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Review Article

Efficacy of the Cervical Vertebral Maturation Method: A Systematic Review

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Main Points

- The aim of the study is to evaluate whether the cervical vertebral maturation (CVM) method is effective in terms of predicting the growth spurt.
- Most of the previous studies have stated that the CVM method is an effective method for assessing skeletal maturity.
- The CVM method and skeletal analysis of the hand-wrist method do not show significant differences.
- No further radiographic investigations are required other than the lateral cephalogram.

ABSTRACT

Objective: The present systematic review was carried out to evaluate both qualitatively and quantitatively the effectiveness of the cervical vertebral maturation (CVM) method in predicting the pubertal growth spurt.

Methods: PubMed, PMC, Scopus, SciELO, Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science databases were searched. The research included every article published from 1970 to June 2019, featuring the keywords: ("cervical vertebrae" OR ("cervical" AND "vertebrae") AND ("orthodontics" OR "growth and development" OR ("growth" AND "development") OR ("growth"). The Preferred Reporting Items for Reporting Systematic Reviews and Meta Analyses (PRISMA) protocol was adopted, and quality assessments modified from the "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) and the "Standards for the Reporting of Diagnostic Accuracy Studies" (STARD) were performed to conduct this systematic review.

Results: Initially, 1284 articles were found. All the articles were then examined, and 43 studies met the inclusion criteria. Sixteen articles had low-quality scores, 25 had moderate scores, and 2 had high scores. The results showed a moderate to high statistically significant correlation between the CVM and other maturation methods.

Conclusion: Overall, the CVM method can be considered an effective method and may be used with other skeletal indices for the radiographic assessment of skeletal maturity, and also to identify the growth peak in growing patients.

Keywords: Cervical vertebrae, skeletal maturation, growth spurt, systematic review, lateral cephalograms

INTRODUCTION

Timing is considered one of the most important factors for the success of an orthodontic treatment procedure. Recently, the issue of optimal timing has attracted the attention of both researchers and clinicians. Clinical research has shown that greater therapeutic effects are obtained when the mandibular growth peak is included in the treatment period. Therefore, the use of an effective biological indicator to estimate the pubertal growth spurt represents an effective diagnostic tool to treat patients with skeletal discrepancies.

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Typically, patients treated during the growth peak demonstrate significant skeletal effects, while patients treated during the pre-peak period show only dentoalveolar modifications.

Growth assessment is essential for functional orthodontic therapy, which performs its function best in the growing patient. For this reason, it is important to identify the growth peak of patients who undergo this treatment. In addition, other types of treatment should ideally be performed in certain growth stages, for example: the facial mask is ideal for use at a young age, that is, the cervical vertebral stage 2 (CVS2), while orthognathic surgery and implant positioning are not undertaken until growth ceases (CVS6). For this reason, the CVM stage can be a useful indicator in all ages and for a wide range of orthodontic treatments rather than just for functional treatment.

There are several biological indicators to estimate skeletal maturation such as chronological age, dental formula and tooth development, menarche in girls, and the change of voice in boys, height increase, non-invasive biomarkers taken from serum or from gingival crevicular fluid, and skeletal age assessed by radiography. However, the assessment of skeletal age is considered the best biological index related to the growth of facial bones. The classic and most generally used method for assessing skeletal age is the radiographic analysis of the hand-wrist bones, whose validity has been confirmed by numerous scientific studies.[1] However, the main disadvantages of this method are the additional radiograph of the hand necessary to perform the study, and the great difficulty in assessing the staging. Therefore, in recent years, the evaluation of the CVM has been increasingly utilized in determining the skeletal maturity of the growing patient. In 1972, Lamparski[1] introduced this method, allowing skeletal age estimation and eliminating the necessity for extra radiographic exposure since the cervical vertebrae were already recorded on lateral cephalograms taken as a diagnostic pretreatment record. Lamparski's method is predicated on the study of changes in size and shape of the 5 cervical vertebral bodies from the second to the sixth cervical vertebrae (C2-C6) and includes 6 phases of cervical vertebral stage development. However, the utilization of a lead collar to guard the thyroid during the execution of the x-ray can hinder the entire vision of the cervical spine. Thus, in 1995, Hassel and Farman[2] conceived a replacement CVM method, which evaluated the visible lateral profiles of C2, C3, and C4. Furthermore, Baccetti et al.[3] limited the number of cervical vertebrae analyzed during the evaluation of bone age, and published a CVM method to evaluate the maturation of the cervical spine. According to this method, only 3 vertebrae were evaluated—C2, C3, and C4—which are visible even with a protective collar for the thyroid.

Nevertheless, within the literature, there are conflicting results regarding the efficacy of the CVM method for the right identification of the growth spurt.[4,5] To get an accurate summary of the best available evidence when considering the CVM method, a scientific review of the literature seems necessary. Thus, the aim of this systematic review was to throw the spotlight on whether the CVM method is scientifically effective to determine skeletal maturity. The question of our research was: How effective is that the CVM method in terms of predicting the growth spurt?

METHODS

Information Sources

A global electronic database search was conducted to identify relevant publications. The following databases were searched: PubMed, PMC, Scopus, SciELO, Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science. All studies published from 1970 to June 2019 have been included in our research.

Search Study

The electronic search strategy focused on the following key words: ("cervical vertebrae" OR ("cervical" AND "vertebrae") AND ("orthodontics" OR "growth and development" OR ("growth" AND "development") OR "growth"). The Preferred Reporting Items for Reporting Systematic Reviews and Meta Analyses (PRISMA) protocol were adopted for this systematic review[6]; and the PROSPERO registration number of our review was: CRD42020155719.

