Diagnostic performance of skeletal maturity for the assessment of midpalatal suture maturation

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Introduction: The aim of this study was to analyze the diagnostic performance of the cervical vertebral maturation (CVM) method in estimating accurately the stages of maturation of the midpalatal suture. **Methods:** Cone-beam computed tomography (CBCT) images from 142 subjects (84 female, 58 male; mean age, 14.8 ± 9.7 years) were analyzed by 2 calibrated examiners to define, by visual analysis, the maturational stages of the cervical vertebrae and the midpalatal suture. These CBCT images were required by orthodontists and surgeons for diagnosis and treatment purposes. Positive likelihood ratios (LHRs) were calculated to evaluate the diagnostic performance of the CVM stages in identifying the maturational stages of the midpalatal suture. **Results:** Positive LHRs greater than 10 were found for several cervical vertebral stages (CSs), including CS1 and CS2 for the identification of midpalatal suture stages A and B, CS3 for the diagnosis of midpalatal suture stage C, and CS5 for the assessment of midpalatal suture stages D and E. These positive LHRs indicated large and often conclusive increases in the likelihood that the CVM stages were associated with specific stages of midpalatal suture maturation. At CS4, there were a moderate positive LHR for stage C and low positive LHRs for stages D and E. **Conclusions:** Most CVM stages can be used for the diagnosis of the stages of maturation of the midpalatal suture, so that CBCT imaging may not be necessary in these patients. In the postpubertal period, however, an assessment of the midpalatal suture maturation using CBCT images may be indicated in deciding between conventional rapid maxillary expansion and surgically assisted rapid maxillary expansion. On the other hand, if the CVM stage cannot be assessed, chronologic age may be a viable alternative to predict some midpalatal suture stages (particularly the early stages). (Am J Orthod Dentofacial Orthop 2015;148:1010-6)

Rapid maxillary expansion (RME) is an orthopedic procedure that produces separation of the midpalatal suture, thus widening the maxilla. RME has been used routinely in orthodontic practice for many reasons, including the correction of crossbites and dental crowding.[1-5]

Histologic studies[6-10] and investigations with microcomputed tomography[11] on autopsy material have demonstrated large variability in the chronologic age for fusion of the midpalatal suture. Persson and Thilander[7] observed fusion of the midpalatal suture in subjects from 15 to 19 years of age. On the other hand, patients at the ages of 27,[7] 32,[7] 54,[9] and even 71[11] years have been reported to have no signs of fusion of this suture. Such findings indicate that the variability in the developmental stages of fusion of the midpalatal suture is not related directly to chronologic age, particularly in young adults.[6-9,11]

The maturation of the facial sutures has been demonstrated by Björk[12] to be related to growth in height, and the start of fusion of the midpalatal suture has been associated with the rate of skeletal growth.[7] It is well known that skeletal growth has periods of acceleration and maturation that are not associated directly with chronologic age.[13,14] Therefore, several biologic indicators have been proposed for individual assessment of skeletal maturity, including the hand-

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wrist method[15] and the cervical vertebral maturation (CVM) method.[16]

The CVM method is performed on lateral cephalograms that are used routinely for orthodontic diagnosis and treatment planning, avoiding the need for an additional radiograph.[16] This method has demonstrated reliability and reproducibility for evaluating the pubertal peak and further maturation in skeletal growth.[17-21]

Cone-beam computed tomography (CBCT) provides 3-dimensional images of the oral and maxillofacial structures with no image overlap, allowing a reliable diagnosis of the maturation of the midpalatal suture before RME.[22] Angelieri et al[22] proposed 5 maturational stages of the midpalatal suture: stage A, straight high-density sutural line, with no or little interdigitation; stage B, scalloped appearance of the high-density sutural line; stage C, 2 parallel, scalloped, high-density lines that are close to each other and are separated in some areas by small low-density spaces; stage D, fusion completed in the palatine bone with no evidence of a suture; and stage E, complete anterior fusion in the maxilla.

