Original Article

Correlations of spheno-occipital synchondrosis, cervical vertebrae, midpalatal suture, and third molar maturation stages

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ABSTRACT

Objectives: To estimate the joint correlations among cervical vertebrae maturation (CVM), spheno-occipital synchondrosis (SOS), midpalatal suture maturation (MPS), and third molar mineralization (TMM) and to assess the predictive potential of SOS on CVM and MPS.
Materials and Methods: 570 pretreatment cone-beam computed tomogram (CBCT) scans from three private practices were analyzed, and MPS, CVM, SOS, and TMM stages were categorized and recorded by two independent investigators. Intra- and inter-rater reliability tests were evaluated with weighted Cohen's kappa tests. Spearman correlation coefficients for ordinal data were used to estimate the pairwise correlations among SOS, CVM, MPS, and TMM. To evaluate if SOS could predict CVM and MPS, ordinal regression models were estimated and cross-validated.
Results: The analysis demonstrated a robust positive correlation between SOS and CVM ($r = 0.845$) and between SOS and MPS ($r = 0.742$). A significant correlation was also observed between CVM and MPS ($r = 0.659$). Further correlations were identified between TMM and SOS ($r = 0.444$), TMM and MPS ($r = 0.392$), and TMM and CVM ($r = 0.358$). Ordinal regression models indicated the potential of using SOS as a predictive marker for CVM and MPS stages.
Conclusions: With a comprehensive analysis, SOS is strongly correlated with CVM and MPS, and SOS stage can be used to predict CVM and MPS using ordinal regression. Since MPS stages are challenging to categorize due to their anatomy, this finding suggests a diagnostic tool using SOS stages or when more information on skeletal maturity of the patient is desired. (*Angle Orthod*. 0000;00:000–000.)

KEY WORDS: Spheno-occipital synchondrosis; Cervical vertebrae; Midpalatal suture; Third molar

INTRODUCTION

The growth and skeletal maturity stages of orthodontic patients are important factors in the treatment planning process. The classic implant studies in craniofacial growth seem to point to an increase in craniofacial growth during the pubertal growth spurt.[1] In Class II treatment, timing functional appliance therapy to the peak pubertal growth period in adolescents is critical.[2] In Class III cases, any future craniofacial growth potential before starting a treatment plan that involves orthognathic surgery may compromise the outcome.[3] Patients requiring rapid maxillary expansion (RME) show greater transverse craniofacial changes at the skeletal level when treated before peak skeletal growth.[4] Thus, the ability to identify biological or morphological characteristics at discrete stages and relate those stages to the skeletal maturity of an orthodontic patient can aid orthodontic treatment planning.

Currently, the most commonly used indicators of skeletal maturity are an increase in height, skeletal maturation of the hand and wrist, and the cervical

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vertebrae maturation method.[5] Other researchers advocate using chronological age to perform just as well as other complicated methods.[6] The advent of three-dimensional imaging using cone beam computed tomography (CBCT) has allowed the visualization of internal structures, such as the midpalatal suture (MPS) and spheno-occipital synchondrosis (SOS), that were previously inaccessible with traditional two-dimensional techniques such as anteroposterior and lateral cephalometric, occlusal, or panoramic radiographs.

The developmental stages of the permanent dentition viewed from periapical or panoramic radiographs have long been used to estimate chronological age. Third molar mineralization (TMM) is of particular interest because they are the last set of teeth to develop, often not reaching full development until late adolescence and into early adulthood. TMM correlated with chronological age in many studies; however, results and conclusions surrounding dental age and development are highly population-specific and show great variability among ethnic groups.[7]

The cervical vertebrae maturation (CVM) method was first described in an unpublished master's thesis in 1972 by Lamparksi and has since been refined by many clinicians, most notably McNamara and Franchi. The main reason for the popularity of the CVM method over others, such as the hand-wrist analysis, is that the CVM method is performed on the lateral cephalogram routinely taken in the orthodontic examination, eliminating the need for an additional radiograph.[8]

