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Validity of the Maturation Stage Method in the Individual Assessment of Midpalatal Suture Ossification Before Maxillary Expansion: A Systematic Review

Validez del Método de la Etapa de Maduración en la Evaluación Individual de la Osificación de la Sutura Palatina Mediana Previo a la Expansión Maxilar: Una Revisión Sistemática

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ABSTRACT: In 2013, midpalatal suture maturation stage assessment was proposed for the evaluation of patients before performing maxillary expansion. In this study, we aimed to analyze the association between the midpalatal suture maturation stages assessed by CBCT, according to the method described by Angelieri *et al*., and other objective methods used to assess skeletal maturation or bone fusion. A computerized database search was conducted using PubMed, Cochrane Library, SciELO, LILACS, Web of Science, and Scopus, without language restriction. Unpublished literature was searched on ClinicalTrials.gov, the National Research Register, and Pro-Quest Dissertation Abstracts and Thesis database. Authors were contacted when necessary, and reference lists of the included studies were screened. Search terms included midpalatal suture, maturation, correlation, diagnostic performance, classification, evaluation, assessment, and relationship. Quality assessment was performed using the Observational Cohort and Cross-Sectional Studies tool developed by the National Heart, Lung, and Blood Institute. Eleven studies met the inclusion criteria. Of all the studies included, 81.9% had fair quality and 18.1% good quality, respectively. Eight out of eleven studies assessed the correlation between the midpalatal suture maturation method and the skeletal maturity evaluated by CVM method (Spearman's correlation coefficient: 0.244-0.908). Two out of eleven studies evaluated the correlation between midpalatal suture maturation method and the skeletal maturity assessed by HWM method (Spearman's correlation coefficient: 0.904-0.905) Even though midpalatal suture maturation stage assessment needs an exhaustive training and calibration process, it is a valid method to evaluate skeletal maturation or bone fusion. From a clinical perspective, for patients at CS4, CS5 and CS6, an assessment of the midpalatal suture on CBCT is indicated. A similar assessment should be done in patients at SMI 7-9.

KEY WORDS: midpalatal suture maturation method, cranial sutures, maxillary expansion, skeletal maturation, cervical vertebrae; hand-wrist.

INTRODUCTION

Maxillary transverse deficiency may be one of the most common skeletal problems among orthodontic patients (McNamara, 2000).

Transverse maxillary deficiency can be associated with several changes such as posterior crossbite; dental crowding; occlusal disharmony;

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changes in tongue posture and mouth breathing, producing significant effects on muscle function and aesthetics (Haas, 1961).

The most effective orthopedic treatment that aims to increase the maxillary transverse width is rapid maxillary expansion (RME) (Haas, 1965).

Rapid maxillary expansion (RME) is an orthopedic procedure that produces separation of the midpalatal suture, thus widening the maxilla. The heavy forces generated by the expander transmit through the teeth into the maxillary bones and are intended to open the midpalatal suture by separating the hemi maxilla; this leads to subsequent bone deposition. RME has been used routinely in orthodontic practice for many reasons, including the correction of crossbites and dental crowding (Bishara, 1987; Chang *et al*., 1997; McNamara *et al*., 2003; McNamara, 2006). The goals of RME are typically to maximize skeletal expansion and to minimize dentoalveolar expansion (Grünheid *et al*., 2017).

Closure of the craniofacial sutures, especially the midpalatal suture, eventually makes skeletal expansion by conventional RME impossible (Liu *et al*., 2015), which makes it essential to consider other alternatives, such as: miniscrew assisted rapid palatal expansion (MARPE) (Shin *et al*., 2019) or surgically assisted rapid palatal expansion (SARPE) (Chrcanovic *et al*., 2009).

In adults, SARPE has advantages such as improved nasal breathing, aesthetic enhancement due to reduction of the buccal corridor, and reducing the potential need for extraction treatment (Koudstaal *et al*., 2009).

The time point to shift from RME to SARPE is not clear enough, especially in young adults (Angelieri *et al*., 2013 ; Acar *et al*., 2015; Grünheid *et al*., 2017). Most studies suggest that RME should be presented before puberty (Baccetti *et al*., 2002; Thadani *et al*., 2010). In contrast, other case reports have shown a successful expansion by RME without surgical weakness in adult patients (Capelozza *et al*., 1996; Handelman, 1997; Handelman *et al*., 2000).

Determining the level of bone fusion is important in relation to the staging of craniofacial bone maturation and the evaluation of bone growth potential during pre-adolescent or adolescence (Angelieri *et al*., 2015; Jang *et al*., 2016; Lee & Mah, 2019a).

Bone fusion of the MPS has been evaluated using analysis methods such as occlusal radiographs (Ennes & Consolaro, 2004), histological studies (Persson & Thilander, 1977; Knaup *et al*., 2004) and visual methods in dry skulls (Mann *et al*., 1991) where a great variability was found between the bone fusion stage and the chronological age of the individual (Korbmacher *et al*., 2007; Estrada *et al*., 2022).

To help with the clinical decision whether correction of a transverse discrepancy should be attempted with conventional RME or whether surgically assisted expansion is necessary, indicators of midpalatal suture maturation have been proposed (Grünheid *et al*., 2017).

These indicators include sutural morphology as assessed on occlusal radiographs (Wehrbein & Yildizhan, 2001), skeletal maturity indicators on hand-wrist radiographs (Fishman *et al*., 1982; Revelo & Fishman, 1994), and cervical vertebral maturation (CVM) indicators on lateral cephalograms (Baccetti *et al*., 2001).

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 (Jang *et al*., 2016). Angelieri *et al*. (2013) 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.

