Multiple Regression Modeling for Age Estimation by Assessment and Comparison of Spheno-Occipital Synchondrosis Fusion and Cervical Vertebral Maturation Stages

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Abstract

Objectives The aim of this study was (1) to evaluate the relationship between spheno-occipital synchondrosis (SOS) fusion stages, cervical vertebral maturation (CVM) stages, and clivus sizes with chronological age on cone-beam computed tomography (CBCT) images, and (2) to compare these methods for accurate age estimation using regression analysis.

Materials and Methods The CBCT images of 200 individuals (102 females and 98 males) were included in the study. The SOS fusion stages and CVM stages were evaluated. The width and length of the clivus were measured. The effects of SOS fusion stages, CVM stages, clivus width, and clivus length on age estimation were evaluated by univariate tests and the effects of coexistence with ANCOVA and regression model. Spearman rank correlation analysis was also used to investigate the relationship between the SOS fusion stage, CVM stage, clivus width, and clivus length.

Results The SOS stages, CVM stages, and clivus width were not shown statistically significant differences between the sexes (p-values = 0.205, 0.162, and 0.277, respectively), whereas clivus length was significantly longer in males (42.9 ± 4.26 mm) than in females (41.04 ± 3.74 mm). Multiple regression analysis showed 80% success when all parameters (SOS fusion stages, CVM stages, clivus width, and clivus length) were taken into consideration.

Conclusion In conclusion, with the use of CVM stages and SOS fusion stages together, an accurate and reliable age estimation can be obtained in forensic medicine.

Keywords
- spheno-occipital synchondrosis
- cervical vertebra maturation
- clivus
- cone-beam computed tomography
- age estimation

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Introduction

It is a necessity to estimate the age of living individuals and human remains in social, criminal, civil, and anthropological purposes. Age estimation has become more important worldwide due to criminal investigations, asylum applications, asylum seekers, adoption, immigrants, child workers, and especially individuals who do not have official documents.[1,2]

Skeletal maturation models tend to show clear and distinct age estimation patterns for different populations. The skeletal maturation varies among different populations due to genetic and socioeconomic factors.[3,4] Although there are different skeletal age estimation methods, multifactor and noninvasive approaches are recommended to make the most accurate estimation of age.[5,6]

Spheno-occipital synchondrosis (SOS) is the growth center between the occipital and sphenoid bone, which forms of cartilage in the growth phase of the cranial base until the stage of skeletal maturation.[7–9] As the ossification of the synchondrosis process, ecto-endo fusion begins between occipital and sphenoid bones and the maturation is completed by closing the gap between bones.[10] The late ossification of this synchondrosis than any other in the cranium makes it popular in age estimation.[11]

Cervical vertebra maturation (CVM) is another method of evaluating skeletal maturation, which is based on the evaluation of morphological changes in the cervical vertebrae.[12] Hassel and Farman evaluated morphological changes in the cervical vertebrae based on the presence or absence of curvature at the inferior border of the vertebrae, the shape of the vertebral bodies, and the width of the intervertebral spaces.[13]

Clivus is a part of the cranium between the dorsum sella and foramen magnum. The genesis of clivus result from the fusion of synchondrosis between basioccipital and exoccipital bones, and the ossification process starts from 3 years old and continues until 25 years old.[14,15]

Macroscopic, histological, and radiographic examinations are performed to evaluate different parameters in age estimation.[11,16,17] Among those methods, radiographic methods are noninvasive procedures and evaluate the anatomic structures that are examined. Cone-beam computed tomography (CBCT) is widely used in dentistry because of its advantages such as low radiation doses, rapid scanning, and high quality and accurate three-dimensional display of hard tissues, providing submillimeter slice thickness in multiplanar reformation.[18,19]

The aim of this study was (1) to evaluate the relationship between SOS fusion stages and CVM stages and clivus sizes with chronological age on CBCT images and (2) to compare these methods for accurate age estimation using regression analysis.