SOS is the site of the union of the sphenoid and occipital bones in the cranial base, located just anterior to the foramen magnum and inferior to the pituitary fossa. It is an active growth center of the craniofacial skeleton. Early in life, the synchondrosis is composed of cartilage and remains open to allow for skeletal growth before becoming ossified and converted into bone in adolescence/early adulthood.[9] Given the fact that the SOS fusion stage is viewable with CBCT and the beginning of its fusion is related to the onset of puberty in teenagers, there is hope that its fusion stage can be used as an additional indicator of skeletal maturity in orthodontic patients.[10]

MPS plays an important role in orthodontic treatment planning and diagnosis. It is routinely opened during RME to fix transverse discrepancy issues. However, as this suture ossifies in adolescence and early adulthood, RME and sutural separation no longer become safe treatment options, and surgically assisted expansion is often considered. MPS fusion stage is viewable on a CBCT; however, the nature of its anatomy, such as thickness and curvature, makes this anatomical landmark challenging to classify.[11]

Multiple studies have shown that SOS and CVM show a statistically significant correlation.[10,12–14] Given this strong correlation, an ordinal prediction equation was developed for CVM using SOS, sex, and age as predictors, with the understanding that rank correlations are not directly pertinent to (logistic) ordinal regression goodness of fit to the extent that parametric (Pearson's) correlations are to linear parametric regression fitting. The predictive model was cross-validated and was found to be reproducible in the validation sample.[10] Additionally, CVM and MPS correlation was investigated with controversial outcomes.[15–18] Previous studies reported mixed results on the correlation of third molar mineralization and skeletal maturity. Some studies reported a good correlation between third molar mineralization and skeletal maturity from hand-wrist radiographs,[19]. In contrast, others showed that the third molar was the least reliable tooth to judge skeletal maturity.[20] Recently, two studies investigated correlations between SOS and MPS and concluded that there was a positive relationship and simultaneous progression of MPS and SOS.[21,22]

The aim of this study was to examine the correlations between CVM, SOS, MPS, and TMM comprehensively in the same large sample group, determine if sex was a biological factor in the correlation, and assess the predictive potential of SOS stages on MPS maturation using ordinal regression.

MATERIALS AND METHODS

A total of 570 pretreatment CBCT images of distinct subjects who required orthodontic treatment (242 males and 328 females with ages ranging from 7–66 years old and a mean $\pm$ SD of 18.18 $\pm$ 12.66 years old) were analyzed by two independent reviewers. The CBCT scans were obtained with institutional review board exemption (University of Illinois, Chicago) from deidentified pretreatment diagnostic records from three orthodontic private practices in Illinois, USA. The CBCT images were taken with a CBCT (i-CAT FLX, Quakertown, PA) machine with the same parameters at 120V, 5 mA with FOV of 16x13 cm^2 and 0.4 mm^3 voxel size and 8.9-second scan time.

The CBCT three-dimensional (3D) images were analyzed using Dolphin Imaging Software version 11.95 (Dolphin Imaging, Chatsworth, CA USA). The DICOM file was imported into the Dolphin 3D imaging program. All relevant diagnostic structures in the cervical spine and cranial base were required to be fully viewable in the CBCT images to be included. If third molars had been extracted or had not yet formed, those scans were still included, but third molars were not rated. The 3D rendering was oriented with the Frankfort horizontal plane parallel to the floor.

Table 1. Correlation Values of Age, CVM, SOS, MPS, and TMM

	CVM (r)			SOS (r)			MPS (r)			TMM (r)		
Parameters	Male	Female	Overall	Male	Female	Overall	Male	Female	Overall	Male	Female	Overall
Age (r)	0.723**	0.676**	**0.692****	0.734**	0.724**	**0.720****	0.653**	0.609**	**0.623****	0.597**	0.460**	**0.517****
CVM (r)				0.822**	0.849**	**0.845****	0.659**	0.657**	**0.659****	0.463**	0.275**	**0.358****
SOS (r)							0.747**	0.744**	**0.742****	0.511**	0.378**	**0.444****
MPS (r)										0.445**	0.343**	**0.392****

[a] CVM indicates cervical vertebrae maturation; MPS, midpalatal suture maturation; SOS, spheno-occipital synchondrosis.