This systematic review aimed to analyze the association between the midpalatal suture maturation stages assessed by CBCT, according to the method described by Angelieri *et al*. (2013) and other objective methods used to assess skeletal maturation or bone fusion.

A secondary and subsidiary aim was to assess the association between MPS maturation stages and chronological age.

MATERIAL AND METHOD

Protocol and Registration. The systematic review was conducted and written in accordance with the

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Liberati *et al*., 2009; Moher *et al*., 2009). The protocol for this systematic review was registered on the International Prospective Register of Systematic Reviews (www.crd.york.ac.uk/ PROSPERO,CRD42022356017).

Eligibility criteria. The following inclusion and exclusion criteria were applied:

P: human subjects of any gender without restriction of ethnicity or age
I: midpalatal suture maturation method proposed by Angelieri *et al*. (2013)
C: Other validated or quantitative methods used to assess midpalatal suture maturation
O: assessment of maturation/interdigitation/ossification of MPS before maxillary expansion treatment
Study design (S): observational studies (cohort studies either prospective or retrospective and cross-sectional studies).

Exclusion criteria were as follows: articles including subjects who had undergone any type of (1) orthodontic or (2) orthopedic treatment, (3) nonhuman studies, (4) syndromic conditions, (5) case reports, (6) cleft lip, and (7) palate, and (8) review articles.

Information sources and search strategy. To identify relevant articles, the electronic databases of PubMed, Cochrane, Web of Science, Scopus, SciELO and LILACS were comprehensively searched up to December 3, 2022. Gray literature was checked by using Google Scholar and Open Gray database. A broad search strategy was formulated by the main reviewer (A.S) with the assistance of a specialized librarian from the Biomedical Sciences Library of Universidad de La Frontera, Chile, and after discussion with one of the reviewers (P.S.V.).

Finally, manual searches in the reference list of included articles were also carried out. There was no restriction of year or status of publication for inclusion.

Detailed search strategies were developed for each database based on the strategy developed for MEDLINE, and subsequently adapted for the other databases.

Study selection. Study selection was performed in three phases. First, the main researcher (A.S) excluded the duplicate articles using the Reference Manager EndNote X9 (Clarivate Analytics, Philadelphia, Pa). Secondly, two reviewers (A.S and P.S.V) blindly assessed the titles and abstracts of identified records. Then, the same reviewers separately applied eligibility criteria to the full-text studies using the systematic review web application Rayyan (rayyan.qcri.org) (Ouzzani *et al*., 2016). Information was cross-checked in a consensus meeting in which disagreements were solved between them. If there was no consensus, a third reviewer was consulted to make a final decision (M.M.G).

Data charting process and Data items. The data was extracted independently by two reviewers (A.S and P.S.V) using a data extraction sheet designed in Microsoft Excel (Redmond, Wash), and any differences were resolved by discussion and consensus with a third reviewer (I.G.C). The following data were extracted from each included study: first author, publication year, study design, sample size, sex distribution, objectives, inclusion criteria, equipment used, number of examiners, calibration, training, blinding process, inter and intra-evaluator agreement, Pearson's correlation coefficient, likelihood ratio, statistical analysis used, and the author's conclusion.

Quality assessment of included studies Synthesis of results. As suggested by Ma *et al*. (2020), the Observational Cohort and Cross-Sectional Studies tool developed by the National Heart, Lung, and Blood Institute & National Institutes of Health (2017) was used to assess the quality of the articles that met the inclusion criteria.

Two reviewers independently assessed the articles and subsequently discussed each study's quality (A.S and P.S.V). In case of discrepancy, a third author was consulted for further evaluation (I.G.C).

RESULTS

A total of 1.380 studies were identified by electronic searches, and 611 studies remained after removing duplicates. After initial screening, a total of nine studies met the predetermined inclusion criteria. After the full text review, four studies were included for this review. In addition, seven eligible studies were identified via hand searches. As a result, eleven studies were included in this systematic review (Fig. 1). Summary of characteristics of each included study are presented in Table I.