Materials and Methods

This retrospective study was approved by the Clinical Researches Ethics Committee of X University, and the study protocol was prepared according to the principles stated in the Helsinki Declaration.

Table 1 The distribution of patients by age groups

Age (y)	Number of samples
≤10	38
11–14	45
15–20	67
25≤	50
Total	200

Overall, 200 CBCT scans (102 females and 98 males) that had been taken for various reasons (cyst, tumor, impacted teeth, orthodontic treatment, etc.) were randomly selected from the archive of the department of dentomaxillofacial radiology. Patients selected for this study had no pathological fracture or trauma that affected the morphological structure or integrity in the head and neck region. Moreover, only good-quality CBCT images were chosen; images with motion artifact or technical error were excluded from the study. The distribution of patients by age groups is shown in ►**Table 1**.

All images were taken with the I-CT system (Imaging Sciences International, Hatfield, Pennsylvania, United States), 120 kVp, 5 mA, 0.3-mm isotropic voxel size, and 16 × 9–13 cm field of view. Image measurements were performed using I-CT Vision software (Imaging Science International), which provided three planes of 0.3-mm slice thickness and 0.3-mm slice interval. All measurements were analyzed by the same observer who has 10 years of experience and was recorded in millimeters using a spreadsheet (Microsoft Office Excel, Redmond, Washington, United States).

Determination of Spheno-Occipital Synchondrosis Fusion Stages

The SOS fusion stages were evaluated in four stages following Franklin and Flavel[9] (►**Fig. 1**):

- Stage 0 (unfused): No bone present in the between the basilar portion of the occipital and the sphenoid (no bone present in the gap)
- Stage 1 (fusing endocranially): The fusion that proceeds endo-ectocranially is not reached more than half the length of synchondrosis
- Stage 2 (fusing ectocranially): Greater than half the length of the synchondrosis is fused (the ectocranial [inferior] border remains unfused)
- Stage 3 (complete fusion): The basilar portion of the occipital and the sphenoid bone is completely fused (a fusion scar may be present).
- All assessments for standardization of the review were made in the mid-sagittal plane.

Measurement of Clivus Width and Length

The length of the clivus was measured as the longest point in the sagittal plane, from the upper point of the dorsum sella to the lowest point on the anterior margin of the foramen magnum. The width of the clivus was measured as the longest distance from left to right near the anterior

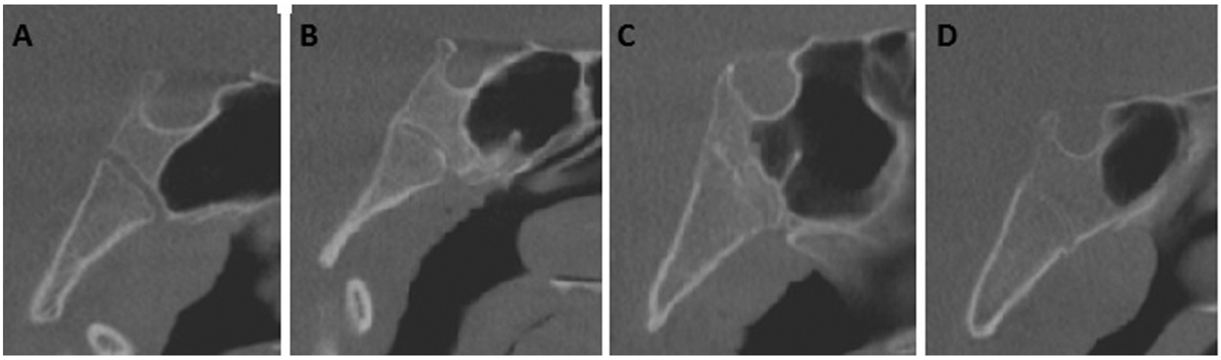

Fig. 1 Spheno-occipital synchondrosis fusion stages. (**A**) Stage 0, (**B**) Stage 1, (**C**) Stage 2, and (**D**) Stage 3.

