

Recent Methods Used for Analysis of Midpalatal Suture Closure Before Maxillary Expansion in Humans: A Systematic Review

Métodos Recientes Utilizados para el Análisis del Cierre de la Sutura Palatina Mediana Previo a Expansión Maxilar en Humanos: una Revisión Sistemática

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ABSTRACT: The evaluation of the maturation of the midpalatal suture is highly important before making the clinical decision on whether to correct a transverse discrepancy in a conventional or surgical way. For this purpose, there are methods such as hand and wrist analysis, evaluation of maturation of the cervical vertebrae, and evaluation by means of occlusal radiographs. The main objective of this systematic review is to identify in the current literature the use of new methods and technologies to evaluate the maturation of the midpalatal suture before performing maxillary expansion. A bibliographic search was carried out using PubMed, Cochrane Library, SciELO, LILACS, Web of Science and Scopus using the terms midpalatal suture, cranial sutures, palate, maturation, interdigitation, ossification, maxillary expansion, evaluation, assessment and assess. The 119 articles were obtained, of which only 7 meet the selection criteria, which describe qualitative, quantitative and semiquantitative evaluation methods. During the last few years, due to advances in technology and science, various promising methods and techniques have been proposed for the evaluation of median palatal suture maturation. The quality of the available evidence is not enough to support the use of any one of these methods on their own. We recommend that clinicians use multiple diagnostic methods for an objective assessment of the maturation of the midpalatal suture, to guide them in their clinical decisions.

KEY WORDS: midpalatal suture, ossification, maxillary expansion, evaluation, cranial sutures.

INTRODUCTION

The decrease in the transverse diameter of the maxilla is associated with various conditions, among which, the following are mentioned: posterior crossbite (dental and / or skeletal), dental crowding, occlusal disharmonies, narrowing of the pharyngeal airway, postural alterations of the tongue, mouth breathing and muscle alterations producing effects on orofacial function and aesthetics (McNamara Jr., 2000; McNamara Jr. *et al.*, 2003; McNamara Jr., 2006).

The evaluation of the maturation of the midpalatal suture (MPS) is very important when making clinical decisions about whether to correct a transverse

discrepancy in a conventional way, with micro screws, or to perform assisted surgery.

Histological studies (Melsen, 1975; Persson & Thilander, 1977; Persson *et al.*, 1978; Wehrbein & Yildizhan, 2001; Knaup *et al.*, 2004) and research with computed microtomography (Korbmacher *et al.*, 2007) in cadavers have shown that there is great variability in the chronological age of fusion of MPS. Patients aged 27, 32, 54 and up to 71 years have been reported without signs of fusion at the MPS level. These methods have the limitation of not being able to be performed in living human beings.

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It is key to understand that the maturation of MPS varies from one individual to another. Therefore, identifying in which adolescents or young adults it is possible to perform rapid conventional maxillary expansion (RME) as a less invasive alternative to surgically assisted expansion (SARME) is of vital importance (Kao *et al.*, 2018).

Since chronological age is not reliable in determining the developmental stage of the suture during growth, it becomes essential to understand individual variability in the development of MPS (Melsen, 1975; Gueutier *et al.*, 2016).

Bjork (1966) showed that facial suture maturation is related to growth in stature, and the onset of MPS fusion has been associated with skeletal growth rate. Nevertheless, he does not propose a specific method but only a general conclusion (Bjork, 1966).

To help with the clinical decision-making on whether the correction of a transverse discrepancy should be performed conventionally or surgically, various indicators of MPS maturation have been proposed, which have been traditionally used for the evaluation of skeletal maturation, including hand radiography (Greulich & Pyle, 1960; Flores-Mir *et al.*, 2004) and the cervical vertebral maturation method by means of the lateral skull radiography (Hassel & Farman, 1995; Baccetti *et al.*, 2002).

Revelo & Fishman (1994) proposed individual assessment of midpalatal suture morphology using occlusal radiographs prior to RME therapy. However, occlusal radiographs are not reliable in analyzing MPS morphology because the vomer and structures on the outside of the nose cover the midpalatal area, which could lead to a false radiographic interpretation in which the suture will appear to be ossified.

With the advent of Cone Beam (CBCT) a 3D visualization has been possible, which makes all this process much more objective. However, a gold standard in the evaluation of suture closure has not yet been established and the proposed methods differ in their sensitivity and specificity.

The main aim of the present article is to identify in the current literature the use of new methods and technologies to assess the maturity of MPS before performing a maxillary expansion.

The secondary aim of the present study is to assess the methodological quality of the articles that propose new methods and technologies to evaluate the maturity of MPS before performing a maxillary expansion.

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 study protocol was registered on the International Prospective Register of Systematic Reviews (ID: CRD42022344402).

Eligibility criteria. Articles included in this review fulfilled the following inclusion criteria according to the Population, Exposure, Comparator, and Outcomes format:

Population: human subjects without any history of orthopedic treatment, orthodontic treatment, syndromic condition, or cleft lip and palate.

Exposure: new methods or technologies used to assess midpalatal suture maturation

Condition: not applicable.

Outcome: degree of ossification-maturation-interdigitation of midpalatal suture before maxillary expansion treatment

Study design: observational studies (cohort studies either prospective or retrospective and cross-sectional studies).

Articles including subjects who had undergone any type of orthodontic treatment, nonhuman studies, case reports, and review articles were excluded.