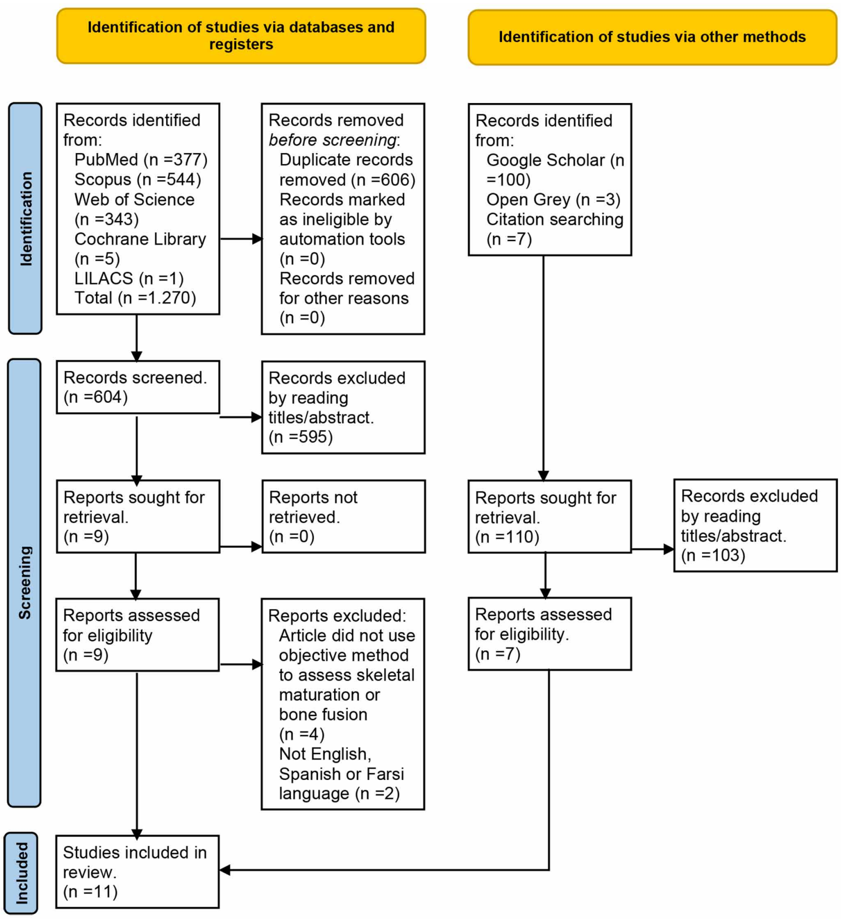

Fig 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only (Page *et al*., 2021).

A summary of the blinding and calibration processes performed in each one of the included articles is presented in Table II.

I. Results of individual sources of evidence and synthesis of results.

a) Angelieri *et al*. 2015. Angelieri *et al*. (2015) analyzed the diagnostic performance of the CVM method in correctly identifying the stages of maturation of the midpalatal suture in 142 subjects (58 male and 84 female) of 5.3 to 58.4 years old.

The degree of correlation between the maturational stages of the midpalatal suture and CVM was r = 0.908 (Table III).

CS2 and CS3 stages showed positive LHRs greater than 10 for diagnosis of stages B (32.333) and C (11.310), respectively.

When trying to predict midpalatal suture maturation stages by using chronological age, the total number of correct predictions for both sexes was 90. When trying to predict midpalatal suture maturation stages by using CVM method the total correct predictions were 97. That is why the authors mention that when using regression analysis, it appears that the CVM method and chronological age were almost equally effective in predicting MPS stages. When the CVM stage cannot be assessed, chronologic age may be a viable alternative to predict some midpalatal suture stages (particularly the early stages).

b) Jang *et al*. 2016. Jang *et al*. (2016) classified the maturation degree based on the morphology of the midpalatal suture by using CBCT images and investigated the relationship with conventional developmental age indices in 99 patients (40 male and 59 female) of 6 to 20 years old. Between the indices of maturation used we can mention skeletal maturation indicator (SMI), CVM method and dental age by Hellman's index. The HWM and MPS stage showed an especially strong correlation (r= 0.904), CVM and MPS stage showed a strong correlation (r= 0.874) and the correlation between MPS - Hellman's index was relatively weak (r= 0.777). The correlation between the midpalatal suture maturation and chronological age was r = 0.774 (Table III).

c) Kwak *et al*. 2016. Kwak *et al*. (2016) evaluated the correlation between fractal dimension and maturation of the midpalatal suture with CBCT data in 131 subjects (69 male and 62 female) of 18.1 to 53.4 years old. At the optimal fractal dimension cut-off value of 1.0235, a test in which fractal dimension was used to predict the variable that splits maturation stages into A-C and D or E, resulted in the following values: Sensitivity 64.9 %, specificity 86.6 %, false positive rate 35.1 %, false negative rate 13.4 %, positive predictability 80.3 %, and negative predictability 74.6 %. Also, a strong negative correlation between maturation stage and fractal dimension was found (r= -0.623) (Table III).

Table I. Summary of characteristics of included studies.

Authors (y)	Country	Sample Size	Age	Study design	Equipment used	Specifications
Angelieri *et al.* (2015)	Brazil - USA	142 (58M-84F)	5.3-58.4 y	CS	Not mentioned	Not mentioned
Jang *et al.* (2016)	Korea	99 (40M-59F)	6-20 y	CS	PaX-Zenith3D	105 kV, 6.2 mA, 15-24 s, 0.2 to 0.3 mm voxel sizes, FoV 16 cm x 14 cm
Kwak *et al.* (2016)	Korea	131 (69M-62F)	18.1-53.4 y	CS	Not mentioned	FoV 20 x19 cm; 90 kV; 4.0 mA; 24 s
Gorucu Coskuner *et al.* (2018)	Turkey	50 (21M-29F)	15-30 y	CS	i-CAT Cone Beam 3D Imaging System	FoV23 x 17 cm, voxel 0.30 mm,120-kV, 2 mA, 17.8s
Kim *et al.* (2018)	Korea	40 (20M-20F)	8.2-23.6 y	CS	i-CAT Cone Beam 3D Imaging System	Not mentioned
Lee & Mah (2019a)	Korea	480 (240M-240F)	7-15 y	CS	Not mentioned	9 mA; tube voltage, 80 kV; scanning time, 24 s; and field of view, 20 x 15 cm.
Chutasripanich & Mahatumarat (2020)	Thailand	103 (44M-59F)	8-18 y	CS	3D Accuitomo 170 machine	80-90 kVp, 1-10 mA and 17.5 s
Mahdian *et al.* (2020)	Iran	93 (42M-51F)	9-30 y	CS	Planmeca ProMax 3D	Kv: 82, 12 mA, exposure time of 12 to 30 seconds, field of view of 8*8 cm
Yu & Kim (2021)	Korea	267 (132M-135F)	7-15 y	CS	Not mentioned	9 mA; tube voltage, 80 kV; scanning time, 24 s; and field of view, 20 x 15 cm
Luz *et al.* (2022)	Brazil	42 (17M-25F)	11-14 y	CS	i-CAT Cone Beam 3D Imaging System	120 kV, 18 mA, exposure time of 8.9 seconds, voxel size of 0.2 mm, and field of view (FOV) of 160 x 60 mm
Estrada *et al.* (2022)	Peru	351 (175M-176F)	10-20 y	CS	Point 3D Combi 500	90 kV, 5 mA, and 19 s, FoV 24.4 cm x19.5 cm, voxel size of 127 mm^2

