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Morphometric analysis of cervical vertebrae in relation to mandibular growth

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Introduction: Cervical vertebral maturation (CVM) methods have been criticized because of their subjective nature. The aims of this study were (1) to analyze the morphometric changes in the outline of the second to fourth cervical vertebrae with growth and (2) to test the validity of the CVM method for determining the mandibular growth peak. **Methods:** Lateral cephalograms of 25 participants from ages 10 to 16 years were acquired from the Burlington Growth Study, and the CVM stage was qualitatively determined. Mandibular and cervical vertebral semilandmarks were then digitized, and point distribution models were used to describe the morphometric templates of the vertebrae in relation to chronologic age and the timing of peak mandibular growth. Mixed model analysis was used to determine the relationship between mandibular length, sex, CVM stage, and chronologic age. **Results:** Morphometric changes of the second to fourth cervical vertebrae during growth were consistent with the CVM descriptions. However, mandibular length changes were not significantly associated with CVM stages after adjusting for chronologic age. Morphometric templates of vertebral shapes before and during the mandibular growth peak were similar, with changes detectable only after the growth peak had passed. Morphometric vertebral shape changes varied between the sexes. **Conclusions:** Morphometric changes of the cervical vertebrae and the CVM method could not accurately identify the mandibular growth peak. (Am J Orthod Dentofacial Orthop 2016;149:92-8)

The importance of the determination of periods of accelerated growth to the timing of dentofacial orthopedics has been often advocated.[1-3] To date, evaluations of secondary sex characteristics, height and weight, hand-wrist maturation, and dental development have been used as alternatives to chronologic age.[4-12] The usefulness of the evaluation of skeletal maturity using the second (C2), third (C3), and fourth (C4) cervical vertebrae has also been widely investigated, since the vertebrae can be seen on conventional lateral cephalometric radiographs even when a protective collar is worn.[3] Despite controversy surrounding the specific radiation dose, a major advantage of the cervical vertebral maturation (CVM) methods over other maturation methods, such as the hand-wrist method, is that they eliminate the need for additional radiation exposure.[1,12,13] The so-called CVM methods are based on the shape and size of changes of the cervical vertebrae with growth.

It has often been suggested that concavities in the inferior borders of C2 through C4 increase with age, and that C3 and C4 increase in height and become less trapezoid and more rectangular with time.[1-3,14-18] However, these reported changes in vertebral shapes are mostly based on subjective evaluations. Hence, there has been criticism over the reproducibility and qualitative nature of maturational assessments from current cervical maturation methods.[19,20]

Quantitative analytical methods are more useful than qualitative methods because they are accurate, allow numeric comparisons between groups, and do not rely on individual interpretations.[21] Point distribution models have been shown to be a useful way of quantitatively describing shape for a variety of purposes.[22-25] Point distribution models are a type of active shape model that derives the statistics of a set of labeled points or "semilandmarks." After scaling and aligning all sets of data points, we can find the typical

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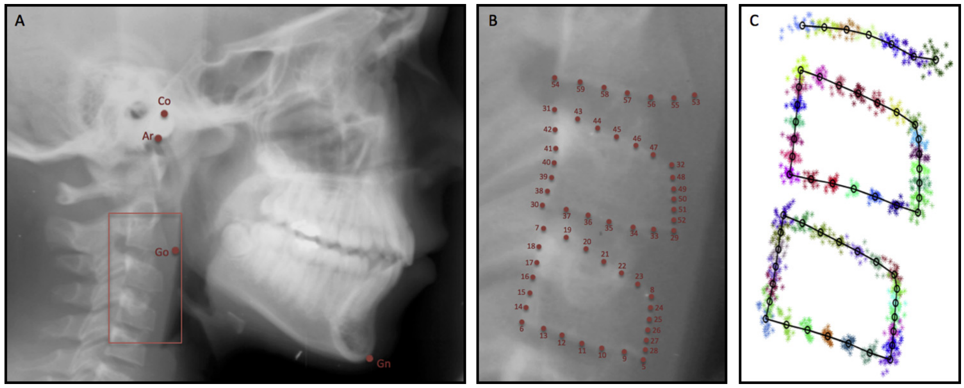