Information sources and search strategy. To identify relevant articles, the electronic databases of PubMed, LILACS, Scopus, SciELO, Cochrane Library and Web of Science were searched from 2010 to July 26th, 2022. Gray literature was checked by using the 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.).

Table I. Skeletal maturation stages of the MPS proposed by Angelieri *et al.*

Stage	Description
A	Represents the earliest maturation stage of the suture, and in this stage the suture was identified as a relatively straight high-density line at the midline
B	The suture presents an irregular shape and was identified as a scalloped high-density line at the midline
C	The suture is seen as two parallel, scalloped, high-density lines close to each other and separated in some areas by small low-density spaces
D	The complete fusion of the suture has occurred in the palatine bone and the radiographic image of the suture was identified as two scalloped, high-density lines at the midline on the maxillary portion of the palate that were not visible in the palatine bone
E	Fusion of the suture has occurred in the maxilla. It is not possible to identify the MPS. As to bone density, it is the same as in other parts of the palate

The search strategy was adapted for each database. The detailed search strategy for all the databases have been reported in Table I.

References cited in the selected articles were also screened for relevant studies.

Study selection. Articles were selected in 3 phases. In the first phase, 1 author (A.S.) excluded the duplicate articles using the Reference Manager EndNote X9 (Clarivate Analytics, Philadelphia, Pa) and the systematic review web application Rayyan (Ouzzani *et al.*, 2016) (rayyan.qcri.org). Articles were then independently selected by 2 reviewers (A.S. and I.G.C.) based on their title and abstract. In the second phase, the same 2 reviewers independently screened the full texts to identify those papers that satisfied the inclusion criteria. Finally, phase 3 resolved the conflicts of the selection process by a discussion with the third reviewer (P.S.V.).

Data collection and analysis. Data extraction for the included studies was performed by the first reviewer (A.S.) and was later rechecked by the second reviewer (P.S.V.). Finally, a data extraction sheet was formulated in Microsoft Excel (Redmond, Wash) after a discussion with the third reviewer (I.G.C.).

Data extraction was performed for the following items: (1) participant characteristics: sample size, sex distribution, age of the included subjects (mean and standard deviation or age range); and (2) study characteristics: author and year of publication, study design, objectives, diagnostic method to evaluate MPS maturation, equipment used, sample size, calibration and blinding process, examination region, inter and intra-evaluator agreement, results, and conclusions.

Quality assessment of included studies. As suggested by Ma *et al* (2020) the Observational Cohort and Cross-Sectional Studies tool developed by the

National Heart *et al* (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 119 studies were identified by electronic searches, and 66 studies remained after removing duplicates. After initial screening, a total of 50 studies met the predetermined inclusion criteria. After the full text review, 6 studies were included for this review. In addition, 1 eligible study was identified via hand searches. As a result, 7 studies were included in this systematic review (Fig. 1).

Results of individual sources of evidence and synthesis of results.

Franchi *et al.* (2010). Franchi *et al.* (2010) performed a quantitative measurement of the MPS, evaluating its density, using low-dose computed tomography (CT), parallel to the palatal plane, at three different times: before rapid expansion of the maxilla (T0), at the end of active expansion (T1) and after a passive retention period of 6 months (T2).

Standardized axial images were acquired by passing through the trifurcation of the upper right first molar. These were enlarged with a magnification factor x3 (Light-Speed 16 software, General Electric Medical System, Milwaukee, Wisconsin). Images spanning an area of 1 square millimeter were evaluated by a blinded examiner for calculation of density values in Hounsfield units (HU). This quantitative scale is a linear transformation of the tissue attenuation