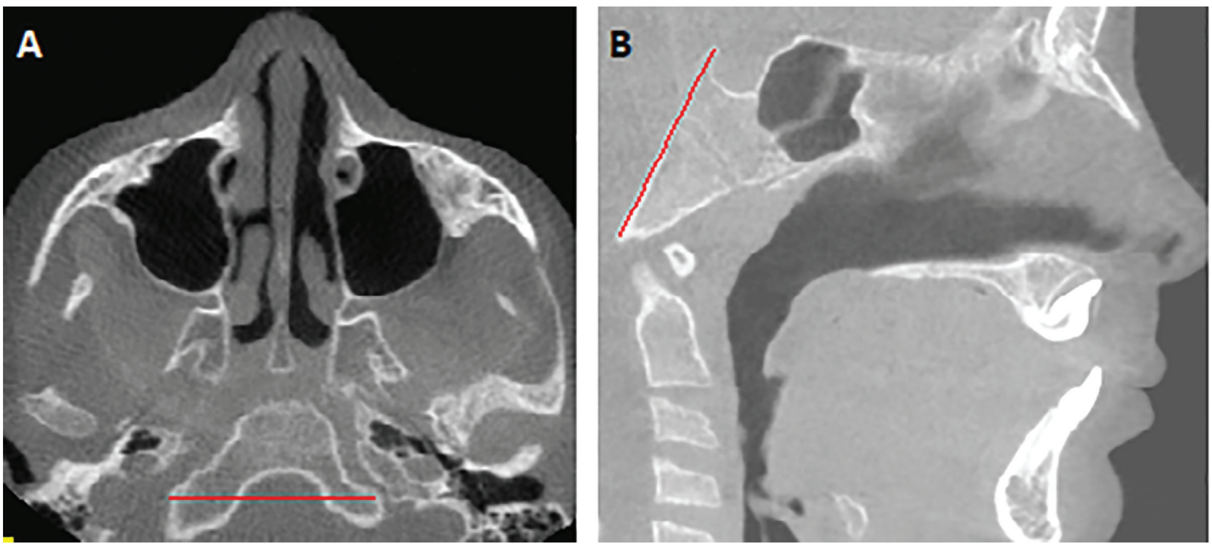

Fig. 2 Measurement of clivus width (**A**) and clivus length (**B**).

peripheral margin of the foramen magnum in axial sections[20] (►**Fig. 2**).

Evaluation of Cervical Vertebral Maturation

The CVM was evaluated into one to six stages based on the morphology of the CV2, CV3, and CV4, which was previously described by Hassel and Farman[13] (►**Fig. 3**).

This method divides skeletal maturation into one to six stages based on the morphology of the three CVs (CV2, CV3, and CV4) as follows:

- Stage 1 (initiation): CV2, CV3, and CV4 inferior vertebral body borders are flat. The superior vertebral borders are tapered posterior to anterior taking the shape of a trapezoid.
- Stage 2 (acceleration): Concavities progress in the lower borders of CV2 and CV3, while the lower border of CV4 vertebral body is still flat.
- Stage 3 (transition): Distinctive concavities in the lower borders of CV2 and CV3. Developing concavity in the lower border of CV4, CV3 and CV4 are rectangular.
- Stage 4 (deceleration): Distinctive concavities in the lower borders of CV2, CV3, and CV4 seen on the images, CV3, and CV4 are nearly square.
- Stage 5 (maturation): Distinctive concavities are seen on inferior borders of C2, C3, and C4, and bodies of C3 and C4 are nearly square; well-defined concavities appear on the on lower borders of bodies of all cervical vertebrae.
- Stage 6 (completion): Representing the maturation stage with deep concavities for the inferior vertebral body borders of CV2, CV3, and CV4, which are vertical rectangular.