However, CBCT is characterized by additional radiation and increased costs for patients compared with the lateral cephalograms and panoramic radiographs obtained routinely in orthodontic practices. Therefore, the aim of our study was to analyze the diagnostic performance of the CVM method in identifying correctly the stages of maturation of the midpalatal suture in growing and adult patients.

MATERIAL AND METHODS

Baseline diagnostic CBCT images acquired for clinical purposes in 142 subjects (84 female, 58 male) with a mean age of 14.8 ± 9.7 years (range, 5.3-58.4 years) were examined. The CBCT images were required by clinicians for diagnosis and treatment of these patients. These CBCT images were obtained from the archives of private practices of orthodontists and surgeons as well as from researches conducted at Methodist University of São Paulo, São Bernardo do Campo, Brazil, and the University of Michigan, Ann Arbor. This study was approved by the institutional review board of the University of Michigan.

The images of the midpalatal suture were analyzed using Invivo5 software (Anatomage, San Jose, Calif). The adjustment of the patient's head in the 3 planes of space and the selection of the slice for evaluation the midpalatal suture maturation were performed according to the protocol described previously by Angelieri et al.[22] The central cross-sectional axial slice in the superior-inferior dimension (from the nasal to the oral surfaces) of the palate was used for the staging of the midpalatal suture.

All axial central cross-sectional slices used for assessment of the midpalatal suture were arranged by the principal investigator (F.A.) in a PowerPoint (Microsoft, Redmond, Wash) presentation with a black background and codes that were displayed sequentially on a high-definition computer monitor. For subjects with a thick palate, 2 axial cross-sectional slices were used.[22] No adjustments in contrast or brightness of these images were made. In a darkened room, each image of the midpalatal suture was classified blindly by an expert examiner (F.A.) according to the visual analysis method described previously by Angelieri et al.[22]

Using the Invivo5 software, lateral cephalograms were derived from the same CBCT images. The cephalograms then were cropped so that only the images of the cervical vertebrae were visible; images of the dentition and adjacent skeletal structures were not visible. The cropped images were arranged in a similar PowerPoint presentation with a black background and identification codes. The vertebral images were analyzed according to the CVM method by 1 expert examiner (J.A.M.).[16]

Thirty images of the cervical vertebrae and 30 images of the midpalatal sutures from the same subjects were selected randomly from the total sample and reclassified by the same examiners a month later. A weighted kappa coefficient was calculated for evaluation of the intraexaminer agreement for the CVM method and classification of the midpalatal suture maturation.

Statistical analysis

The correlations between the midpalatal sutures and the CVM stages were evaluated by the Spearman correlation test.

The relationship between skeletal maturity assessed with the CVM method and the maturational stages of the midpalatal suture was evaluated with a measure of diagnostic performance—the positive likelihood ratio (LHR).[23] The positive predictive value of a test is the probability that the patient has the condition (in this case, a specific maturational stage of the midpalatal suture) when restricted to patients who test positive (specific stage of CVM). The LHR incorporates both the sensitivity and the specificity of the test and provides a direct estimate of how much a test result will change the odds of having a condition or "disease."

The LHR for a positive result indicates how much the probability of the condition to be diagnosed (specific maturational stage of the midpalatal suture) increases when a test is positive (specific CVM stage).[23] A result of 1 indicates no diagnostic performance (ie, no

Table I. Relative distributions of the midpalatal suture stages according to the skeletal maturation stages (N = 142)

	Midpalatal suture stages					*Correlation coefficient*
Skeletal maturation stages	*Stage A*	*Stage B*	*Stage C*	*Stage D*	*Stage E*	*0.908**
CS1 (n = 41; 22 F, 19 M; mean age, 8.5 ± 2.7 y)	15 (36.6%)	26 (63.4%)	–	–	–	
CS2 (n = 16; 7 F, 9 M; mean age, 10.4 ± 2.1 y)	1 (6.2%)	15 (93.8%)	–	–	–	
CS3 (n = 23; 10 F, 13 M; mean age, 12.4 ± 1.3 y)	–	4 (17.4%)	19 (82.6%)	–	–	
CS4 (n = 25; 18 F, 7 M; mean age,14.2 ± 1.7 y)	–	–	18 (72.0%)	3 (12.0%)	4 (16.0%)	
CS5 (n = 37; 27 F, 10 M; mean age, 25.6 ± 13.4 y)	–	–	5 (13.5 %)	13 (35.1%)	19 (51.4%)	

Correlations between midpalatal suture and skeletal maturation stages (CVM stages) are quantified through the Spearman rho correlation coefficient.
– Null value; **P* <0.01.
F, Female; *M*, male.

relationship), whereas a result smaller than 1 must be interpreted as a decrease in the likelihood of disease (negative relationship).[24] An LHR greater than 1 indicates that the test result is associated with the disease.