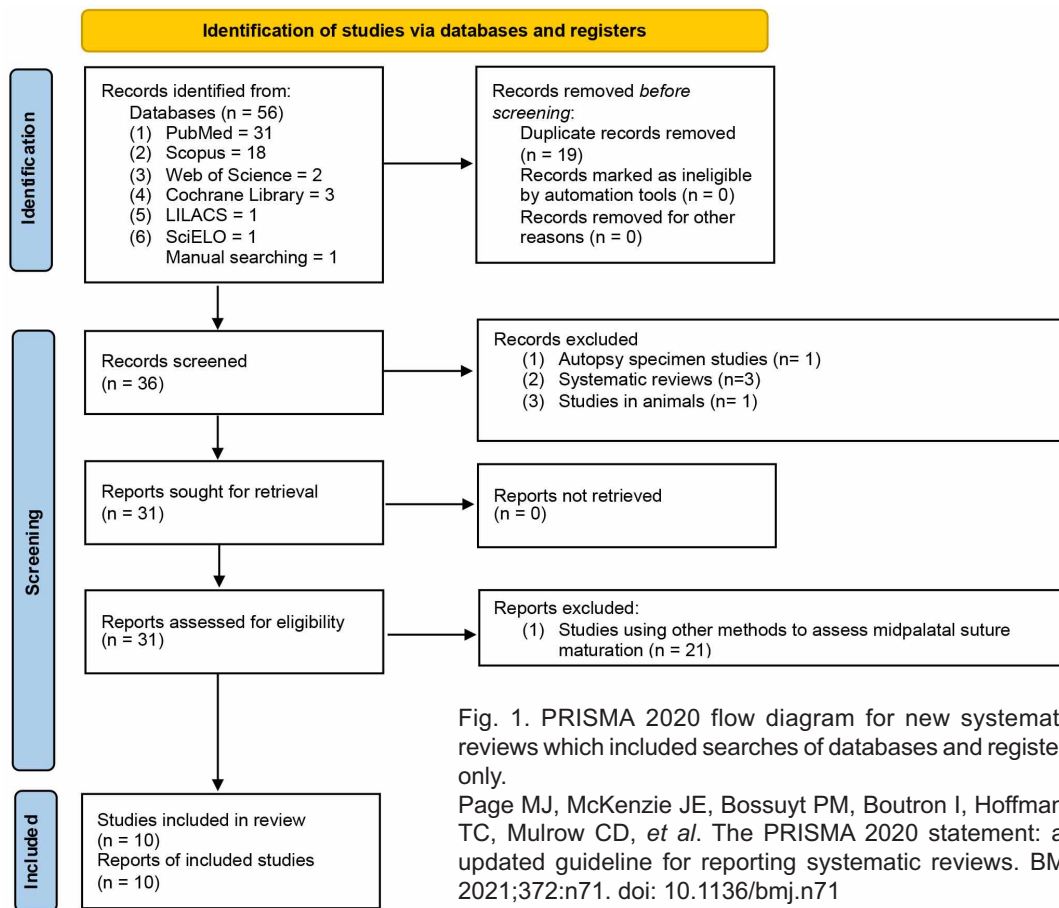


Fig. 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only.

Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

coefficient, where -1000 corresponds to air, distilled water under standardized conditions is equal to 0 HU and very dense bone is defined as equal to or greater than 1000.

The 4 regions of interest (ROI) in the palatal region were identified as follows:

- 1) Anterior Satural ROI (AS ROI)
- 2) Posterior Satural ROI (PS ROI)
- 3) Anterior Bone ROI (ROI AB)
- 4) Posterior Bone ROI (PB ROI)

The last two values were used to reference the density of MPS with that of the hard palate.

The pre-expansion statistical analysis showed a significant difference between the anterior and posterior satural region (563.3 ± 183.29 HU and 741.7 ± 167.1 HU, respectively) with respect to the anterior and posterior bone region (1057.5 ± 129.4 HU and 1102.8 ± 160.9 HU) ($P < 0.05$). The authors reported that in T0, the density in AS ROI was significantly lower than that of PS ROI ($P < 0.05$), but no significant differences

were found between these two sutural regions in T1 or T2 ($P > 0.05$). Both AS ROI and PS ROI showed a significant decrease in density from T0 to T1, significant increases from T1 to T2, and there was no significant difference between T0 and T2.

Sumer *et al.* (2012). Assessed the efficacy of ultrasonography (US) to generate a semi-quantitative measurement of MPS ossification.

Ultrasonography was used to assess the mineralization of MPS at five different times: 14 days after the completion of the expansion protocol by means of SARME, 2 months post expansion, 4 months post expansion, at the time of removal of the expander and 2 months after the expansion device removal. To do this, they used the ultrasound probe intraorally, placing it perpendicularly over the mucosa that is above the MPS, obtaining images in the axial direction.

The authors used a four-point semi-quantitative scale to report bone filling. A score = 0 was assigned to a suture with clean margins and 0 % echogenic ma-

terial. A score = 1 was awarded for having partial transmission, gaps in localized margins, and echogenic material less than or equal to 50 %.

A score = 2 was characterized by partial ultrasound transmission, slightly visible margins, and an increase in echogenic material of over 50 %. A score = 3 was described as a situation in which the ultrasound is not transmitted, 100 % echogenic reading, and unidentifiable margins. All evaluations were performed by the same radiologist. Bone filling trends were qualitatively supported by comparison with conventional occlusal radiography.

Immediately after expansion, all subjects had an echolucent suture, without echogenic material and allowing the complete passage of ultrasound waves, being able to observe a small amount of bone at the level of the margins (gap), for which a bone filling value equal to 0 was assigned. At two- and four-months post expansion, two of the three subjects were identified with a bone filling value = 1, while the remaining subject had a bone filling score=2. On the occlusal radiograph of these stages, the appearance of the bone within the space was more similar to that of the adjacent normal bone.

When the device was removed, at 6 months and at the 8-month follow-up, the amount of echogenic material at the suture level increased but did not reach 100 %. The score for two of the subjects was equal to 2. The remaining patient received a bone filling score = 3 due to incomplete wave transmission and 100 % echogenicity. On occlusal radiography, the suture was almost completely ossified.

Angelier *et al.* (2013). presented and validated a new classification system for the individual evaluation of the individual morphology of MPS using CBCT. The proposed method consists of an individual and qualitative evaluation of the maturation of the MPS. This standardized methodology seeks to capture the best axial cross-section of MPS observed on a CBCT, providing an individual categorization of MPS maturation with letters from A to E.

Each one of the stages is described below:

- A: MPS is almost a straight, high-density suture line with little or no interdigitation.
- B: MPS is irregularly shaped and appears as a high-density scalloped line
- C: MPS has 2 parallel, scalloped, high-density lines

close to each other, separated by small, low-density spaces in the maxillary and palatine bones. The suture may have a straight or irregular pattern.

D: The fusion of MPS with the palatine bone is observed, so MPS cannot be visualized in the palatine bone, since fusion generally occurs from the posterior to the anterior portion. Parasutural bone density is increased (high bone density) compared to maxillary parasutural bone density. In the maxillary portion of the suture, fusion has not yet occurred, and the suture can still be seen as two lines of high density separated by small spaces of low density.