Fig 1. A, Four mandibular semilandmarks were identified: *Gn* (gnathion, the most anterior and inferior part of the chin), *Go* (gonion, the most posterior and inferior part of the angle of the mandible), *Co* (condylion, the most superior part of the head of the condyle), and *Ar* (articulare, the point of intersection between the zygomatic arch and the posterior border of the mandibular ramus). **B,** Example of the 55 semilandmarks to be used for digital tracing of C2 through C4. Points 5-28 show the outline of C4, points 29-52 show the outline of C3, and points 53-59 show the inferior border of C2. **C,** Example of how the point distribution model is used to find the template shape of the cervical vertebrae. The *different colors* represent the different semilandmark points, and the *crosses* represent a subject's semilandmark point.

semilandmark position using an assigned weighting. After this, the shape template of an object can be determined in a quantitative way.

The aim of this study was to analyze and quantitatively describe the morphometric changes in the outlines of C2, C3, and C4 between the ages of 10 and 16 years, as seen on lateral cephalograms. Furthermore, we tested the validity of the assumptions underlying the CVM method and its relationship to observed changes in the mandibular length during growth.[18]

MATERIAL AND METHODS

Participants were selected from the records of the Burlington Growth Study, housed in the American Association of Orthodontists Foundation Craniofacial Growth Legacy Collection. At the time of data collection, 67 participants were available for downloading. Subjects were selected for inclusion if they had at least 5 of 6 lateral cephalograms available in the collection taken at ages 10, 11, 12, 13, 14, and 16 years, and if C2 through C4 were visible on all films. Exclusion criteria were incomplete records, radiographs of poor diagnostic quality, subjects with known craniofacial (or other) conditions or syndromes, and subjects treated orthodontically. Twenty-five participants (13 boys, 12 girls) fulfilled these criteria and were included in the study. The mean ANB angle for them was 3.9° (standard deviation, 1.9°). Images were scaled according to the American Association of Orthodontists guidelines. One principal investigator (S.G.) performed all data collection and the initial analysis after training and calibration.

Qualitative visual analysis was conducted for each head film to determine the CVM stage; this method has been previously described.[18] Semilandmarks were digitized and then converted to Cartesian coordinates using MATLAB software (R21012; MathWorks, Natick, Mass). A total of 63 mandibular and cervical semilandmarks were identified and analyzed per radiograph.

The reliability of the 4 mandibular semilandmarks was assessed (Fig 1, *A*). Mandibular length was measured using the distance between articulare and gnathion for each year-long time period. The distance was preferred to the distance from condylion to gnathion because of greater reliability.

Fifty-five semilandmarks were used to trace the inferior border of C2 and the outlines of C3 and C4 (Fig 1, *B*). One point was placed on each corner of the vertebra, and 5 equally spaced points were placed between each corner along the x-axis for the superior and inferior borders, or the y-axis for the anterior and posterior borders. When a semilandmark was to be placed on the corner of a vertebra with a curvature, 2 lines of best fit were taken along the adjacent edges, and the angle was bisected so that the semilandmark was placed on the midpoint of the curvature. The assumptions of the CVM methods were tested in a separate study.[26]

Intraobserver reliability of cervical and mandibular semilandmarks and CVM stage was evaluated by duplicate assessments of 25 cephalograms over a 4-week

Fig 2. Template shape of the cervical vertebrae before the peak according to chronologic ages for boys and girls, considered together and separately. There is a slight increase in the curvature of the lower borders of C2, C3, and C4 with age. Also, there is a tendency for the vertebrae to become taller and more square with time. Girls were more advanced than boys.

period. One image was randomly selected from each participant. The assessor (S.G.) was blinded to the chronologic age and sex of the participants. Agreement for the CVM staging was determined using the percentage of agreement, as well as unweighted and weighted kappa statistics.

Data were clustered according to chronologic age. In addition, 3 more clusters were formed with regard to mandibular growth: before peak, during peak, and after peak. In each cluster, each shape was defined by "n" points (semilandmarks) in 2-dimensional space. Using Procrustes analysis, which finds the minimum of the least-squared error of all shapes in the same cluster subject to scale, rotation, and translation, we constructed a point distribution model as described by Cootes et al.[25] After this, a vertebral template was made for each vertebra by finding the mean semilandmark point after aligning the shapes in each cluster (Fig 1, *C*). All morphometric analyses were carried out for the sexes together and separately.