F, female; M, male; Y, years; FoV, Field of View

d) Gorocu-Coskuner *et al*. 2018. Gorocu-Coskuner *et al*. (2018) assessed the stage of maturation of the MPS by using CBCT and determined the association between the stage of MPS maturation with CVM and chronological age in 50 patients (21 male and 29 female) of 15 to 30 years old. No significant correlation was observed between the CVM and MPS maturation stages (r = 0.030). The correlation between the midpalatal suture maturation and chronological age was r = 0.212 (Table III).

e) Kim *et al*. 2018. Kim *et al*. (2018) evaluated ossification and maturation of the midpalatal suture via evaluation of the morphological stages and measured Hounsfield units (HU) using cone beam computed tomography (CBCT) in 40 patients (20 male and 20 female) of 8.2 to 23.6 years old. A strong correlation was observed between morphological stages and HU ratio (r= 0.909). The correlation between the midpalatal suture maturation and chronological age was r = 0.816 (Table III).

f) Lee & Mah 2019a. Lee & Mah (2019a) analyzed the association of MPS maturation stages with CVMI and chronological age by evaluating the MPS morphology using CBCT images in 480 children (240 male and 240 female) of 7 to 15 years old. The correlation coefficient between MPS maturation stage and CVMI was r= 0.602, indicating a strongly positive correlation. CVMI 1-3 showed high positive LHR value (44.79) for the diagnosis of stages A-C. MPS maturation stage and chronological age showed positively significant correlation in boys and girls (0.499 and 0.560, respectively) (Table III).

g) Chutasripanich & Mahatumarat 2020. Chutasripanich & Mahatumarat (2020) evaluated the relationship between the maturation stage of midpalatal suture, CVM, and dental age (Demirjian method) in 103 patients (44 male and 59 female). No significant correlation was observed between the midpalatal suture maturation stage and CVM (r= 0.244) and a weak correlation between the midpalatal suture maturation stage and dental age (r = 0.279) (Table III). The correlation between the midpalatal suture maturation and chronological age was not measured.

Table II. Blinding and Calibration process of included studies.

Authors (y)	Methods used	Nº examiners	Intraexaminer agreement	Interexaminer agreement	Washout period	Randomization of images (second examination)	Blinding
Angelieri *et al.* 2015	MPS suture maturation CVM method	2 (1 for each method)	*k* MPS: 0.935 *k* CVM: 0.978	Not applicable	30 days	30 images for each method	Yes
Jang *et al.* 2016	MPS suture maturation CVM method HWM method Hellman's index	1	ICC MPS: 0.995 ($p < 0.05$) ICC CVM: 0.991 ($p < 0.05$) ICC HWM: 0.996 ($p <0.05$) ICC H. index: 0.992 ($p < 0.05$)	Not applicable	60 days	30 images for each method	Yes
Kwak *et al.* 2016	MPS suture maturation CVM method Fractal dimension	3	*k* MPS: not mentioned *k* CVM: 0.71 *k* Fractal: 0.84	*k* MPS: not mentioned *k* CVM: 0.53-0.86 *k* Fractal: 0.67-0.72	2 days	30 images	Not mentioned
Gorucu Coskuner *et al.* 2018	MPS suture maturation CVM method	2 (worked together)	*k* MPS: 0.837 *k* CVM: 0.865	Not applicable	15 days	All images	Yes
Kim *et al.* 2018	MPS suture maturation Gray density ratio (HU)	1	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Lee & Mah (2019b)	MPS suture maturation CVM method	2	*k* MPS: 0.974 *k* CVM: 0.976	*k* MPS: 0.952 *k* CVM: 0.969	14 days	30 images	Not mentioned
Chutasripanich & Mahatumarat 2020	MPS suture maturation CVM method Demirjian method	1	Not mentioned	Not applicable	Not mentioned	Not mentioned	Not mentioned
Mahdian *et al.* 2020	MPS suture maturation CVM method	2	*k* MPS: 0.89 *k* CVM: 0.93	*k* MPS: 0.90 *k* CVM: 0.88	Not mentioned	Not mentioned	Not mentioned
Yu & Kim 2021	MPS suture maturation HWM method MP3 stages	1	ICC MPS: 0.806 ICC MP3:0.836 ICC HWM: 0.993	Not applicable	14 days	All images	Not mentioned
Luz *et al.* 2022	MPS suture maturation CVM method	2	*k* MPS: 0.9115 *k* CVM: 0.9461	*k* MPS: 0.9067 *k* CVM: 0.9325	30 days	All images	Yes
Estrada *et al.* 2022	MPS suture maturation CVM method	2	*k MPS:* 0.86 *k* CVM: 0.85	*k MPS:* 0.82 *k* CVM: 0.83	30 days	35 images	Yes

h) Mahdian *et al*. 2020. Mahdian *et al*. (2020) determined the correlation of CVM stage and MPS maturation stage in 93 patients (42 male and 51 female). Spearman correlation coefficient between the CVM stage and the MPS maturational stage was positive but moderate (r= 0.691 in female patients and r=0.754 in male patients). Stages D and E, which show suture fusion, were not observed before CVM stage 4 (CS4).

The Spearman correlation coefficient between age and MPS maturational stage was positive but relatively weak (r =0.543 in female and r =0.594 in male patients) (Table III).

i) Yu & Kim 2021. Yu & Kim (2021) evaluated the correlation between the maturation of the midpalatal suture and the skeletal maturity assessed by SMI and MP3 stages in 267 subjects of 7 to 15 years old (132 male and 135 female). They also analyzed the diagnostic reliability of SMI and MP3 stages in predicting the maturational stages of the midpalatal suture. The degree of correlation between the maturational stages of the midpalatal suture and the SMI was r = 0.905 (Table III).