E: Fusion of MPS with the maxilla occurs. The actual suture is not visible in at least a portion of the maxilla. Bone density is the same as in other regions of the palate.

They concluded that there is great variability in the distribution of MPS maturation stages in relation to chronological age.

Kwak *et al* (2016). Performed an objective and quantitative evaluation of MPS. The purpose of this study was to evaluate the correlation between the fractal dimension, which had been used to evaluate mammalian cranial sutures, and the maturation of the MPS by evaluating the data obtained from CBCT, and to determine if it is possible to use the results obtained through fractal analysis as a criterion to determine the maturation stage of MPS in a clinical context.

Each of the subjects underwent a cone beam computed tomography scan. Subsequently, these images were processed to evaluate the stage of maturation of cervical vertebrae (CVM) and the evaluation of the maturation of MPS according to the protocol proposed by Angelier *et al* (2013), in which the maturation stage is categorized with letters from A-E. In addition, the Region of Interest was isolated for the calculation of the fractal dimension of MPS.

Regarding the calculation of the fractal analysis, once the region of interest had been selected, a program for image processing was used (Photoshop CS6 Extended; Adobe Systems, San Jose, CA, USA) according to the method proposed by White & Rudolph (1999). A Gaussian filter (sigma = 35 pixels) was applied to each ROI to remove structures with small or intermediate sizes and a blur was performed until only structures with large differences in density were visualized, known as Gaussian blur. This blurred image was subtracted from the original. Image J version 1.48

software (National Institute of Health, Bethesda, MD, USA) was used to create a skeletonized binary image. Finally, the fractal dimension was calculated using the box counting option of the Image J program.

At an optimal cutoff value of the fractal dimension of 1.0235, the statistical analysis to evaluate the predictive ability of the fractal analysis to determine the maturation stage (A, B, C) vs (D or E) reported the following values: specificity 86.6 %, sensitivity 64.9 %, false positive 35.1 %, false negative 13.4 %, positive predictive value 80.3 % and negative predictive value 74.6 %.

Grünheid *et al.* (2017). Tested a new method called midpalatal density ratio. Their main objective was defining if the density ratio, obtained from a pretreatment CBCT image, could be used as a valid predictor of the amount of skeletal response to RME treatment.

CBCT scans were obtained at T1 (before orthopedic treatment) and T2 (after orthopedic treatment). To quantify the skeletal effects of RME, they used T1 and T2 slices to draw linear measurements between 3 bilateral skeletal structures. These structures were:

- 1) Distance between the greater palatine foramina
- 2) Maximum width of the nasal cavity
- 3) Distance between the infraorbital foramina

To determine the midpalatal suture density ratio, gray density measurements were made on 0.3-mm slices using Invivo5 software (version 5.5.2; Anatomage, San Jose, Calif). Average gray density values were determined for defined regions of the suture (GD_s), soft palate (GD_{sp}), and palatal process of the maxilla (GD_{ppm}).

The average gray density values were used to calculate the midpalatal suture density (MPSD) ratio by the following equation:

$$MPSD \text{ ratio} = \frac{GD_s - GD_{sp}}{GD_{ppm} - GD_{sp}}$$

This ratio ranges from 0 to 1. Lower values indicate that the suture region is closer in density to the soft palate (less calcified). Values close to 1 indicate that the suture region is closer in density to the palatal process of the maxilla (highly calcified).

Grünheid *et al.* (2017). Concluded that the midpalatal suture density ratio was found to have a significant correlation with measures of skeletal response to RME treatment, making it a suitable tool to predict the skeletal response to RME and help to accurately diagnose the amount of MPS maturation, leading the clinicians towards a less invasive approach when performing maxillary expansion treatments.

Abo Samra & Hadad (2018). Performed a quantitative evaluation of the maturation of the MPS. The purpose of their study was to evaluate the relationship between the morphological stages of maturation of the MPS and the density of MPS (MPSD) to support the reliability of these stages as a determining factor when indicating a protocol of treatment.

The classification of the morphological maturation stage of MPS was carried out according to the protocol described by Angelieri *et al.* (2015, 2017).

Bone density measurements were carried out as follows: in the mid-sagittal section, passing through the anterior and posterior nasal spine, the maxillary region was divided into three equal sections (M1, M2 and M3), while the palatal region was divided into two equal sections (P1, P2). Then, in the coronal section passing through each of these sections, the mean MPD value was measured using a rectangular region of interest (ROI) at 3 mm wide and along the total height of the MPS (the cancellous bone between superior and inferior cortical bone) using the OnDemand 3D app.

The bone density of MPS in the maxillary region (MPD_m) was the average of the bone density values of its three sections (M1, M2, M3).

The bone density of MPS in the palatal region (MPD_p) was the average of the bone density values of its two sections (P1, P2).

Significant differences were found in MPD_m between Stage E and Stages A (p = 0.001) -B (p <0.001) -C (p = 0.003) -D (p = 0.198) and between stage B and stages C (p = 0.037) -D (<0.001). Also, significant differences were found in MPD_p between stages D and stages A (p = 0.002) -B (p <0.001) -C (p = 0.024), between stage E and stages A (p = 0.001) -B (p <0.001) -C (p = 0.003). Also, between stage B and stage C (p = 0.037).