An LHR between 1 and 2 can be interpreted as a minimal increase (15%) in the likelihood of disease.[25] An LHR between 2 and 5 indicates a small increase (15%-30%) in the likelihood of disease. An LHR between 5 and 10 can be interpreted as a moderate increase (30%-45%) in the likelihood of disease.[25] LHRs above 10 indicate large and often conclusive increases in the likelihood of the disease (ie, strong association). A positive LHR of 10 or more for any CVM stage was considered a reliable indicator for the diagnosis of any of the maturational stages of the midpalatal suture.

The statistical analyses were performed with a statistical software package (version 12; SPSS, Chicago, Ill) and an interactive statistical calculator (http://statpages.org/ctab2x2.html). Statistical significance for all statistical tests was set at $P < 0.05$.

RESULTS

The weighted kappa coefficients for the evaluation of the intraexaminer agreement for the CVM method and the classification of the midpalatal suture maturation were 0.978 and 0.935, respectively. This result indicates very good intraexaminer reproducibility.

The prevalence rates of the different CVM stages according to the maturational stages of the midpalatal suture are reported in Table I, as are the demographics of the subjects at the different CVM stages. There were statistically significant positive correlations between the CVM stages and the maturational stages of the midpalatal suture (Spearman r = 0.908 at $P < 0.01$).

The positive LHRs of the cervical vertebral stages (CSs) for the identification of the maturational stages of the midpalatal suture are given in Table II. The presence of CS2, CS3, CS4, and CS5 produces a minimal to small decrease in the likelihood of stages A, B, E, and C, respectively. The values of positive LHRs of CS1 for the diagnosis of stages A and B in the midpalatal suture and of CS5 for the identification of stage D were between 2 and 5, indicating a small increase in the likelihood (15%-30%) of detecting the maturational stages of the midpalatal suture.[25] Both CS4 and CS5 showed a moderate increase (30%-35%) in the likelihood of detecting the maturational stages C and E, respectively.[25] Only CS2 and CS3 showed positive LHRs greater than 10 for the diagnosis of stages B and C, respectively (Table II).

Table II. Positive LHRs for the CVM stages for the diagnosis of midpalatal suture stages (N = 142)

Skeletal maturation stages	*Midpalatal suture stages*				
	Stage A	*Stage B*	*Stage C*	*Stage D*	*Stage E*
CS1	4.543	3.736	–	–	–
CS2	0.525	32.333	–	–	–
CS3	–	0.454	11.310	–	–
CS4	–	–	6.122	1.074	0.986
CS5	–	–	0.372	4.266	5.461

– Null value.
LHR, Likelihood ratio.

In a previous study, the midpalatal maturational stages A and B were indicated as the stages in which a conventional RME approach would have encountered less resistant forces and probably more skeletal effects than at stage C. With either stage D or E, surgically assisted RME should be considered because fusion of the midpalatal suture already has occurred partially or totally.

To give more clinical relevance to the results of this investigation, data from the CVM stages and the midpalatal suture stages were combined (Table III). Five

Table III. Diagnostic performance parameters of prepubertal stages CS1 and CS2 for the identification of midpalatal suture stages A and B, of pubertal stage CS3 for the identification of midpalatal suture stage C, and of postpubertal stage CS5 for the identification of midpalatal suture stages D and E