CVM and SOS were analyzed from a midsagittal slice of the CBCT image. The midsagittal plane was adjusted to pass through the anterior and posterior nasal spines in the axial plane, following the midpalatal suture, with Frankfort horizontal parallel to the floor. This method was consistent with previous studies that analyzed CVM from CBCT sagittal sections.[23,24] CVM was analyzed using the classification method of McNamara et al.[8] Previous studies showed near-perfect agreement in CVM evaluation between sagittal sections extracted from a CBCT and traditional lateral cephalograms.[23,24] SOS was evaluated from the same midsagittal image following the five-stage scoring scheme outlined by Bassed et al.[9]

The MPS maturation stages were analyzed on an axial cross-section using the five-stage technique of Angelieri et al.[11] In cases with thick or curved hard palates, more than one cross-section was investigated to correctly classify the MPS fusion stage. Mandibular third molars were classified using the eight-stage classification system of dental development described by Demirjian et al.[25] Although most studies using that method for third molar development use a panoramic radiograph for analysis, the developmental stages were directly evaluated from the CBCT 3D rendering to simplify the methods. Studies have shown no significant difference in the staging accuracy between analyzing extracted teeth, panoramic radiographs, or CBCT to evaluate third molar development.[26] The lower right third molar image was taken from the 3D rendering facing to the right, with the mandibular bony structure density reduced so that the entirety of the mandibular right third molar was visible.

Statistical Analysis

Intra-examiner and inter-examiner agreement was evaluated with weighted Cohen's Kappa tests. Descriptive statistics using frequency distributions (%), cross-tabulations, and Spearman correlation coefficients for ordinal data were used to estimate the pairwise correlations among age, SOS, CVM, MPS, and TMM by sex. To confirm the predictive ability of SOS on MPS, ordinal regression models were estimated for SOS, CVM, and MPS. Statistical significance was set at 0.05. Data analyses were performed with IBM SPSS Statistics (version 29.0; IBM, Armonk, NY). Cross-validation and resampling estimations were programmed in 2024 SageMath (https://sagemath.org).

RESULTS

Intra- and inter-rater reliability tests were evaluated with weighted Cohen's Kappa Tests. The Kappa values for intra- and inter-rater reliability on each variable, respectively, were CVM: 0.882, 0.771; SOS: 0.884, 0.766; MPS: 0.758, 0.872; and Third Molar: 1.000, 1.000.

Spearman rank correlation showed a statistically significant positive correlation ($P < .001$) between the following maturation indices: CVM and SOS (r = 0.845), CVM and MPS (r = 0.659), CVM and TMM (0.358), SOS and MPS (r = 0.742), SOS and TMM (r = 0.444), MPS and TMM (r = 0.392). Age showed a significant positive correlation with all the other variables (Table 1).

When analyzed by sex, males and females showed the following correlations, respectively: CVM and SOS (r = 0.822, 0.849), CVM and MPS (r = 0.659, 0.657), CVM and TMM (0.463, 0.275), SOS and MPS (r = 0.747, 0.744), SOS and TMM (r = 0.511, 0.378), MPS and TMM (r = 0.445, 0.343) (Table 1). The correlations, ranked from highest to lowest, were as follows: SOS and CVM, SOS and MPS, CVM and MPS, SOS and TMM, and MPS and TMM. Similar correlations were found between males and females; however, certain parameters were found to have lower correlations in females, such as CVM and TMM and SOS and TMM.

As suggested by the relatively higher ordinal correlations between SOS and CVM and SOS and MPS, ordinal regression models were tested with SOS as the independent variable and CVM and MPS as the dependent variables. The analysis showed that SOS was a significant predictor of CVM (Pseudo R^2= 0.673). The resulting estimated proportion of correct classification (observed vs predicted) by resampling with replacement (bootstrapping resampling) was 0.469 with a corresponding 95% confidence interval (CI) (0.411; 0.525) (Figure 1).