Kajan *et al.* (2018). Proposed a new method in which they chose an axial view with the clearest image of

MPS as possible. Afterwards, on this selected axial view, coronal images having 1 mm thickness and 2 mm distance were reconstructed on a line in the direction of MPS from behind the nasopalatine foramen to the transverse palatal suture. These coronal images had a width of 100 mm. Subsequently, the coronal images were divided into three groups (anterior, middle, and posterior sections). Each one of these groups had three to four cuts that were assessed. The percentage of opening depth of the MPS in all cuts of every region was reported in such a way that the opening depth of MPS was divided to total visible depth of MPS in each cut. Finally, the mean percentage of opening of the MPS depth section was calculated and reported as the opening percentage.

They found a statistically significant association between the opening of MPS depth and the age groups

in the middle (P = 0.008) and posterior (P = 0.001) sections of the suture. The percentage of suture opening decreased with increasing age and from anterior to posterior region. In the three groups, the lowest percentage of MPS opening depth was observed in the posterior palatal region. They finished by concluding that the middle portion of the MPS is a good place for evaluating the effect of increasing age on the opening depth of MPS.

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 % to 85.7 %. One study (Sumer *et al.*, 2012) had poor quality, five studies (Franchi *et al.*, 2010; Angeli *et al.*, 2013; Kwak *et al.*, 2016; Abo Samra & Hadad, 2018; Kajan *et al.*, 2018) had fair quality and one study (Grünheid *et al.*, 2017) had good quality.

Table II. Electronic literature search strategy.

Database	Keywords	Time frame	Result	Included articles
MEDLINE/ PubMed	("midpalatal suture maturation" OR "midpalatal suture maturation method") AND ("cranial suture" OR "cranial sutures*" OR "midpalatal suture") AND ("maturation" OR "interdigitation" OR "ossification") AND ("evaluation" OR "assess" OR "assessment")	January 2013- July 2022	31	10
Scopus			18	
Web of Science			23	
Cochrane Library			3	
LILACS			1	
SciELO			1	

Table III. Summary of characteristics of included studies.

Authors (y)	Country	Sample Size	Age	Study design	Equipment used	Specifications
Angeli <i>et al.</i> (2013)	United States	140 (54 M- 86 F)	5.6 – 58.4 years	Cross-sectional	iCAT cone-beam 3D imaging system	8.9 to 20 seconds, FoV at least 11 cm, voxel 0,2 a 0,3 mm
Tonello <i>et al.</i> (2017)	Brazil	84 (40 M- 44 F)	11 – 15 years	Cross-sectional	iCAT scanner	8.9 to 30 seconds, FoV at least 11 cm, voxel 0,2 a 0,3 mm
Angeli <i>et al.</i> (2017)	Brazil	78 (14 M – 64 M)	18 – 66 years	Cross-sectional	iCAT Cone Beam 3D Imaging system scanner	17.8 seconds, coxel 0,3 mm
Barbosa <i>et al.</i> (2018)	Brazil	60 (27 M – 33 F)	11 – 21 years	Cross-sectional	Not mentioned	Not mentioned
Ladewig <i>et al.</i> (2018)	Brazil	112 (68 M- 44F)	16 – 20 years	Cross-sectional	iCAT scanner	40 seconds, FoV 22x16 cm, 120kV, 36 mA, 0,4 voxel
Jimenez <i>et al.</i> (2019)	Peru	200 (95 M- 105 F)	10 – 25 years	Cross-sectional	Planmeca ProMax 3D Mid scanner	13,68 seconds, FoV at least 11 cm, 90 kV, 10 mA, 0,2 a 0,3 mm voxel
Vahdat <i>et al.</i> (2020)	Iran	178 (89 M- 89 F)	10 – 70 years	Cross-sectional	Newtom VGi Cone Beam CT	18 seconds, 110 kV, 1-20 mA. The equipment was automatically adjusted
Katti <i>et al.</i> (2020)	India	200 (95 M – 105 F)	11 – 50 years	Cross-sectional	NewTom Giano CBCT machine	Not mentioned
Gatti Reis <i>et al.</i> (2020)	Brazil	487 (198 M – 289 F)	15 – 40 years	Cross-sectional	iCAT scanner	120 kV, 8 mA, 26.9 s rotation, 0.25 mm voxel FOV between 6 _ 23 and 8 _ 23 cm.
Villarroel <i>et al.</i> (2021)	Chile	150 (73 M – 77 F)	15 – 30 years	Cross-sectional	Sirona Orthophos XG3D	14 segundos, FoV 8x8, 85 kV, 7 mA, voxel 0,16

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

Table IV. Blinding, Calibration process of included studies.