	Skeletal maturation stages		
Diagnostic tests	*CS1 and CS2 Variable diagnosed: stages A and B Value (95% CI)*	*CS3 Variable diagnosed: stage C Value (95% CI)*	*CS5 Variable diagnosed: stages D and E Value (95% CI)*
Sensitivity (%)	93.4 (87.9-93.4)	45.2 (34.4-51.5)	82.1 (70.5-89.2)
Specificity (%)	100.0 (95.8-100.0)	96.0 (91.4-98.6)	95.1 (90.8-97.9)
Positive predictive value (%)	100.0 (94.1-100.0)	82.6 (62.9-93.0)	86.5 (74.3-94.0)
Positive LHR	infinity (21.1-infinity)	11.3 (4.0-37.8)	16.9 (7.6-41.7)

LHR, Likelihood ratio.

diagnostic performance parameters were calculated for prepubertal stages CS1 and CS2 for the identification of midpalatal suture stages A and B, pubertal stage CS3 for the diagnosis of midpalatal suture stage C, and postpubertal stage CS5 for the assessment of midpalatal suture stages D and E. In all cases, the positive LHRs were greater than 10, thus indicating a large and often conclusive increase in the likelihood that the CVM stage of diagnosis corresponds to a specific stage in midpalatal suture maturation.

According to the 4 parameters of sensitivity, specificity, positive predictive value, and positive LHR, the prepubertal stages CS1 and CS2 showed the highest diagnostic performance for identification of stages A and B in midpalatal suture maturation, with specificity and positive predictive values of 100%. However, the 95% confidence intervals for the positive LHRs of these CVM stages for the identification of maturational stages in midpalatal suture were variable, with the widest range seen for CVM stages 1 and 2 (21.1-infinity).

DISCUSSION

RME often is unpredictable for adolescents and young adults because there is substantial variability in the rate and extent of fusion of the midpalatal suture according to chronologic age.[6-9,11] The identification of the midpalatal sutural stage with CBCT images is a reliable method for the prediction of RME without the often confusing overlay of the vomer and other external structures of the nose that occur when a 2-dimensional occlusal radiograph is used for diagnosis.[8,22] On the other hand, CBCT imaging requires higher costs and increased radiation exposure for patients.

The start of fusion of the midpalatal suture has been associated with the rate of skeletal growth as well as the transverse growth pattern of the maxilla.[7] Both have been related to velocity curves of body height with similar times of growth spurt and growth completion.[12,26] Skeletal maturation has been evaluated in orthodontics by hand-wrist[13] and CVM methods[15,16] for assessing the adolescent growth peak. The CVM method has been shown to be a biologic indicator for somatic skeletal maturity in growing subjects,[17-20] with good reproducibility when specific training is provided along with precise guidelines for assessing each stage visually.[21]

We investigated the diagnostic performance of the CVM stages for the identification of the stages of maturation of the midpalatal suture. Despite the overall large sample size (N = 142), subjects at CS6 could not be included because the sample was derived primarily from CBCT images of juveniles, adolescents, and young adults, the age groups most commonly seeking orthodontic treatment.

These results showed a high correlation coefficient between the CVM stages and the stages of maturation of the midpalatal suture, demonstrating that the maturation of the midpalatal suture is related to skeletal growth. However, the usefulness of a specific CVM stage for the assessment of the stages of maturation of the midpalatal suture is variable when analyzing the stages individually with measures of diagnostic accuracy such as positive LHRs.

As described earlier, positive LHR values smaller than 1 are interpreted as a decrease in the likelihood of the investigated condition (maturational stage of the midpalatal suture). Positive LHRs greater than 1 indicate that the test result (CVM stage) increases the likelihood of the given condition (maturational stage of the midpalatal suture). However, only with a positive LHR of 10 or more is the test considered to be a reliable diagnostic aid.[24]

When analyzing the values of positive LHRs of each CVM stage for the assessment of each stage of maturation of the midpalatal suture, the results indicated

that only CS2 and CS3 can be used for reliable identification of stages B and C, respectively (Table II). From a clinical perspective, these results are positive because a patient in whom RME is undertaken at CS2 should show a good response to RME, probably with more skeletal response than if the patient began this orthopedic treatment at CS3. On the other hand, patients at CS3 have large and often conclusive increases in stage C of midpalatal suture maturation, indicating that RME is possible, but probably with fewer skeletal effects, because of many initial ossification areas along the midpalatal suture, described by Melsen[27] as "bony islands." The timing of RME may be critical at stage C because the start of fusion of the palatine portion of the suture could be imminent. In these instances, the use of CBCT imaging may not be necessary before treatment.