When SOS was set as the independent variable and MPS as the dependent variable, the analysis showed that SOS with the combination of (log) Age was a significant predictor of MPS (Cox and Snell

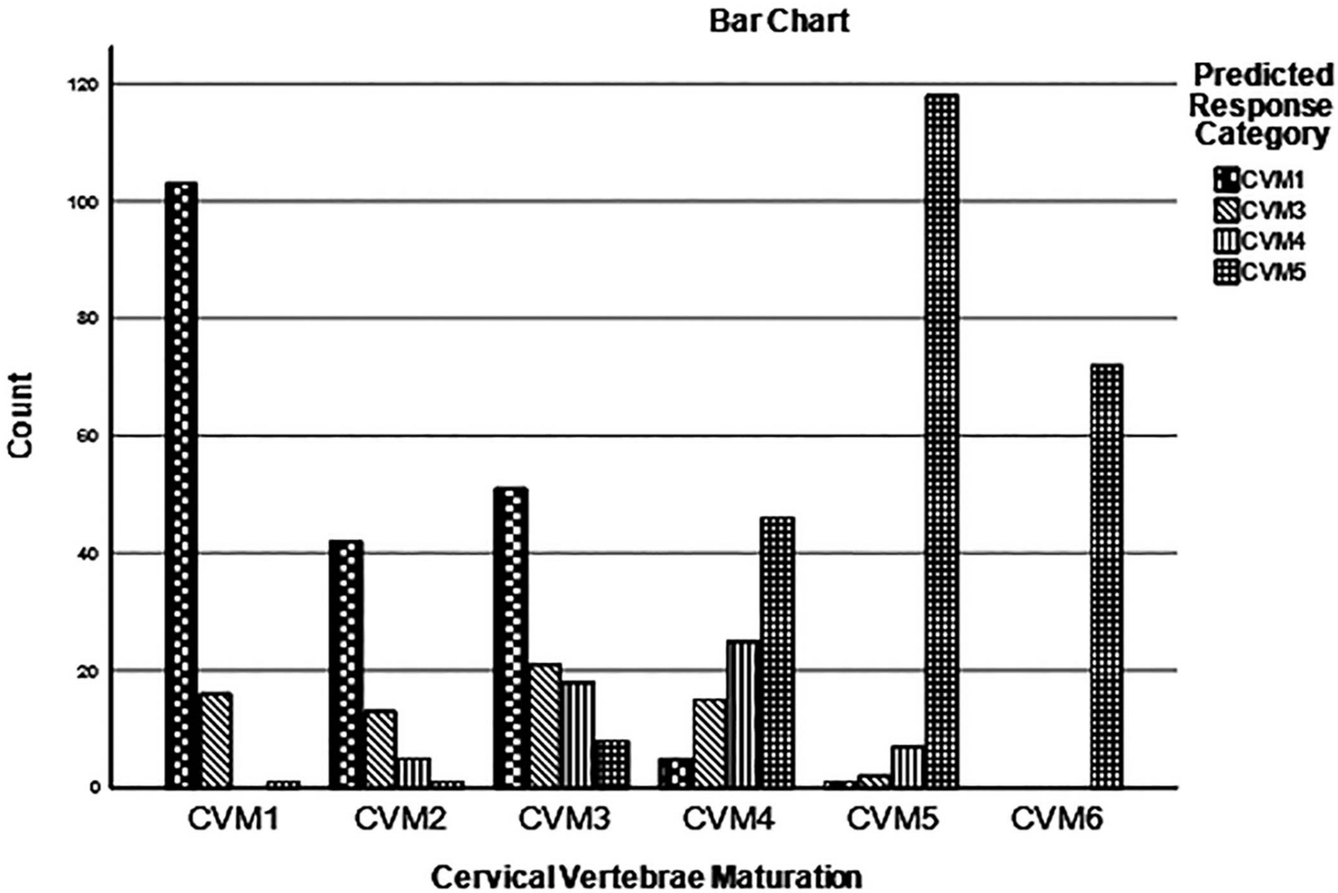

Figure 1. Predicted outcome of CVM stage when the ordinal regression was tested using SOS stage as an independent variable. CVM indicates cervical vertebrae maturation; SOS, spheno-occipital synchondrosis.