Authors (y)	Nº examiners	Calibration-validation process	Intraexaminer agreement	Interexaminer agreement	Washout period	Images included in second examination	Randomization of images (second examination)	Blinding
Angelieri <i>et al.</i> (2013)	3	Yes (10 images calibration-30 images calibration)	K: 0.77 (0.75-0.79)	K: 0.87 (0.82-0.93)	2 days	30 images	Yes	Yes
Tonello <i>et al.</i> 2017	2	Not mentioned	Not mentioned	Not mentioned	15 days	All images	Not mentioned	Yes
Angelieri <i>et al.</i> 2017	1	Not mentioned	K: 0.80	Not applicable	30 days	30 images	Yes	Yes
Barbosa <i>et al.</i> 2018	21	Not mentioned	K: 0.42	K: 0.34	21 days	All images	Yes	Yes
Ladewig <i>et al.</i> 2018	2	Yes (used images included in main study)	K: 0.87	K: 0.89	15 days	All images	Not mentioned	Yes
Jimenez <i>et al.</i> (2017)	2	Yes (not clear if they used same images included in main study)	K: 0.89	K: 0.90	30 days	All images	Yes	Yes
Vahdat <i>et al.</i> (2018)	1	Not mentioned	Not mentioned	Not applicable	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Katti <i>et al.</i> 2020	1	Not mentioned	ICC > 0.8	Not applicable	5 days	All images	Not mentioned	Not mentioned
Gatti Reis <i>et al.</i> 2020	1	Not mentioned	K: 0.8774	Not applicable	30 days	49 images	Yes	Not mentioned
Villarroel <i>et al.</i> 2021	1	Yes (used 10 images)	PCC: 0.94	PCC 1.0	Not mentioned	Not mentioned	Not mentioned	Yes

K; Cohen's kappa, ICC; interclass correlation, PCC; Pearson correlation coefficient

Table V. 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 <i>et al.</i> 2013	Yes	No	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	8/12 (66,6 %)
Tonello <i>et al.</i> 2017	Yes	No	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	8/12 (66,6 %)
Angelieri <i>et al.</i> 2017	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	9/12 (75 %)
Barbosa <i>et al.</i> 2018	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	9/12 (75 %)
Ladewig <i>et al.</i> 2018	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	9/12 (75 %)
Jimenez <i>et al.</i> 2019	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	10/12 (83,3 %)
Vahdat <i>et al.</i> 2020	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	No	NA	Yes	8/12 (66,6 %)
Katti <i>et al.</i> 2020	Yes	No	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	7/12 (58,3 %)
Gatti Reis <i>et al.</i> 2020	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	No	NA	Yes	8/12 (66,6 %)
Villarroel <i>et al.</i> 2021	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	Yes	NA	Yes	10/12 (83,3 %)

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)?

Table VI. Distribution of maturational stages of midpalatal suture by age in the included studies.

	Age groups	5<11 y	11-<14 y	14-18 y	> 18y	
Angelieri <i>et al.</i> 2013	MPS Stages (n)	A:4; B:22; C:2; D:0; E:0	A:1; B:28; C:13; D:1; E:5	A:0; B:6; C:12; D:6; E:8	A:0; B:1; C:4; D:10; E:17	-
Tonello <i>et al.</i> 2017	Age groups	11	12	13	14	15
	MPS Stages (n)	A:1; B:4; C:8; D:0; E:0	A:0; B:9; C:14; D:3; E:1	A:0; B:5; C:6; D:1; E:0	A:0; B:1; C:8; D:3; E:3	A:0; B:2; C:2; D:3; E:4
Angelieri <i>et al.</i> 2017	Age groups	<30 y	>30 y			
	MPS Stages (n)	A:0; B:1; C:3; D:11; E:21	A:0; B:2; C:3; D:8; E:29	-	-	-
Ladewig <i>et al.</i> 2018	Age groups	16	17	18	19	20
	MPS Stages (n)	A:1; B:3; C:9; D:4; E:5	A:0; B:4; C:13; D:5; E:4	A:0; B:0; C:13; D:5; E:6	A:0; B:0; C:7; D:8; E:8	A:0; B:1; C:8; D:8; E:4
Jimenez <i>et al.</i> 2019 ⁽³³⁾	Age groups	10 - 15	16 - 20	21 - 25		
	MPS Stages (n)	A:2; B:13; C:20; D:9; E:4	A:0; B:1; C:10; D:21; E:20	A:0; B:2; C:15; D:28; E:55	-	-
Katti <i>et al.</i> 2020 ⁽³⁴⁾	Age groups	11 - 20	21 - 30	31 - 40	41 - 50	
	MPS Stages (n)	A:15; B:25; C:10; D:0; E:0	A:0; B:5; C:30; D:0; E:0	A:0; B:5; C:20; D:15; E:10	A:0; B:5; C:10; D:5; E:25	-
Vahdat <i>et al.</i> 2020 ⁽³⁵⁾	Age groups	10 - 19	20 - 29	30 - 39	40 - 49	50 - 59
	MPS Stages (n)	A:0; B:12; C:0; D:0; E:0	A:0; B:6; C:7; D:5; E:0	A:0; B:2; C:26; D:12; E:2	A:0; B:0; C:20; D:13; E:7	A:0; B:1; C:11; D:8; E:17
Gatti Reis <i>et al.</i> 2020 ⁽³⁶⁾	Age groups	15 - 20	21 - 25	26 - 30	31 - 35	36 - 40
	MPS Stages (n)	A:0; B:0; C:43; D:17; E:34	A:0; B:1; C:71; D:34; E:102	A:0; B:1; C:25; D:15; E:44	A:0; B:2; C:13; D:10; E:32	A:0; B:1; C:14; D:5; E:23
Villaroel <i>et al.</i> 2021 ⁽³⁷⁾	Age groups	15 - 20	21 - 25	26 - 30		
	MPS Stages (n)	A:0; B:0; C:32; D:10; E:7	A:0; B:2; C:18; D:8; E:23	A:0; B:0; C:15; D:20; E:20	-	-

DISCUSSION

Summary of evidence. After an exhaustive review of the literature, seven methods for evaluating the maturation of MPS were reported. Five of them quantitative and two qualitative. While it is true that qualitative methods tend to be subjective, recent literature relies on them in high esteem, thanks to the use of CBCTs, but grants them the corresponding caution and the difficulty of reliability among uncalibrated observers.