The values of positive LHRs of SMI 1 - 2, SMI 3, SMI 4 - 6, and SMI 10 - 11 were greater than 5 for the identification of stage A (7.264), B (6.271), C (7.875),

Table III. Spearman correlation between MPS maturation and other objective methods.

Authors (y)	CBCT - CVM	CBCT- HWM (SMI)	CBCT- HWM (MP3)	CBCT- Demirjian method	CBCT- Hellman's index	CBCT- Fractal analysis	CBCT - Hounsfield units	CBCT- Chronologic age
Angelieri *et al.* (2015)	r= 0.908, p<0.01	-	-	-	-	-	-	-
Jang *et al.* (2016)	r=0.874, p<0.01	r=0.904, p<0.01	-	-	r=0.777, p<0.01	-	-	-
Kwak *et al.* (2016)	-	-	-	-	-	r=-0.623, p<0.01	-	-
Gorucu Coskuner *et al.* (2018)	r=0.030, p=0.839	-	-	-	-	-	-	r=0.212, p=0.139
Kim *et al.* (2018)	-	-	-	-	-	-	r=0.909, p<0.01	r=0.816, p<0.01
Lee & Mah (2019b)	r=0.602, p<0.001	-	-	-	-	-	-	r=0.499, p<0.001 (M) r=0.560, p<0.001 (F)
Chutasripanich & Mahatumarat (2020)	r=0,244, p=0,098	-	-	r=0.279, p=0.007	-	-	-	-
Mahdian *et al.* (2020)	r=0.754, p<0.001 r=0.691, p<0.001	-	-	-	-	-	-	r=0.594, p<0.001 (M) r=0.543, p<0.001 (F)
Yu & Kim (2021)	-	r=0.905, p<0.05	r=0.830, p<0.05	-	-	-	-	r=0.864, p<0.05 (M) r=0.892, p<0.05 (F)
Luz *et al.* (2022)	r=0.6916, p<0.0001	-	-	-	-	-	-	r=0.0665, p= 0.7997 (M) r=0.0352, p=0.8674 (F)
Estrada *et al.* (2022)	r=0.395, p<0.001	-	-	-	-	-		-

and D/E (5.454 and 6.917) in the midpalatal suture, respectively.

On the other hand, the correlation between the maturational stages of the midpalatal suture and the MP3 was r = 0.830. The values of positive LHRs of MP3 FG for the identification of stage C (5.885) and of MP3 I for the identification of stages D (5.464) and E (6.917) in the midpalatal suture were greater than 5. The correlation between the midpalatal suture maturation and chronological age was r = 0.868.

j) Luz *et al*. 2022. Luz *et al*. (2022) evaluated whether the CVM method can be predictive of the stage of maturation of the midpalatal suture in 42 individuals (17 male and 25 female) of 11 to 14 years old. The degree of correlation between the maturational stages of the midpalatal suture and the CVM was r = 0.6916 (Table III).

They found positive LHRs between CS1 and stages A and B (1.5), and a strong relationship between CS2 and stage B (6.0). Stage C had a strong relationship with suture CS3 (3.833), and stages CS5 and CS6 strongly correlated with stage E (2.857). The correlation between the midpalatal suture maturation and chronological age was r = 0.0135.

k) Estrada *et al*. 2022. Estrada *et al*. (2022) determined the correlation between CVM and the stages of MPS ossification in 351 patients (175 male and 176 female) of 10 to 20 years old.

The degree of correlation between the maturational stages of the midpalatal suture and the CVM was r = 0.395 (Table III).

Although they found positive LHRs, none of them was higher than 5 (CS1- Stage A= 4.91 and CS2-Stage B= 4.75 were the highest). The correlation between the midpalatal suture maturation and chronological age was not measured.

Quality assessment of included studies. The obtained grade of quality assessment for each study is included in Table IV. Grades for the selected studies ranged from 50.0 % to 83.3 %. Two studies (Angelieri *et al*., 2015; Lee & Mah, 2019a,b) had poor quality, seven studies (Kwak *et al*., 2016; Gorocu-Coskuner *et al*., 2018; Kim *et al*., 2018; Chutasripanich & Mahatumarat, 2020; Mahdian *et al*., 2020; Yu & Kim, 2021; Luz *et al*., 2022) had fair quality and two studies (Jang *et al*., 2016; Estrada *et al*., 2022) had good quality.

Table IV. Quality assessment of the included studies using the Observational Cohort and Cross-Sectional Studies (NHBLI) tool.

Included studies	Quality assessment criteria														Quality score (%)
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Angelieri *et al.* 2015	Yes	No	NR	No	No	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	6/12 (50 %)
Jang *et al.* 2016	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	10/12 (83.3 %)
Kwak *et al.* 2016	Yes	Yes	NR	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	7/12 (58,3 %)
Gorucu Coskuner *et al.* 2018	Yes	No	NR	Yes	No	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	7/12 (58,3 %)
Kim *et al.* 2018	Yes	Yes	NR	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	7/12 (58,3 %)
Lee & Mah 2019a	Yes	No	NR	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	6/12 (50 %)
Chutasripanich & Mahatumarat 2020	Yes	Yes	NR	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	7/12 (58,3 %)
Mahdian *et al.* 2020	Yes	Yes	NR	Yes	Yes	No	No	Yes	Yes	NA	Yes	No	NA	Yes	8/12 (66,6 %)
Yu & Kim 2021	Yes	Yes	NR	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	7/12 (58,3 %)
Luz *et al.* 2022	Yes	No	NR	Yes	Yes	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	8/12 (66,6 %)
Estrada *et al.* 2022	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	9/12 (75 %)