Statistical Analysis

Descriptive statistics of the data were made as follows: mean, standard deviation, and frequencies (n, %). Kolmogorov–Smirnov test was used to check for normality distributions of the age, clivus width, and clivus length. These three continuous variables have shown normal distributions according to the test. The unadjusted effects of SOS, CVM, clivus width, and clivus length on age were evaluated by univariate tests, and the adjusted effects were evaluated by using the ANCOVA model. Moreover, the effects of these variables on sex were investigated by using multiple binary logistic regression models. Spearman rank correlation analysis was used to investigate the relationship between the SOS fusion stage, CMV stage, clivus width, and clivus length. Intraclass correlation (ICC) values were calculated for intraobserver compliance. Statistical significance was accepted as $p < 0.05$ and SPSS (version 22) program was used in the calculations.

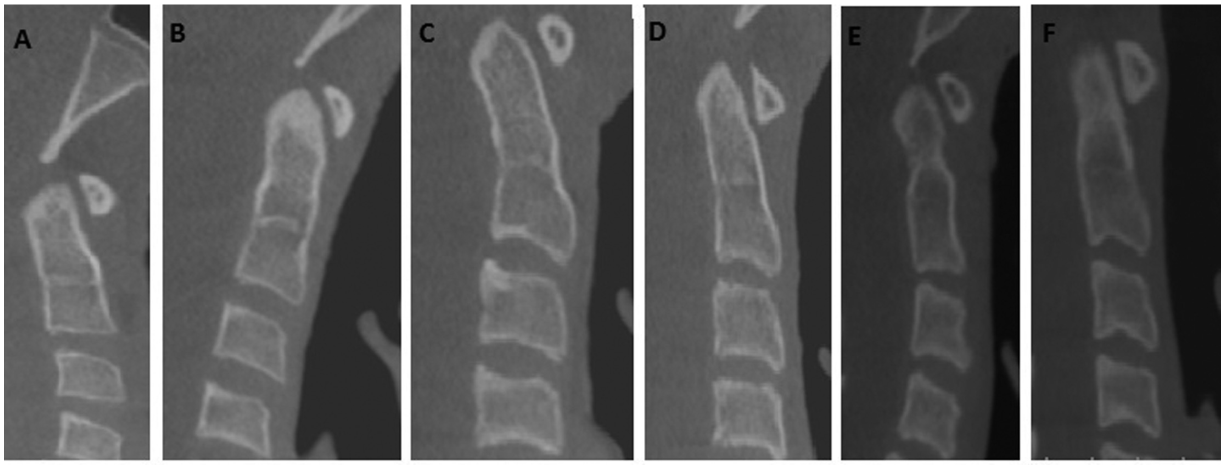

Fig. 3 Cervical vertebral maturation stages. (**A**) Stage 1, (**B**) Stage 2, (**C**) Stage 3, (**D**) Stage 4, (**E**) Stage 5, and (**F**) Stage 6.

Results

The ICC values indicated high reliability for all measurements (0.900). Of all patients included in the study, 102 (51%) were females and 98 (49%) were males. The mean age was 16.5 ± 5.3 years. The mean clivus width 42.3 ± 3.37 mm and the mean clivus length was calculated as 41.97 ± 4.11 mm. The descriptive analysis of the SOS fusion stage and CVM stage are presented in ►**Tables 2** and **3**, respectively.

The SOS fusion stages, CVM stages, and clivus width did not show a statistically significant difference between the sexes (p-values = 0.205, 0.162, and 0.277, respectively), whereas clivus length was significantly longer in males (42.9 ± 4.26 mm) than in females (41.04 ± 3.74 mm; $p < 0.001$).

The age estimation accuracy was evaluated separately for SOS fusion stages, CVM stages, clivus width, and clivus length.

The SOS fusion stages had a statistically significant effect on age estimation ($p < 0.001$), and the success of SOS fusion stages in predicting age (R^2) was calculated as 70.2% when the other three factors were ignored. Besides, it was found that age increased at a statistically significant level of 3.815 years in each increase of SOS fusion stages.