Quantitative methods have gained ground, but the sophistication to reach mass use is still high. With the evolution of artificial intelligence, it is assumed that the recognition of ossification patterns in CBCTs or ultrasound images, should soon provide us with an analysis tool of the ossification stage of the patient, as well as help us in decision-making to perform maxillary disjunctions with the different modalities that are proposed today.

Each one of these methods has inherent advantages and disadvantages, which we will discuss below.

One of the advantages of the low radiation CT protocol proposed by Franchi *et al.* (2010) is that the voltage is reduced to 80 kV, exposing the patient to a lower dose of absorbed radiation. Additionally, when the kilovoltage is reduced, the contrast of the

anatomical structures increases, while still being acceptable to assess bone quality through this protocol.

Ultrasound, used in the study by Sumer *et al.* (2012), has the great advantage of being a non-invasive and low-cost method, allowing the evaluation of the patient sitting in the dental chair. Additionally, US has proven to be a reliable method to assess early bone formation, as supported by previous studies involving osteogenic distraction (Troulis *et al.*, 2003; Bruno *et al.*, 2008). A study comparing US with panoramic radiographs showed that the efficacy of US to measure an osteotomy gap during osteogenic distraction is equal to that of conventional radiographs (Bruno *et al.*, 2008). One disadvantage of US is the inability to penetrate cortical bone. However, after successful REM or SARME, the gap generated by the osteotomy and its margins are easily visualized. An area of significant interest in the future is to ascertain whether this technology can penetrate an immature MPS before and after carrying out a RME treatment, allowing the clinician to make a subjective assessment of maturation and interdigitation throughout the entire suture while the patient is sitting in the dental clinic. Among the limitations of this study, we can mention a very small sample size of three patients and the lack of a Gold Standard (Histological) or CT to validate these results. Furthermore, it is important to mention that the authors did not report statistical analyzes for this study.

Consequently, an area of future research is the use of this technology and bone filling scores in a larger sample in conjunction with a standard methodology that supports these results.

The method for assessing the morphological maturation of MPS proposed by Angelieri *et al* (2013) is characterized by being a qualitative and didactic method. By not having a gold standard, the authors propose the concept of "Ground Truth" or fundamental truth; This being the professional opinion of the main researcher, who has more experience, when applying his own proposal related to the stages of maturation suggested to classify the sutural maturation of each patient.

Due to the lack of a gold standard and the inaccurate reporting of p-values in their statistics, the results of the validation should be interpreted with caution. A further limitation of this methodology is the method of classifying the stages of maturation of MPS by itself. The authors developed the stages of maturation (A-E) based on the similarity and comparison of the radiographic morphology with the histological morphology of the suture.

Theoretically, the direct analogy of the histological morphology with the morphology of MPS in CBCT is incompatible because the histological evaluation is made at a microscopic level compared to a macro analysis that is performed when assessing it in the axial sections obtained in CBCT.

In addition, to be able to apply this method, significant training and experience is required to be able to classify the maturation stages appropriately.

Subsequently, any inference or direct translation of the histological appearance of the suture and hence development of the CBCT-based sutural maturation stages is not possible.

Therefore, the findings and maturation stages of MPS should be used with caution and should not be used for clinical decision-making. Rather, at best, this classification can be used as an extensive process of subjective assessment of MPS maturation during treatment planning.

Among the strengths of this method, we can mention that it has been validated against the Hand and Wrist (Jang *et al.*, 2016) and Cervical Vertebral Maturation methods (Angelier *et al.*, 2015). Another

strength is that this method has been replicated in populations from different countries, such as Brazil (Tonello *et al.*, 2017, Ladewig *et al.*, 2018; Barbosa *et al.*, 2019), Chile (Villaruel *et al.*, 2021), Irán (Haghanifar *et al.*, 2017; Vahdat *et al.*, 2020), India (Katti *et al.*, 2020), Korea (Kim *et al.*, 2018) and Peru (Jimenez-Valdivia *et al.*, 2019).

Kwak *et al* (2016) assessed MPS maturation using fractal analysis. The authors noted a significant correlation between the fractal pattern and the degree of maturation of the MPS. Consequently, the authors feel that the proposed method can provide a quantitative and objective method to assess the maturation stage of MPS.

Although this method is an excellent way to determine the degree of ossification of MPS, it requires that the clinicians have a significant familiarity with image processing and have the necessary software to do so. Consequently, the time, cost and resources required can act as prohibitive agents for the use of this method.

Grünheid *et al.* (2017). proposed an objective method based on bone density for evaluating MPS maturation on CBCT scans.

It is mentioned in their article that midpalatal suture density is one of the most important factors that determine the resistance of MPS to expansion forces and to predict the skeletal effects of RME.

One of the difficulties of this method is that low standardization between CBCT machines exists, and the Hounsfield scale may vary among studies (Poggio *et al.*, 2006). Therefore, it is difficult to compare the MPSD taken from different CBCT machines or to depend on absolute values to decide between a conventional or more invasive treatment plan.