Mixed model analyses were used to determine the relationships between mandibular length, sex, CVM stage, and chronologic age. Mandibular length represented the response variable, and sex and CVM stage were entered as covariates. A term for subject was included as a random effect. An interaction term between CVM stage and sex was also entered into the model. A diagonal correlation matrix was used when implementing the mixed model.

The data were analyzed with the Statistical Packaging for the Social Sciences (version 19; IBM, Armonk, NY), and we set type I error at 0.05 (2-tailed).

RESULTS

Cervical semilandmarks could be reliably identified over duplicate measurements; the standard deviations ranged from 0.2 to 0.3 mm for the x-axis and from 0.3 to 0.4 mm for the y-axis. Mandibular semilandmark reliability for articulare was 0.6 mm for the x- and y-coordinates; for gnathion, reliability was 0.4 mm for the x- and y-coordinates, compared. Condylion had poor reproducibility, at 1.4 and 2.1 mm for the x- and y-coordinates, respectively. The overall percentage of agreement for

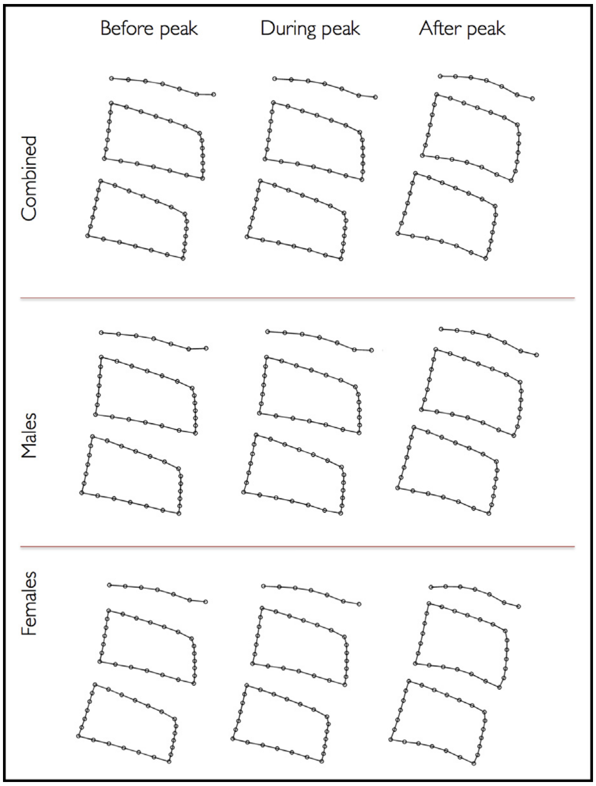

Fig 3. Template shape of the cervical vertebrae before the peak, during the mandibular growth peak, and after the growth peak for the sexes, considered together and separately. There are a slight increase in the curvature of the lower borders of C2 and C3 during the mandibular growth peak and distinct concavities in all 3 inferior borders after the mandibular growth peak. Also, the height to the width ratio, and the anterior to the posterior ratio, appear to increase during mandibular growth, showing a tendency for the vertebrae to become taller and more square with time.

the CVM scores was 84%. The unweighted kappa value was 0.80 (95% CI, 0.61-0.97), and the weighted kappa value was 0.89 (95% CI, 0.78-0.99).

Point distribution models were used to find the morphometric templates of C2 through C4 according to chronologic age (Fig 2) and mandibular growth peak (Fig 3). In relation to mandibular growth, the morphometric templates were remarkably similar before and during the peak growth, whereas more distinct differences could be identified after the peak.

CVM stage was assessed for each cephalogram, and the distribution of all the CVM stages was plotted as a function of chronologic age (Fig 4). As expected, there was a general increase in chronologic age as cervical stage (CS) increased, but the age spans corresponding to the CVM stages were broad: up to 6 years for CS3.