For patients at CS4 and CS5 (as observed in a lateral cephalogram), however, an assessment of the midpalatal suture on CBCT is indicated before making the clinical decision between conventional RME (still possible at stage C) or surgically assisted RME (stages D and E). This more thorough evaluation of midpalatal suture morphology will provide additional information as to whether palatal expansion is possible orthopedically (stage C) or whether partial fusion (stage D) or complete fusion (stage E) of the midpalatal suture already has occurred. In the latter 2 stages of midpalatal suture maturation, surgically assisted expansion may be a better approach to optimize widening of the maxilla without substantial tooth movement, serious pain, mucosal ulceration or necrosis, and accentuated buccal tipping and gingival recession in the posterior teeth, which are expected when RME is unsuccessful.[28,29]

Based on the data in Table III, the prepubertal phases of skeletal maturity (CS1 and CS2) can be used as reliable indicators for stages A and B in midpalatal suture maturation. In a previous investigation, it was suggested that most favorable skeletal effects produced by RME can be obtained at stages A and B[22]; the midpalatal suture appears as a straight high-density line without interdigitation and bone bridges with less resistance to RME. Our results, therefore, corroborate the findings of Baccetti et al,[30] who verified more favorable skeletal changes when RME begins before the pubertal peak in skeletal growth. Patients approaching the pubertal growth spurt (CS3) presumably have more resistance to RME (with respect to those at earlier CVM stages) because the positive LHR greater than 10 indicates the reliable presence of stage C that is characterized by many bony bridges along the midpalatal suture (Table III). Once again, this result agrees with that of Baccetti et al, who found that fewer skeletal and more dentoalveolar effects must be expected when RME is performed at puberty.

Table IV. Chronologic age for subjects at the different midpalatal suture stages

	Chronologic age (y)			
Midpalatal suture stages	*Mean*	*SD*	*Minimum*	*Maximum*
Females				
Stage A (n = 6)	6.2	0.5	5.5	6.7
Stage B (n = 24)	9.0	2.1	5.6	13.6
Stage C (n = 25)	14.8	9.2	9.8	58.4
Stage D (n = 11)	21.7	10.0	13.6	47.4
Stage E (n = 17)	20.1	11.2	12.8	55.2
Males				
Stage A (n = 10)	6.5	1.6	5.3	10.3
Stage B (n = 21)	11.6	1.7	7.9	14.9
Stage C (n = 17)	14.4	3.5	10.6	26.3
Stage D (n = 5)	24.9	9.6	14.6	37.7
Stage E (n = 5)	32.7	11.1	18.5	44.8

In patients at CS5, surgically assisted RME should be considered because fusion of the midpalatal suture already has occurred partially or totally (stages D and E in midpalatal suture maturation). However, 13.5% of the postpubertal subjects at CS5 had stage C in midpalatal suture maturation. This finding can explain the occasional clinical success of RME treatment in adults. Studies of palatal specimens from human autopsy material have shown substantial interindividual variations with regard to the start of closure as well as the advance of closure with age.[7-9]

It has been proposed that functional forces originating in the masticatory apparatus could play a role in the biology of sutural closure.[7] For postpubertal patients needing RME, the assessment of the midpalatal suture maturation provided by CBCT could avoid an unnecessary surgery for patients at stage C, in whom the midpalatal suture still is open, thus decreasing the morbidity and treatment costs.