Pseudo $R^2 = 0.551$). The resampling estimated proportion of correct classification (observed vs predicted) was 0.467 with a corresponding 95% CI (0.410; 0.527) (Figure 2). Cross-validation based on a random (70% training, 30% validation) sample of the original data set estimated the probability of correct MPS classification in the validation sample to be 0.47 with a resampling approximate 95% CI of (0.32, 0.61), thus sustaining the original level of correct classification.

To predict MPS from SOS, the following model was estimated,

$$P[MPS \leq j \mid SOS = k] = 1/(1 + \exp(\beta_{k+}\beta_{\log(Age)}\log(Age) - \theta_j), k = 1, \ldots .5, j = 1, \ldots, 4,$$

In which
$\theta = (-2.45, -0.517, 2.254, 4.025)$
$\beta = (-4.207, -3.128, -2.423, -1.201, 0)$
$\beta_{\log(Age)} = 0.948$.

A graphical representation of the estimated model that avoids individualized calculations (Figure 3) showed the distinct lines corresponding to the conditional probabilities of MPS classification in the diverse stages (Y-axis) for subjects with SOS = 1 as a function of their age (X-axis). It showed that, in general, subjects with SOS = 1 and ages 10 and younger were expected to be at MPS stage A, subjects with SOS = 1 in the age range 10–40 were expected to be at MPS stage B, whereas older subjects with SOS = 1 were expected to be at stage C. However, in all cases, the MPS probabilities were near or just below 50%, so the level of uncertainty in the predicted MPS stage was not small. Similar classification graphs and interpretations could be generated for the other SOS = 2, 3, 4, 5 instances.

DISCUSSION

This was the first study to compare comprehensively the correlations between growth parameter landmarks, namely, SOS, CVM, MPS, and TMM, extracted from CBCT images from the same pool of subjects with various age groups and further analyzing in a separate sex manner. The strongest correlation in this study was between CVM and SOS ($r = 0.845$) and confirmed the positive correlations reported in the