Peak mandibular growth occurred in the year after CS3 in 8 of the 25 participants (32%). In 7 participants (28%), peak growth occurred after CS1; in 5 participants (20%), it occurred after CS2; and in 5 participants (20%), it occurred after CS4. Peak mandibular growth was not found in any participant at CS5 or CS6. Peak mandibular growth occurred at mean ages of 11.7 years in girls (95% CI, 11.1-12.3) and 12.8 years in boys (95% CI, 12.1-13.5).

The results of the mixed model suggest that mandibular length was significantly associated with both CVM stage and sex (Table). There was a significant interaction between CVM stage and sex, indicating that the effect of CVM stage on mandibular length was sex specific. The model was then run again by entering age as a covariate. These results suggested that mandibular length was associated mostly with age and to a marginal extent with sex. No significant association was found with the cervical stage after adjusting for the other covariates.

DISCUSSION

Current CVM methods have been criticized for being subjective, qualitative, and poorly reproducible.[19,20,27] Therefore, a nonsubjective, quantitative method of determining cervical staging is needed to aid in orthodontic diagnosis and treatment planning. The aims of this research project were to describe the morphometric shape changes of C2 to C4 with growth, and to relate these changes to the currently accepted CVM method.[18] Generally, we found that the overall shape changes of the vertebral bodies of C2, C3, and C4 were consistent with the descriptions of shape in the literature. Morphometric shape analysis was used to determine the vertebral templates in relation to the mandibular growth peak and chronologic age. Also, the relationship of mandibular growth peak to cervical stage, sex, and chronologic age was explored.

Before discussing our findings, we must outline several strengths and limitations of this study. Although previous researchers have quantitatively assessed the CVM methods, most used cross-sectional samples.[16,28] Other studies, although longitudinal, have been purely descriptive.[2,12,15,18] Our study was rare in that it was both longitudinal and quantitative. Longitudinal samples have the advantage that they follow the same subjects through time, thus allowing them to be assessed in each age group. Using primarily quantitative measurements in this study has removed some subjectivity from shape assessments and has helped to confirm some qualitative shape descriptions previously published in the literature. Finally, to the best of our knowledge, this study is the first to use

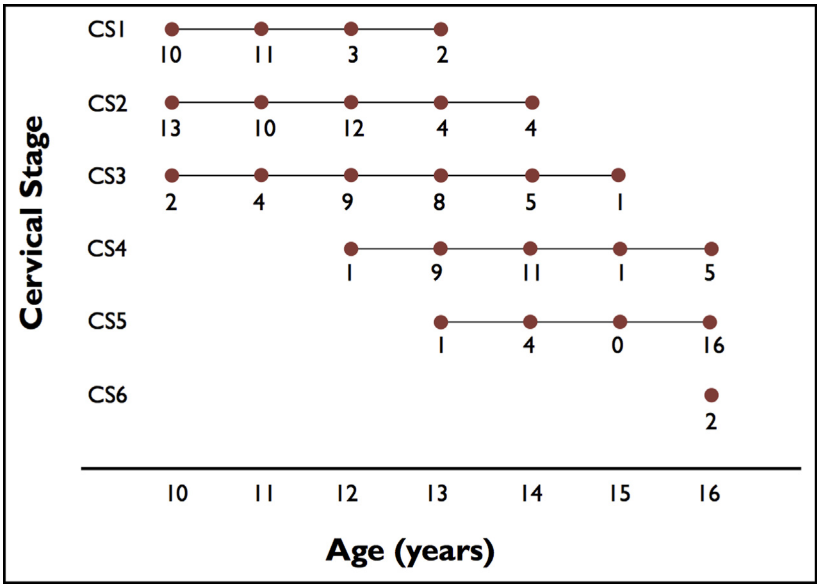

Fig 4. Frequency of CVM stage of individual radiographs by chronologic age. In CS1 (n = 26), 21 radiographs were taken at ages 10 to 11 years; in CS2, most of the radiographs (n = 35) were taken at ages 10 to 13 years. In CS3, most of the films (n = 17) were taken at ages 12 to 13 years. In CS4, most of the films (n = 20) were taken at ages 13 to 14 years. At both CS5 and CS6, most of the radiographs (n = 16 and n = 2, respectively) were taken at age 16 years.

