MxI2 root length and volume to the contralateral side also found significantly smaller dimensions on the impaction side but did not further differentiate between coronal and apical root sections.²⁰

The applied instrumental variables approach relies on the initial formation of a causality model (as illustrated in the directed acyclic graph, Figure 3).

Table 2. Incidence (n) of Differences in Root Length (mm) Between Eruption and Impaction Side (i.e. Eruption Minus Impaction Side)

<table>
<thead>
<tr>
<th>Root length difference (mm)</th>
<th>-4</th>
<th>-3</th>
<th>-2</th>
<th>-1</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence (n)</td>
<td>0</td>
<td>1</td>
<td>10</td>
<td>34</td>
<td>59</td>
<td>43</td>
<td>24</td>
<td>7</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 3. Descriptives for Apical, Coronal and Total Root Volume (mm³); Apical Root Volume as Percentage of the Total Root Volume

<table>
<thead>
<tr>
<th>Side</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Median</th>
<th>Interquartile Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apical root volume (mm³)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eruption</td>
<td>31.4</td>
<td>9.6</td>
<td>31.1</td>
<td>11.5</td>
</tr>
<tr>
<td>Impaction</td>
<td>27.2</td>
<td>10.5</td>
<td>27.7</td>
<td>15.0</td>
</tr>
<tr>
<td>All</td>
<td>29.3</td>
<td>10.2</td>
<td>29.3</td>
<td>12.8</td>
</tr>
<tr>
<td>Coronal root volume (mm³)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eruption</td>
<td>179.3</td>
<td>45.0</td>
<td>174.3</td>
<td>52.1</td>
</tr>
<tr>
<td>Impaction</td>
<td>174.3</td>
<td>45.6</td>
<td>173.6</td>
<td>53.0</td>
</tr>
<tr>
<td>All</td>
<td>176.8</td>
<td>45.3</td>
<td>173.8</td>
<td>53.0</td>
</tr>
<tr>
<td>Total root volume (mm³)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eruption</td>
<td>210.7</td>
<td>52.5</td>
<td>205.8</td>
<td>60.9</td>
</tr>
<tr>
<td>Impaction</td>
<td>201.5</td>
<td>52.5</td>
<td>203.7</td>
<td>60.8</td>
</tr>
<tr>
<td>All</td>
<td>206.1</td>
<td>52.6</td>
<td>204.4</td>
<td>57.6</td>
</tr>
<tr>
<td>Apical root volume percentage (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eruption</td>
<td>14.9</td>
<td>2.7</td>
<td>15.1</td>
<td>3.0</td>
</tr>
<tr>
<td>Impaction</td>
<td>13.5</td>
<td>3.7</td>
<td>13.9</td>
<td>4.9</td>
</tr>
<tr>
<td>All</td>
<td>14.2</td>
<td>3.3</td>
<td>14.7</td>
<td>3.7</td>
</tr>
<tr>
<td>Root length (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eruption</td>
<td>13.8</td>
<td>1.9</td>
<td>14.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Impaction</td>
<td>13.4</td>
<td>2.0</td>
<td>14.0</td>
<td>3.0</td>
</tr>
<tr>
<td>All</td>
<td>13.6</td>
<td>2.0</td>
<td>14.0</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Figure 4. Flowchart of patient recruitment and applied exclusion criteria.

Therein, per patient variables (e.g. genetics) should pose no problem since they are accounted for by the study design (i.e. split-mouth). It was assumed that ARV would relate primarily to PDC with no influence of CRV (instrument) on PDC. However, it should be noted that it is generally accepted that such a model will never perfectly correspond to reality. The more interesting question is not whether there are any variables X (Figure 3) but how influential those are.¹⁴,²¹ Further, the presented model of MxI2 ARV affecting PDC cannot differentiate between the causes for a reduced ARV. An alternative explanation to impeded root development may be root resorption at the apex. While originally all cases with visible signs of root resorption (lacuna formation) were excluded, minimal resorption at the tip of the apex may be indistinguishable in CT data.²² However, root resorption of MxI2 is most commonly situated in the middle third of the root²³ and anomalous MxI2s with reduced size or abnormal shape are considered less at risk to develop severe root resorption compared with patients with regularly shaped and sized MxI2s.²⁴ Nonetheless, root
resorption at the apex should be considered an alternative explanation to developmental impairment of the root.

Clinically, the benefit of a clear and causal effect of reduced MxI2 dimensions on PDC would be the indication for early treatment, such as deciduous canine extraction,25,26 in order to avoid a manifestation of the malocclusion or root resorption.2,23 The primary clinical indicator would naturally be MxI2 crown size, which has been associated with PDC.8,9,27 The current data did not contain information about MxI2 crown size, as crowns were often partially outside the field of view of the CT scans. Also, the correlation between MxI2 crown and root dimensions is not undisputed.28 Therefore, radiographic indicators may be better suited for the early detection of PDC.29,30 However, the present data indicate only subtle differences in MxI2 ARV which may not qualify as a reliable clinical indicator.

The prominent theories of the underlying mechanisms behind an impeded canine eruption are the guidance theory1 and the genetic theory.31 MxI2 size has been used as an argument for both.1,7 The present results cannot resolve this more than 20-year-old dispute between etiologic theories.31,32 Instead, an additional effect is suggested, where PDC is also partially responsible for MxI2 size anomalies, either due to the impediment of root development or due to resorption at the very apex. The presence of an existing, but not necessarily causal, link between MxI2 ARV and PDC should therefore be considered in either etiologic theory.

CONCLUSIONS

- The present results support the widely reported association between MxI2 size anomalies and PDC: a reduced MxI2 ARV is associated with PDC.
- Reduced MxI2 ARV may be a cause for PDC but possibly also the result thereof.

Figure 5. Comparison between eruption and impaction sides of the coronal (A) and apical root volumes (B).

Figure 6. Coronal root volume vs apical root volume of lateral incisors. Prediction lines are due to a local polynomial regression fit. Gray shade represents a pointwise 95% confidence interval.
• The presence of an existing, but not necessarily causal, link between MxI2 ARV and PDC should be considered in etiologic theories.

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