An additional interesting aspect is represented by the possibility of predicting the midpalatal suture stages by using chronologic age. Because boys and girls do not mature at the same age, they were analyzed separately. Means and standard deviations for age at each midpalatal suture stage were calculated separately for the sexes (Table IV). These values defined a Gaussian distribution of age for each midpalatal suture stage. Predicted values for each patient were based on the probability that a patient belongs to 1 of the 5 Gaussian distributions. Gaussian values for female subjects were computed after removing 1 outlier with an age of 58 years and midpalatal suture stage C. The total correct predictions for both sexes with chronologic age were 90 (Table V). Using logistic multinomial regression, we can also calculate the

Table V. Predicted values for each patient were based on the probability that a patient belongs to each of the 5 Gaussian distributions of age for each midpalatal suture stage

	Actual MSMS value for male subjects (n = 58)					
	1	*2*	*3*	*4*	*5*	*Total*
Predicted by age (Gaussian)						
1	9	3				12
2	1	17	8			26
3		1	8	2	1	12
4			1	2	1	4
5				1	3	4
Total	10	21	17	5	5	58
	Actual MSMS value for female subjects (n = 84)					
	1	*2*	*3*	*4*	*5*	*Total*
Predicted by age (Gaussian)						
1	6	4				10
2		16	4			20
3		4	20	4	10	38
4				6	5	11
5			1	1	3	5
Total	6	24	25	11	18	84

Total correct (diagonal entries): 90.
MSMS, Midpalatal suture maturational stage.

Table VI. Predicted values for each patient were based on the probability that a patient belongs to each of the 5 Gaussian distributions of age for each midpalatal suture stage, predicted by the CVM method

	Actual MSMS value					
	1	*2*	*3*	*4*	*5*	*Total*
1	0	0	0	0	0	0
2	16	41	0	0	0	57
3	0	4	37	3	4	48
4	0	0	0	0	0	0
5	0	0	5	13	19	37
Total	16	45	42	16	23	142

Total correct (diagonal entries): 97.
MSMS, Midpalatal suture maturational stage.

number of correct predictions of the midpalatal suture stages with the CVM method as the predictor variable. The total correct predictions with the CVM method were 97 (Table VI). When using regression analysis, it appears that the CVM method and chronologic age were almost equally effective in predicting the midpalatal sutural stages, with the CVM method performing slightly better than chronologic age. When the CVM stage cannot be assessed for any reason, chronologic age may be a viable alternative to predict the maturation of the midpalatal suture.

CONCLUSIONS

The diagnostic performance of the CVM method for the assessment of midpalatal suture maturation showed the following.

1. Prepubertal CVM stages (CS1 and CS2) can be used as reliable indicators for the midpalatal maturational stages A and B.
2. CS3 in CVM indicates reliably stage C in maturation of the midpalatal suture.
3. CS5 in CVM indicates that fusion of the midpalatal suture already has occurred partially or totally (stages D and E in midpalatal suture maturation). However, for postpubertal patients (CS4 and CS5), an individual assessment of the midpalatal suture with CBCT should be undertaken, since 13.5% of patients at CS5 presumably could be treated with conventional RME.
4. When the CVM stage cannot be assessed, chronologic age may be a viable alternative to predict some midpalatal suture stages (particularly the early stages).