Table. Mixed model analyses to assess the interactions among mandibular length, sex, and CVM stage

	Unadjusted for age		*Adjusted for age*	
Variable	*F ratio*	*P value*	*F ratio*	*P value*
CVM	63.6	<0.001	1.71	0.138
Sex	6.49	0.018	4.26	0.055
CVM × sex	5.29	0.001	9.40	<0.001
Chronologic age	-	-	33.92	<0.001

geometric morphometrics to assess cervical vertebral shape, making it an original area of research that was required in this field.

Several limitations also need to be considered. First, a relatively small sample size of 25 was used for this research. However, this is not unique to this study, with similar sample sizes reported in most other longitudinal growth studies assessing CVM in orthodontics.[2,15,18] When the initial data collection for this research was undertaken, only 67 subjects were found in the Burlington Growth Collection, 25 of whom met the inclusion criteria for our study. Since this time, the subjects included in the collection have increased to 100. If the study had been undertaken later or is repeated in the future, an increased sample size would have been possible. Second, we used a historical sample of convenience. Hence, it may not fully represent children today because secular trends and differences in ethnicity cannot be corrected for. Finally, it must be assumed that our sample was untreated orthodontically, healthy, and not exposed to any environmental factors that might have altered growth of the mandible or the cervical vertebrae in any way.

For the morphometric analysis, the images were clustered according to chronologic age and mandibular growth peak. Increasing concavity of the inferior border of all 3 vertebrae could be seen with increasing age. Also, the vertebrae appeared to become taller and less trapezoid in shape with time. The general shape changes were similar in the sexes; however, girls appeared to be more advanced than boys, reaching each stage earlier than their male counterparts. When the mandibular growth peak clusters were compared, it was easy to identify the difference between the morphometric vertebral templates during the mandibular growth peak and after it. After the peak, the vertebrae showed more pronounced curvatures, and they were also distinctly more square in shape (rather than trapezoid). However, it was almost impossible to distinguish a difference between the before-peak and the during-peak clusters. Thus, when this research is applied to orthodontic treatment planning, it would appear that it is possible only to identify a patient who has passed the growth peak, rather than one who is approaching it. Despite this finding, it has been reported that there is still considerable skeletal growth occurring before the pubertal growth spurt.[29] In addition, some authors have also reported that adults can benefit from growth modification treatment.[30] Therefore, treatment undertaken outside the periods of peak mandibular growth should not necessarily be ruled out if there is the potential for some clinical benefit to the patient.

Both the reliability and the validity of the CVM methods are controversial.[17,19,20,31,32] For the CVM methods to be valid, the maximum change in mandibular length would need to occur between set cervical stages in most subjects (eg, between CS3 and CS4). This has been confirmed in some studies but not in others.[2,15,18,33] Our findings do not support the validity of the CVM method to identify the mandibular growth peak. In fact, maximum mandibular growth occurred after CS3 in only 32% of our participants when the sexes were combined. Maximum growth was also seen after CS1, CS2, and CS4 in 28%, 20%, and 20% of our subjects, respectively. Our findings are consistent with previous ones, suggesting large individual variations in the cervical stage of peak mandibular growth.[12,27,33,34]

We used mixed models to determine the relationship between mandibular length, sex, and CVM stage or chronologic age. A mixed model was first run for mandibular length, sex, and CVM stage. In this model, we found that mandibular length was significantly associated with both sex and CVM stage. There was also an interaction between sex and CVM stage, suggesting that the effect of CVM stage on mandibular length was sex specific. A mixed model was then run again for mandibular length, sex, and CVM stage, adding chronologic age as an additional term. The model showed that mandibular length was associated mostly with age and to a marginal extent with sex. No significant association could be found with cervical stage after adjusting for the other covariates. This means that chronologic age is a better predictor of the mandibular growth peak than CVM stage; this is consistent with previous findings.[27,33,35]

CONCLUSIONS

Our findings indicate that quantitative and morphometric vertebral shape changes over time are consistent with the stages described by the CVM methods. However, neither morphometric templates nor subjectively assessed CVM stages could accurately identify the mandibular growth peak. Nonetheless, morphometric analysis of the cervical vertebrae may be useful to determine whether the mandibular grow peak has passed.

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