The CVM stage was calculated to have a statistically significant effect on age estimation ($p < 0.001$), and the success of CVM stages in predicting age (R^2) was calculated as 79.4% when the other three factors were removed.

Furthermore, it was found that the difference in the age increased gradually at a statistically significant level of 2.935 years in each increase of CVM stages.

On the other hand, there was no statistically significant among between clivus length ($p = 0.230$) or clivus width ($p = 0.374$) and age. The results showed that in each millimeter increased in the clivus length and the clivus width, the age was decreased by 0.602 and 0.350 years, respectively, without significant difference (►**Table 4**). Additionally, it was calculated that the success of clivus length in predicting age (R^2) as 21.4% by measuring only clivus length and the success of predicting age (R^2) by measuring only clivus width was calculated to be 7.9%.

Table 2 The descriptive analysis of spheno-occipital synchondrosis fusion stage

	Sex	*n*	Min–max age (y)	Mean (y) ± SD
Stage 0	Female Male	17 18	7–13	12.85 ± 3.54
Stage 1	Female Male	12 22	8–16	13.70 ± 3.04
Stage 2	Female Male	21 13	9–23	15.39 ± 2.76
Stage 3	Female Male	52 45	14–25	16.72 ± 5.15

Abbreviations: *n*, sample size, min, minimum; max, maximum; SD, standard deviation.

Table 3 The descriptive analysis of cervical vertebral maturation stage

	Sex	*n*	Min–max age (y)	Mean (y) ± SD
Stage 1	Female Male	4 3	7–10	10.67 ± 2.80
Stage 2	Female Male	14 25	7–13	11.87 ± 3.38
Stage 3	Female Male	14 16	8–16	13.59 ± 2.65
Stage 4	Female Male	16 11	10–17	14.81 ± 2.61
Stage 5	Female Male	21 18	14–21	17.04 ± 3.56
Stage 6	Female Male	33 25	15–25	20.02 ± 4.71

Abbreviations: *n*, sample size; min, minimum; max, maximum; SD, standard deviation.

The determination coefficient (R^2) of the ANCOVA model is 80% when all parameters (SOS fusion stages, CVM stages, clivus width, and clivus length) were taken into consideration.

The correlation between the SOS fusion stage, CVM stage, clivus width, and clivus length are shown in ►**Table 5**. There

Table 4 The parameters of the analysis of covariance model

	Parameters	B	SE	*p*-Value
	Intercept	18.108	2.397	0.001
SOS	Stage 0	− 3.869	0.987	0.001
	Stage 1	− 3.023	0.838	0.001
	Stage 2	− 1.331	0.614	0.032
	Stage 3	Reference category		
CMV	Stage 1	− 9.347	1.388	0.001
	Stage 2	− 8.143	1.011	0.001
	Stage 3	− 6.424	0.877	0.001
	Stage 4	− 5.209	0.684	0.001
	Stage 5	− 2.976	0.10	0.001
	Stage 6	Reference category		
Clivus	Length	0.057	0.048	0.230
	Width	0.037	0.041	0.374

Note: The dependent variable is age; B: regression coefficient;, SE: standard error of B.
Abbreviations: CMV, cervical vertebral maturation; SOS, spheno-occipital synchondrosis.

was a statistically significant correlation among these four parameters, but the strongest relationship was found between the CVM stages and SOS fusion stages.

Discussion

It is important to know the characteristics of individuals such as age, sex, and race in forensic cases, uncontrolled migrations, the detection of bodies whose integrity was impaired, and the determination of the growth and development stages of children.[21] The dry skull bone is frequently used in forensic medicine and anthropology. In addition to the morphological,[20] histological measurements[22,23] of anatomical structures, such as the SOS, clivus, and radiological examinations,[1] have also been reported to be useful in age–sex–race determinations.

In the literature, age determination studies using clivus measurements,[15,20] SOS fusion stages,[24,25] and CVM stages[4,26] are available, but to our knowledge no study investigated the rate of predicting age accurately by using these three parameters simultaneously.