CD: cannot determine; NA: not applicable; NR: not reported; NHBLI: National Heart, Blood and Lung Institute, United States.
1) Was the research question or objective in this paper clearly stated? 2) Was the study population clearly specified and defined? 3) Was the participation rate of eligible persons at least 50 %? 4) Were all the subjects selected or recruited from the same or similar populations? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants? 5) Was a sample size justification, power description or variance and effect estimates provided? 6) For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured? 7) Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed? 8) For exposures that can vary in amount or level. did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure or exposure measured as continuous variable)? 9) Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? 10) Was the exposure(s) assessed more than once over time? 11) Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? 12) Were the outcome assessors blinded to the exposure status of participants? 13) Was loss to follow-up after baseline 20 % or less? 14) Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s).

DISCUSSION

Even though RME is a more conservative treatment, if it is indicated in patients with totally or partially closed midpalatal sutures, it can lead to consequences such as significant pain, gingival recession, palatal mucosa ulceration or necrosis, buccal tipping of the posterior teeth, and reduction of buccal bone thickness (Bell *et al*., 1976; Betts *et al*., 1995; Garib *et al*., 2005; Rungcharassaeng *et al*., 2007; Kiliç *et al*., 2008), alveolar bone bending (Northway & Meade, 1997), buccal root resorption (Wertz *et al*., 1970), fenestration of the buccal cortex (Timms & Moss, 1971) and instability of the expansion (Haas *et al*., 1980; Greenbaum & Zachrisson, 1982). On the other hand, it is important to mention that even though a surgical expansion with SARME is possible at any time throughout life, it implies increasing morbidity, cost, risk, and more days required for patient recovery (Angelieri *et al*., 2017). It has also been reported to be the most unpredictable procedure among all orthognathic surgery modalities. This unpredictability of the surgical expansion has to do with its relapse potential (Bailey *et al*., 2004; Proffit *et al*., 2007).

A third option mentioned in the scientific literature is the use of microimplants (MARPE) in cases in which the midpalatal suture is in process of closure (Cunha *et al*., 2017; Brunetto *et al*., 2017; Park *et al*., 2017).

A precise method for evaluation of MPS could prevent the wrong diagnosis regarding treatment plan for maxillary expansion (Mahdian *et al*., 2020).

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 (Persson & Thilander, 1977).

Skeletal maturation has been evaluated conventionally in orthodontics by hand-wrist (Karlberg, 2002) and CVM methods (Fishman, 1982; Baccetti *et al*., 2005) for assessing the adolescent growth peak.

Although the hand - wrist radiograph is the most common and standardized method to evaluate skeletal development due to its objective and simple interpretation, high reproducibility, and minimal radiation exposure, it is not yet described as an absolute “gold standard” for skeletal maturity (Lee & Mah, 2019b).

Between the limitations of this method, we can mention that the ossification sequence and timing of skeletal maturity within the hand-wrist area show polymorphism and sexual dimorphism, which can limit the clinical predictive use of this method (Houston, 1980; Szemraj *et al*., 2018).

Finally, events in the hand and wrist are indicators of the peak and the end of the pubertal growth spurt, but these events do not signal the onset of the pubertal growth spurt (Mellion *et al*., 2013).

The CVM method has been shown to be a biologic indicator for somatic skeletal maturity in growing subjects (Franchi *et al*., 2000; Soegiharto *et al*., 2008; Masoud *et al*., 2008; Perinetti *et al*., 2012), with good reproducibility when specific training is provided along with precise guidelines for assessing each stage visually (Perinetti *et al*., 2014).

In recent years, evaluation of the cervical vertebrae has been increasingly used to determine skeletal maturity (Hassel & Farman, 1995; Bacetti *et al*., 2005; Chen *et al*., 2008; Wong *et al*., 2009).

Cervical vertebrae are visible on lateral cephalometric radiographs, which are routinely acquired in patients undergoing orthodontic treatments; therefore, determining the skeletal age by determining the CVM decreases the exposure of the patient to radiation (Bacetti *et al*., 2005; Flores-Mir *et al*., 2006; Gandini *et al*., 2006; Litsas *et al*., 2010).

The assessment of the skeletal age with the CVM is done on a cephalometric radiograph, routinely used in orthodontic practice, which makes it easy to apply (Lai *et al*., 2008; Szemarj *et al*., 2019).

The individual evaluation of midpalatal suture maturation on CBCT scans has been proposed to identify the morphology of the midpalatal suture prior to maxillary expansion, trying to guide clinicians in choosing the best clinical procedure to accomplish a successful treatment (Angelieri *et al*., 2013; Shayani *et al*., 2022).

Spearman's correlation coefficient, (r, also signified by rs) measures the strength and direction of association between two ranked variables. (Correlation Coefficients: Appropriate Use and Interpretation) (Schober *et al*., 2018).

Eight out of eleven studies (72.7 %) assessed the correlation between the midpalatal suture maturation method and the skeletal maturity evaluated by CVM method.

The values of Spearman's correlation coefficient varied between 0.244 (Chutasripanich & Mahatumarat, 2020) and 0.908 (Angelieri *et al*., 2015), with sample sizes ranging between 42 (Luz *et al*., 2022) - 480 (Lee & Mah, 2019a) and ages ranging from 5.3-58.4 years old.

Five articles mentioned a positive correlation, fluctuating between 0.6916 (Luz *et al*., 2022) and 0.908 (Angelieri *et al*., 2015). Three authors found no significant correlation between these two methods, obtaining values that ranged from 0.030 (Gorucu-Coskuner *et al*., 2018) and 0.395 (Estrada *et al*., 2022).