In the same line, Abo Samra & Hadad (2018) proposed a quantitative method that allows to assess in a simple and quantitative way the maturation of the MPS through bone density and Kajan *et al.*, (2018) suggested a quantitative method called percentage of opening depth. One of the main complications related to these methods is similar to the one presented by Grünheid *et al* (2017): the impossibility to contrast the direct comparison of gray scales between CBCT equipment of different commercial brands. This leads us to determine that it is not possible to make absolute decisions regarding the

maturation stage of MPS or when making the decision to perform RME or SARME by only using these bone density values.

Methodological quality assessment. Methodological quality (risk of bias) assessment is an important step before study initiation usage. Therefore, accurately judging study type is the first priority, and choosing the proper tool is also important (Ma *et al.*, 2020). One of the strengths of this systematic 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 (National Heart *et al.*, 2017).

This differentiates this systematic review from other reviews in which a quality review was not performed (Isfeld *et al.*, 2017; Kao *et al.*, 2018; Mahdian *et al.*, 2019) and another in which intra and inter-operator agreements were used as a variable to evaluate this item (Gao *et al.*, 2022).

Of the 7 included studies, only 1 (Abo Samra & Hadad, 2018) described how the sample size was calculated. Similarly, only 2 studies (Kwak *et al.*, 2016; Kajan *et al.*, 2018) mentioned in detail the demographic background, location, and time period in which they obtained the samples (Table IV).

Another point of vital importance is related to the calibration between the observers, the blinding process and the randomization of the images used to evaluate the intra-observer agreement.

Only one study carried out a calibration process and prior training (Angelieri *et al.*, 2013). 4 studies randomized the images of the second examination (Angelieri *et al.*, 2013; Kwak *et al.*, 2016; Grünheid *et al.*, 2017; Abo Samra & Hadad, 2018) and 4 performed the blinding process (Franchi *et al.*, 2010; Angelieri *et al.*, 2013; Grünheid *et al.*, 2017; Abo Samra & Hadad, 2018) (Table III).

Limitations. The methodology employed in the current review followed well-established guidelines. A possible selection bias was avoided by extensive searches across multiple electronic databases and accessing gray literature publication status restrictions.

Limitations are associated with the included studies methodological differences, characteristics and retrieved data.

Future observational studies should be performed/reported according to guidelines such as STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) (Gao *et al.*, 2022) to increase evidence-based practice information about this topic.

Clinical relevance. Aiming to choose RME in older individuals can lead to consequences such as palatal mucosa ulceration or necrosis, reduction of buccal bone thickness, pain, gingival recession, buccal tipping of the posterior teeth (Bishara & Staley, 1987; Capelozza-Filho *et al.*, 1996; von Elm *et al.*, 2008), fenestration of the buccal cortex (Rungcharassaeng *et al.*, 2007), alveolar bone bending (Timms & Moss, 1971), and buccal root resorption (Wertz *et al.*, 1970). On the other hand, SARME implicates possible unnecessary surgical procedures increasing risk, cost, morbidity, and more days for the patient to recover (Langford & Sims, 1982).

In this context, developing new methods to assess midpalatal suture maturation phase effectively and efficiently is of crucial importance.

CONCLUSIONS

The present study on new methods to assess midpalatal suture maturation revealed some promising and powerful techniques. It is important to mention that few studies were identified, and most of them had methodological and applicability concerns.

Neither of the mentioned methods has sufficient evidence and quality to be recommended as the method of choice to make the clinical decision regarding the development and maturation of the midpalatal suture before maxillary expansion. It is important for clinicians to use a combination of methods when making this important decision.

There is an urgent need for well-designed studies that assess the use of non-invasive techniques and technologies, such as the case of US.

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SHAYANI, A.; SANDOVAL VIDAL, P. & GARAY CARRASCO, I. Métodos recientes utilizados para el análisis del cierre de la sutura palatina mediana previo a expansión maxilar en humanos: Una revisión sistemática. *Int. J. Odontostomat.*, 16(4):504-516, 2022.

RESUMEN: La evaluación de la maduración de la sutura palatina mediana es de suma importancia antes de tomar la decisión clínica sobre si corregir una discrepancia transversal de forma convencional o quirúrgica. Para ello existen métodos como el análisis de la mano y la muñeca, la evaluación de la maduración de las vértebras cervicales y la evaluación mediante radiografías oclusales. El objetivo principal de esta revisión sistemática es identificar en la literatura actual el uso de nuevos métodos y tecnologías para evaluar la maduración de la sutura palatina mediana antes de realizar la expansión maxilar. Se realizó una búsqueda bibliográfica en PubMed, Cochrane Library, SciELO, LILACS, Web of Science y Scopus, utilizando los términos "midpalatal suture", "cranial sutures", "palate, maturation", "interdigitation", "ossification", "maxillary expansion", "evaluation", y "assessment". Se obtuvieron 119 artículos, de los cuales solo 7 cumplieron con los criterios de selección. Estos, describen métodos de evaluación cualitativos, cuantitativos y semicuantitativos. Durante los últimos años, debido a los avances tecnológicos y científicos, se han propuesto varios métodos y técnicas prometedoras para la evaluación de la maduración de la sutura palatina media. La calidad de la evidencia disponible no es suficiente para apoyar el uso de alguno de estos métodos por sí solo. Recomendamos que los profesionales utilicen una combinación de métodos de diagnóstico, que permitan una evaluación objetiva de la maduración de la sutura palatina mediana y ayuden a guiarlos en sus decisiones clínicas.

PALABRAS CLAVE: sutura palatina mediana, osificación, expansión maxilar, suturas craneales.

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