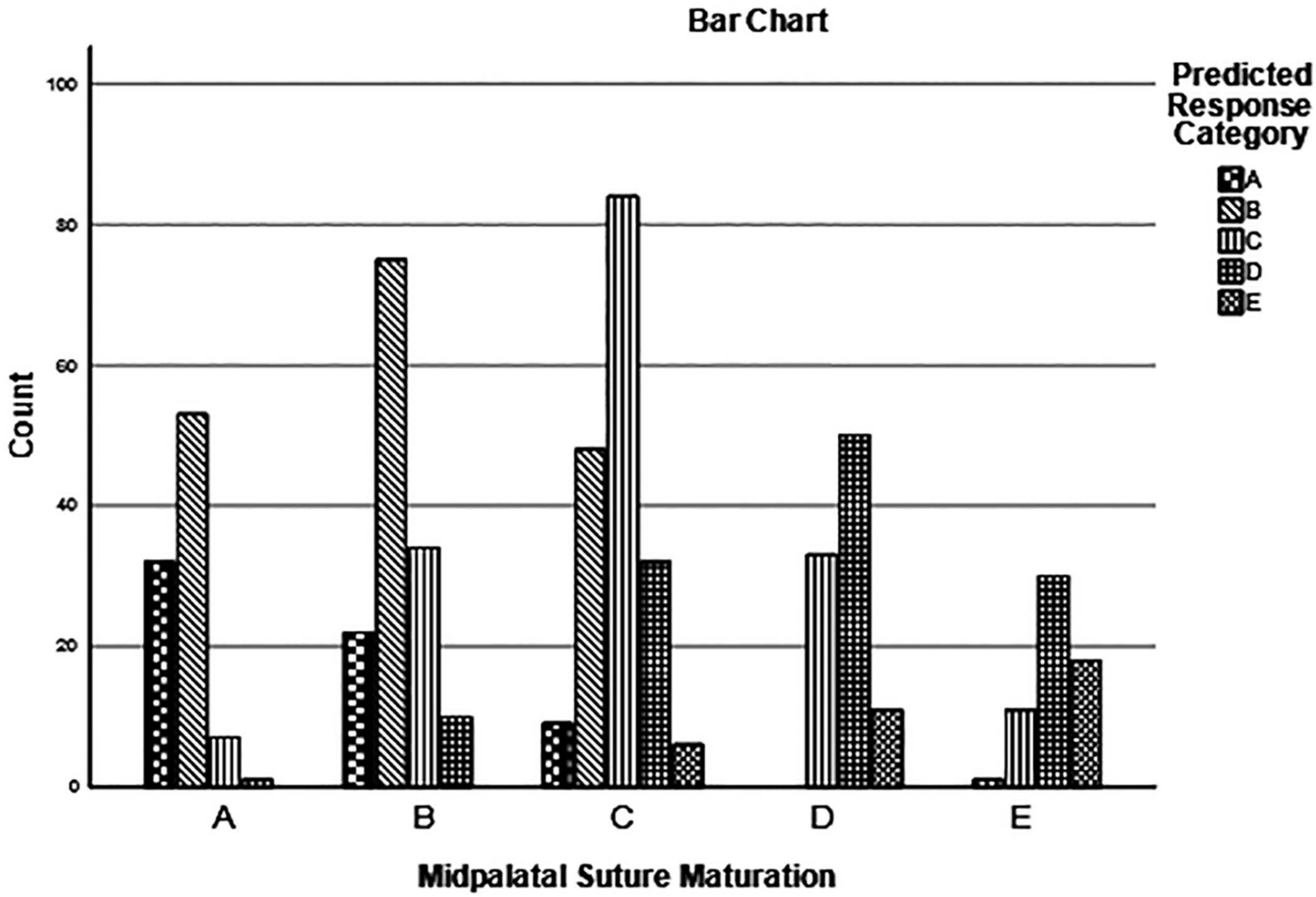

Figure 2. Predicted outcome of MPS stage when the ordinal regression was tested using SOS stage as the independent variable. MPS indicates midpalatal suture maturation; SOS, spheno-occipital synchondrosis.

literature.[10,12–14] Though slightly lower than previous studies, the results from this study were comparable to previous studies and demonstrated a strong positive correlation between CVM and SOS (Table 2).

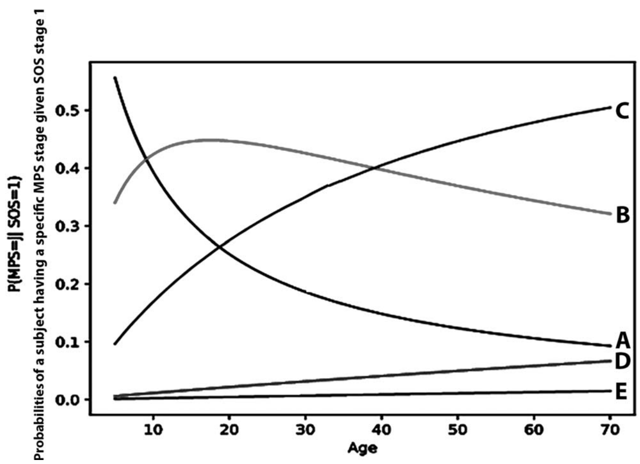

Figure 3. Graph summarizing the results of the ordinal regression model predicting MPS from SOS and log (Age). The five distinct lines show the probability of a subject being at that MPS stage, given the age of the subject and SOS stage. Example SOS = 1. MPS indicates midpalatal suture maturation; SOS, spheno-occipital synchondrosis.