The difference between the Spearman’s correlation coefficients obtained might be because of racial difference, sample size and the inclusion criteria used in every study. For example, Mahdian *et al*. (2020) did not include patients in CS1 and CS2 stages. Something similar happened with Angelieri *et al*. (2015), who only included patients between CS1 and CS5. As mentioned by Luz *et al*. (2022), to obtain more consistent results, it is suggested to increase the sample size, with a similar distribution between genders, of a wider age range, and with a longitudinal follow-up of patients.

In the same way, two out of eleven studies (18.1 %) evaluated the correlation between midpalatal suture maturation method and the skeletal maturity assessed by HWM method (Jang *et al*., 2016; Yu & Kim, 2021).

The sample sizes and ages ranged between 99-237 subjects and 6-20 years, respectively.

The values of Spearman's correlation coefficient varied between 0.904 (Jang *et al*., 2016) and 0.905 (Yu & Kim, 2021), showing a strong correlation between both methods.

There is a great deal of controversy regarding the relationship between chronological age and MPS ossification. Fusion of the MPS may happen in a wide variety of ages.

Only six (Gorucu-Coskuner *et al*., 2018; Kim *et al*., 2018; Lee & Mah, 2019b; Mahdian *et al*., 2020; Yu & Kim, 2021; Luz *et al*., 2022) authors evaluated the relationship between chronological age and MPS method. The values obtained fluctuated between 0.212 (Gorucu-Coskuner *et al*., 2018) and 0.878 (Yu & Kim, 2021). Lee. *et al*. (2019) divided their assessment by sex, obtaining a value of 0.499 for men and 0.560 for women. Luz *et al*. (2022) and Yu & Kim (2021) did a similar analysis. Luz *et al*. (2022) found a higher correlation coefficient in males (0.7809) than females (0.6916). In the meantime, Yu & Kim (2021) found a higher correlation coefficient in females (0.892) than males (0.864).

Angelieri *et al*. (2015) mentioned that if the CVM stage cannot be assessed, chronologic age may be a viable alternative to predict some midpalatal suture stages. This could be partially true only for early stages of maturation. Based on the articles found, we believe that it is essential that clinicians should not be guided exclusively by chronological age when making the decision between performing a conventional or surgical maxillary expansion because initiation and period of maximum growth spurt vary by races, genders, and individuals (Björk & Helm, 1967; Grave & Brown, 1976; Soliman *et al*., 2014).

Likelihood ratio (LHR) is a measure of diagnostic performance (Attia *et al*., 2003). 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 or HWM). 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" (Angelieri *et al*., 2015).

A result of 1 indicates no diagnostic performance (ie, relationship), whereas a result smaller than 1 must be interpreted as a decrease in the likelihood of disease (negative relationship). An LHR greater than 1 indicates that the test result is associated with the disease (Deeks & Altman, 2004).

An LHR between 1 and 2 can be interpreted as a minimal increase (15 %) in the likelihood of disease. 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. LHRs above 10 indicate large and often conclusive increases in the likelihood of the disease (ie, strong association).

Of the included studies, five of eleven (45,4 %) (Angelieri *et al*., 2015; Lee & Mah, 2019a; Yu & Kim, 2021; Estrada *et al*., 2022; Luz *et al*., 2022) used LHR for measuring diagnostic performance. We found controversial information reported by the authors in relation to this powerful tool for incorporating the results of a diagnostic test into clinical decision making. Angelieri *et al*. (2015) mentioned that 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.

This has been reaffirmed by Lee & Mah (2019b), who declared that CVMI 1 - 3 showed positive LHR greater than 10 for the diagnosis of stages A - C (44.79), suggesting that the prepubertal status of cervical vertebrae is a reliable indicator for MPS nonfusion (stages A - C). Luz *et al*. (2022) identified a strong relationship between CS2 and stage B (6.0). In contrast, Estrada *et al*. (2022) reported in their study that no positive LHR greater than 5 was found.

From a clinical perspective, these results are positive because when the treatment plan includes maxillary expansion in patients with CVMI 1 - 3, CBCT is not necessary to confirm the MPS fusion. Additionally, 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.

For patients at CS4, CS5 and CS6 (as observed in a lateral cephalogram), however, an assessment of the midpalatal suture on CBCT is indicated, to minimize the adverse effects of dental expansion and avoid unnecessary invasive procedures, before making the clinical decision between conventional RME (still possible at stage C) or surgically assisted RME (stages D and E). An important finding mentioned by Angelieri *et al*. (2015) was that 13.5 % of the postpubertal subjects at CS5 had stage C in midpalatal suture maturation. This could explain the occasional clinical success of RME treatment in adults.

In the case of HWM, Yu & Kim (2021) established that a positive LHR of 5 or more for any SMI or MP3 stage is considered to be a reliable diagnostic indicator for the estimation of any maturational stages of the midpalatal suture. Based on this, SMI 1 - 2, SMI 3, SMI 4- 6, and SMI 10-11 can be used for reliable identification of stages A, B, C, and D & E, respectively and MP3 FG stage and I stage can be used as valid indicator of stages C and D & E, respectively. From a clinical perspective, it is important to take CBCT for patients in SMI 7 - 9 to evaluate the midpalatal suture more thoroughly before the clinical decision of the more suitable maxillary expansion technique.

II Methodological quality assessment.