Chaurasia et al[20] in their study stated that the mean clivus width and length were 28.8 ± 3.98 and 42.7 ± 3.98 mm, respectively, regardless of age and sex. Moreover, they reported that there was no statistically significant difference in clivus width between sexes, but the clivus length was significantly higher in males. In another study, Chaurasia et al[15] reported that there was a significant positive correlation between length of clivus and age; additionally, the accuracy of estimating sex by clivus measurement was 76.43% in males and 77.94% in females. In line with this study, the current study results also showed clivus length is significantly longer in males than in females. On the other hand, it was found that the success of predicting an age by measuring only clivus length and only clivus width was 21.4 and 7.9% respectively. It is considered that the number of patients, population, and races may change the results.

Sinanoglu et al[24] indicated that a significant positive relationship between age and SOS fusion stages for both sexes. They reported that fusion started 1 year earlier in females and also the early onset of ossification started at ages 11.37 and 10.56 years in males and females, respectively. The average age for complete fusion (Stage 3) was calculated as 18.36 years in males and 18.29 years in females. In another study,[25] the success of the SOS fusion stage in predicting age was reported to be 66.1% in females and 35.5% in males. These results were evaluated as moderately successful, and the authors indicated that this method needs to be developed. Bayrak and Göller Bulut[26] also in a recent study stated that there was a positive correlation between the SOS fusion stage for both sexes and age.

Schmeling et al[4] evaluated the variation of CVM stages according to different races and stated that the change in the age of CVM stages is not clearly affected by ethnic origin, and therefore, CMV stages can be used to estimate age in different races. Uysal et al[27] evaluated the relationship between chronological age and CVM and reported that a high correlation coefficient was found between chronologic age and CVM, and a high correlation was also found in both sexes, although it was significantly better for females. On the other hand, Kulkarni and Dave[28] stated that there was a moderate correlation between chronological age and cervical vertebral bone age. In another study that investigated the effect of CVM age estimation via panoramic radiographs[6] noticed that the R^2 value of CVM was found to be 46%. In the current study, the R^2 value of CVM was found as high as 79%. The reason for this difference may be due to the use of different techniques. As in

Table 5 Correlations between spheno-occipital synchondrosis fusion stages, cervical vertebral maturation stages, clivus width, and clivus length

		Clivus width		Clivus length		Vertebral maturation stages	
		r	*p*-Value	r	*p*-Value	r	*p*-Value
Spearman's rho	SOS stages	0.233	0.001[a]	0.409	< 0.0001[a]	0.878	< 0.0001[a]
	Clivus width			0.306	< 0.0001[a]	0.250	< 0.0001[a]
	Clivus length					0.481	< 0.0001[a]

Abbreviation: SOS, spheno-occipital synchondrosis.
[a]Indicates significant differences.

our study, CBCT was preferred because of its advantages such as being able to allow three-dimensional investigations and giving more detailed images due to its high spatial resolution.

Montasser et al[29] evaluated the CVM stage according to sex and different racial groups and stated that in both sexes; statistically, differences were evident between Hispanics versus both Whites and African Americans. Additionally, they reported no sex differences were detected in stages 4, 5, or 6 in any of three racial groups.

In this study, clivus measurements, SOS fusion stages, and CVM stages were evaluated simultaneously, and the accuracy rate was calculated as 80%. Moreover, a strong statistically significant correlation was found between the CVM stages and SOS fusion stages. However, there was no statistically significant difference in the sex prediction among SOS fusion stages, CVM stages, and clivus width.

There are some limitations to our study. The sample size is small; hence, a larger sample size should be evaluated for further studies. Another limitation is the particular population of the study and larger samples from different populations can be investigated regarding the difference between ethnicities.

Conclusion

In conclusion, an accurate age estimation can be achieved through the assessment of both SOS fusion and CVM stages; this is highly useful in estimating the individual age in forensic practice.

Conflict of Interes
None declared.

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