The second strongest correlation in this study was between SOS and MPS (r = 0.742). While two other studies were found that evaluated SOS and MPS correlation, only one[22] used the same MPS classification as this study, and this study was the first to use a five-stage SOS staging system. The correlation (r = 0.736) reported from 312 Turkish patients in that study was similar to the current study, confirming a robust positive relationship and simultaneous progression of MPS and SOS maturation. In addition, subgroups of

Table 2. Correlation Values Between SOS and CVM From Previous Literature

Study	Reported r value for CVM and SOS
Kim et al. (2023)[12]	r = 0.955 in males and r = 0.964 in females
Fernández-Pérez et al. (2016)[10]	r = 0.89
Fayad et al. (2020)[13]	r = 0.852
Kocasarac et al. (2017)[14]	r = 0.851
Results from this study	**r = 0.845 (males = 0.822, females = 0.849)**

[a] CVM indicates cervical vertebrae maturation; SOS, spheno-occipital synchondrosis.

Table 3. Correlation Values Between CVM and MPS From Previous Literature

Study	Reported r value for CVM and MPS
Angelieri et al. (2015)[15]	r = 0.908
Jang et al. (2016)[16]	r = 0.874
Mahdian et al. (2020)[17]	r = 0.754 in males and r = 0.691 in females
Results from this study	**r = 0.659 (males = 0.659, females = 0.657)**
Estrada et al. (2022)[18]	r = 0.395

[a] CVM indicates cervical vertebrae maturation; MPS, midpalatal suture maturation.

sexes were investigated, reporting a correlation of r = 0.747 in males and 0.744 in females.

The third strongest correlation in this study was between CVM and MPS (r = 0.659). The literature surrounding this correlation was less consistent, and the result from this study confirmed a strong positive relationship with more overall variation between studies (Table 3).

TMM showed a moderate correlation with SOS (r = 0.444), and a weak relationship with MPS (r = 0.392) and CVM (r = 0.358). Demiturtruk et al.[14] reported a strong correlation (r = 0.723) between CVM and TMM in males and a weak correlation (r = 0.371) in females. They also reported a strong correlation (r = 0.759) between SOS and TMM in males and a weak association (r = 0.534) in females. Compared to males, the current study showed weaker correlations between TMM and CVM, and TMM and SOS in females; however, the overall weak correlations combined with the fact that many patients are congenitally missing their third molars or have them previously extracted makes TMM of limited clinical value.

The results of this study confirmed that the ordinal regression of the CVM stage could be accurately predicted from the SOS stage. A previous study[10] reported a χ^2 (6) = 457.54, $P < .001$ (Cox-Snell pseudo R^2 = 0.77), and the current study reported a pseudo R^2 = 0.673, with a resulting estimated agreement (observed versus predicted CVM) probability of 0.469 and a corresponding approximate 95% CI (0.411; 0.525).

For the first time, ordinal regression was used to evaluate whether SOS and age could be used to predict MPS. Previous studies reported SOS to predict CVM when the cervical vertebrae were not fully visible on the CBCT, such as when a thyroid collar is used or a small field scan is taken to evaluate an impacted maxillary canine.[10,13] The clinical application of observing the SOS fusion stage can be expanded by evaluating the correlation and predictive ability of SOS on MPS.

SOS maturation can be considered a diagnostic tool due to its strong correlation with CVM and MPS. In cases where the palatal bone of the patient is significantly curved, requiring evaluation in multiple planes, or the palatal bone is very thin, making an accurate MPS classification difficult or impossible, the SOS stage and the regression equation in this study can be used to estimate a patient's MPS stage.

Some limitations of this study were present since ethnicity was not recorded or evaluated from the sample due to unrecorded information from a private practice setting.

CONCLUSIONS

- The maturation stage of SOS can be used to confirm the skeletal maturity of patients.
- CVM and SOS have a strong positive correlation.
- MPS and SOS have a strong positive correlation.
- SOS and age can be used to predict MPS.

DISCLOSURE

The authors declare no conflicts of interest during the electronic submission process.

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