Methodological quality (risk of bias) assessment is an important step before study initiation usage. One of the strengths of this review is that it is the first one to assess the methodological quality of the articles related to this topic using the Quality assessment of the included studies using the Observational Cohort and Cross-Sectional Studies tool. Also, to the best of our knowledge, this is the first systematic review that aims to analyze the association between the midpalatal suture maturation stages assessed by CBCT, according to the method described by Angelieri *et al*. (2015), and other objective methods used to assess skeletal maturation or bone fusion.

As mentioned by Santiago *et al*. (2012) in a systematic review, common methodological limitations in studies on reliability of diagnostic methods include lack of image randomization, blinding, and sample size calculation.

Of the eleven studies included, only six (Jang *et al*., 2016; Kwak *et al*., 2016; Kim *et al*.,2018; Chutasripanich & Mahatumarat, 2020; Mahdian *et al*., 2020; Yu & Kim, 2021) described and clearly defined the study population, mentioning in detail the demographic background, location, and time period for obtaining the samples. Four out of eleven studies (Jang *et al*., 2016; Mahdian *et al*., 2020; Luz *et al*., 2022; Estrada *et al*., 2022) mentioned how the calculations of their sample size was done.

Another point of vital importance is related to the blinding process. Only five out of the eleven (Angelieri *et al*., 2015; Jang *et al*., 2016; Gorucu-Coskuner *et al*., 2018; Estrada *et al*., 2022; Luz *et al*., 2022) included studies mentioned that the examiners were blinded (Table II).

III Limitations

A limitation of this study has to do with results not being homogeneous, making it impossible to perform a meta-analysis.

The methodological quality of the studies included was assessed rigorously and many deficiencies were found, such as: lack of randomization, blinding and sample calculation.

Another limitation has to do with the method itself. Barbosa *et al*. (2019) mention that an extensive calibration and training program is necessary for more reliable and reproducible applications. On the other hand, it has a very big potential for research and educational purposes.

Also, there is an urgent need for future studies to also include the evaluation of the rest of the circummaxillary sutures. This, because even though the MPS could still be open in some patients, other craniofacial structures could offer resistance to palatal expansion. In fact, other circummaxillary sutures (Isfield *et al*., 2017), zygomatic arch (Wetz., 1970; Bishara *et al*.,1987) and sphenoid bone (Bishara *et al*., 1987) are also involved. Therefore, in order to have a better prediction of the prognosis, these structures should also be taken into consideration in future studies (Reis *et al*., 2020).

CONCLUSION

- Even though midpalatal suture maturation stage assessment needs an exhaustive training and calibration process, it is a valid method to evaluate skeletal maturation or bone fusion.
- Association between MPS stage assessment method and CVM method varied between 0.030 and 0.908.
- Association between MPS stage assessment method and HWM method oscillated between 0.904 and 0.905.
- Most of the literature recommends that chronological age should not be used as an indicator of midpalatal suture maturation on its own.
- From a clinical perspective, for patients at CS4, CS5 and CS6, an assessment of the midpalatal suture on CBCT is indicated. A similar assessment should be done in patients at SMI 7-9.

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SHAYANI, A.; MERINO-GERLACH, M. A.; GARAY-CARRASCO, I. A.; NAVARRO-CÁCERES, P. E. & SANDOVAL-VIDAL, H. P. Validez del método de la etapa de maduración en la evaluación individual de la osificación de la sutura palatina mediana previo a la expansión maxilar: Una revisión sistemática. *Int. J. Odontostomat., 17(3)*:312-326, 2023.

RESUMEN: En 2013, se propuso un nuevo método para la evaluación del estadio de maduración de la sutura palatina mediana para la evaluación de los pacientes antes de realizar la expansión maxilar. En este estudio, nuestro objetivo fue analizar la asociación entre las etapas de maduración de la sutura palatina mediana evaluada en CBCT, según el método descrito por Angelieri *et al*., y otros métodos objetivos utilizados para evaluar la maduración esquelética o la fusión ósea. Se realizó una búsqueda en las bases de datos PubMed, Cochrane Library, SciELO, LILACS, Web of Science y Scopus, sin restricción de idioma. Se buscó literatura no publicada en ClinicalTrials.gov, el Registro Nacional de Investigación y la base de datos ProQuest Dissertation Abstracts and Thesis. Se estableció contacto con los autores cuando fue necesario y se revisaron las listas de referencias de los estudios incluidos. Los términos de búsqueda incluyeron sutura palatina mediana, maduración, correlación, rendimiento diagnóstico, clasificación, evaluación, valoración y relación. La evaluación de la calidad se realizó mediante la herramienta de Estudios transversales y de cohortes observacionales desarrollada por el Instituto Nacional del Corazón, los Pulmones y la Sangre. Once estudios cumplieron con los criterios de inclusión. Del total de estudios incluidos, el 81.9% tuvo calidad regular y el 18.1% calidad buena, respectivamente. Ocho de once estudios evaluaron la correlación entre el método de maduración de la sutura palatina mediana y la madurez esquelética evaluada por el método CVM (coeficiente de correlación de Spearman: 0.244-0.908). Dos de once estudios evaluaron la correlación entre el método de maduración de la sutura palatina mediana y la madurez esquelética evaluada por el método HWM (coeficiente de correlación de Spearman: 0.904-0.905). Aunque la evaluación del estado de maduración de la sutura palatina mediana necesita un proceso exhaustivo de entrenamiento y calibración, es un método válido para evaluar la maduración esquelética o la fusión ósea. Desde una perspectiva clínica, para pacientes en CS4, CS5 y CS6, está indicada una evaluación de la sutura palatina mediana en CBCT. Se debe realizar una evaluación similar en pacientes con SMI 7-9.

PALABRAS CLAVE: método de maduración de la sutura palatina mediana, suturas craneales, expansión maxilar, madurez esqueletal, vértebras cervicales, análisis carpal.

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