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REFERENCES

1. Bishara SE, Staley RN. Maxillary expansion: clinical implications. Am J Orthod Dentofacial Orthop 1987;91:3-14.
2. McNamara JA Jr. Maxillary transverse deficiency. Am J Orthod Dentofacial Orthop 2000;117:567-70.
3. McNamara JA Jr. Long-term adaptation to changes in the transverse dimension in children and adolescents: an overview. Am J Orthod Dentofacial Orthop 2006;129(Suppl):S71-4.
4. Chang JY, McNamara JA Jr, Herberger TA. A longitudinal study of skeletal side-effects induced by rapid maxillary expansion. Am J Orthod Dentofacial Orthop 1997;112:330-7.
5. McNamara JA Jr, Baccetti T, Franchi L, Herberger T. Rapid maxillary expansion followed by fixed appliances: a long-term evaluation of changes in arch dimensions. Angle Orthod 2003;73:344-53.
6. Persson M, Magnusson BC, Thilander B. Sutural closure in rabbit and man: a morphological and histochemical study. J Anat 1978;125:313-21.
7. Persson M, Thilander B. Palatal suture closure in man from 15 to 35 years of age. Am J Orthod 1977;72:42-52.
8. Wehrbein H, Yildizhan F. The mid-palatal suture in young adults. A radiological-histological investigation. Eur J Orthod 2001;23:105-14.
9. Knaup B, Yildizhan F, Wehrbein H. Age-related changes in the midpalatal suture. J Orofac Orthop 2004;65:467-74.
10. Melsen B. Palatal growth studied on human autopsy material. Am J Orthod 1975;68:42-54.
11. Korbmacher H, Schilling A, Püschel K, Amling M, Kahl-Nieke B. Age-dependent three-dimensional micro-computed tomography analysis of the human midpalatal suture. J Orofac Orthop 2007;68:364-76.
12. Björk A. Sutural growth of the upper face studied by the implant method. Acta Odontol Scand 1966;24:109-27.
13. Karlberg J. Secular trends in pubertal development. Horm Res 2002;57(Suppl 2):19-30.
14. Delemarre-van de Waal HA. Secular trend of timing of puberty. Endocr Dev 2005;8:1-14.
15. Fishman LS. Radiographic evaluation of skeletal maturation. A clinically oriented study based on hand-wrist films. Angle Orthod 1982;52:88-112.
16. Baccetti T, Franchi L, McNamara JA Jr. The cervical vertebral maturation (CVM) method for the assessment of optimal treatment timing in dentofacial orthopedics. Semin Orthod 2005;11:119-29.
17. Franchi L, Baccetti T, McNamara JA Jr. Mandibular growth as related to cervical vertebral maturation and body height. Am J Orthod Dentofacial Orthop 2000;118:335-40.
18. Soegiharto BM, Moles DR, Cunningham SJ. Discriminatory ability of the skeletal maturation index and the cervical vertebrae maturation index in detecting peak pubertal growth in Indonesian and white subjects with receiver operating characteristics analysis. Am J Orthod Dentofacial Orthop 2008;134:227-37.
19. Masoud M, Masoud I, Kent RL Jr, Gowharji N, Cohen LE. Assessing skeletal maturity by using blood spot insulin-like growth factor 1 (IGF-I) testing. Am J Orthod Dentofacial Orthop 2008;134:209-16.
20. Perinetti G, Franchi L, Castaldo A, Contardo L. Gingival crevicular fluid protein content and alkaline phosphatase activity in relation to pubertal growth phase. Angle Orthod 2012;82:1047-52.
21. Perinetti G, Caprioglio A, Contardo L. Visual assessment of the cervical vertebral maturation stages: a study of diagnostic accuracy and repeatability. Angle Orthod 2014;84:951-8.
22. Angelieri F, Cevidanes LH, Franchi L, Gonçalves JR, Benavides E, McNamara JA Jr. Midpalatal suture maturation: classification method for individual assessment before rapid maxillary expansion. Am J Orthod Dentofacial Orthop 2013;144:759-69.
23. Attia J. Moving beyond sensitivity and specificity: using likelihood ratios to help interpret diagnostic tests. Aust Prescr 2003;26:111-3.
24. Deeks JJ, Altman DG. Diagnostic tests 4: likelihood ratios. BMJ 2004;329:168-9.
25. McGee S. Simplifying likelihood ratios. J Gen Intern Med 2002;17:647-50.
26. Björk A, Skieller V. Growth of the maxilla in 3 dimensions as revealed radiographically by the implant method. Br J Orthod 1997;4:53-64.
27. Melsen B. A histological study of the influence of sutural morphology and skeletal maturation on rapid palatal expansion in children. Trans Eur Orthod Soc 1972;48:499-507.
28. Garib DG, Henriques JF, Janson G, Freitas MR, Coelho RA. Rapid maxillary expansion—tooth-tissue-borne versus tooth-borne expanders: a computed tomography evaluation of dentoskeletal effects. Angle Orthod 2005;75:548-57.
29. Rungcharassaeng K, Caruso JM, Kan JY, Kim J, Taylor G. Factors affecting buccal bone changes of maxillary posterior teeth after rapid maxillary expansion. Am J Orthod Dentofacial Orthop 2007;132:428.e1-8.
30. Baccetti T, Franchi L, Cameron CG, McNamara JA Jr. Treatment timing for rapid maxillary expansion. Angle Orthod 2001;71:343-50.