Study Selection

At the first stage, 2 reviewers (LA and RG) screened the titles and abstracts of the retrieved records independently, duplicate exclusion was performed, and irrelevant articles were excluded. In the next phase, the complete texts of probably relevant papers were evaluated to determine whether they met the eligibility criteria. The inclusion criteria, supported by PICOS format, were: [1] cross-sectional and longitudinal articles in human studies that evaluate qualitatively and quantitatively the CVM method; [2] studies that compare the CVM method with other methods for assessing skeletal age, for example, the hand-wrist maturation (HWM) method, the middle phalanx of the third finger (MP3) method, body height, chronological age, and dental age; and [3] studies that evaluate at least 20 patients. The exclusion criteria were: [1] lack of a transparent description of inclusion/exclusion criteria; [2] studies with inadequate sample sizes; [3] letters to editor, opinion articles, reviews and meta-analyses; and [4] published articles not written in English.

Eligibility was independently assessed by the 2 authors, and any disagreements were resolved by discussion and consent or by a third expert author (MM) who was asked to arbitrate. Any elements that did not meet the inclusion criteria were excluded.

The PRISMA flowchart diagram for the study selection process has been reported (Figure 1).

Data Extraction and Quality Assessment of Selected Studies

Two review authors independently extracted data, consistent with a pre-set protocol. The extracted data included: first author, year of publication, study design, sample composition by sex and age, CVM evaluation method, standard method to evaluate skeletal age, CVM reproducibility statistical analysis, CVM

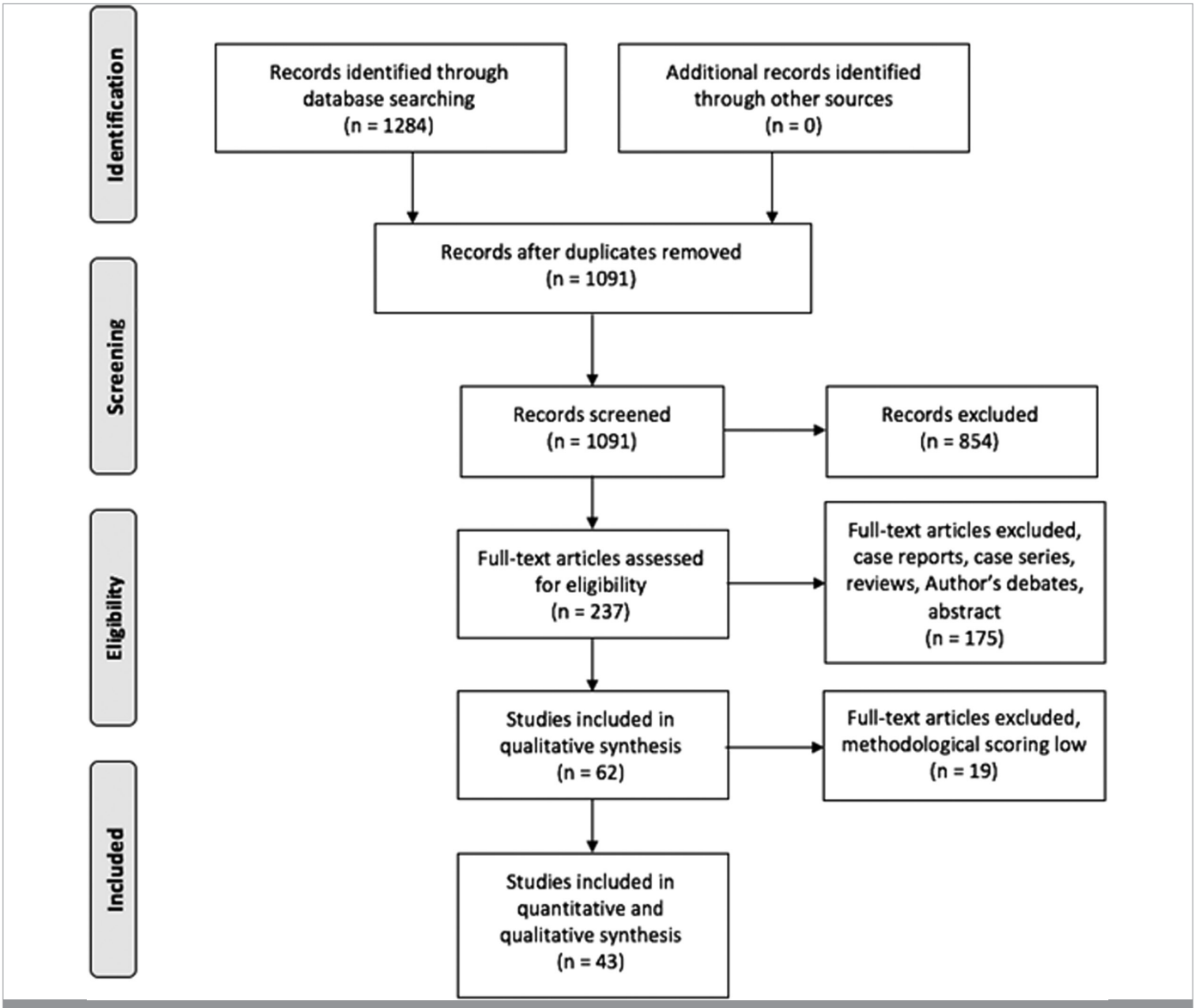

Figure 1. Flow Diagram of the literature search

correlation test versus standard method, CVM and standard method accuracy, and results.

If the data were not clear enough, the authors were contacted by e-mail. Any disagreements between the 2 authors were resolved by discussion and consent or consultation with a third expert author (MM).

Quality Analysis

The methodological quality of the selected articles was assessed using the assessment modified from the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE), and 7 Standards for the Reporting of Diagnostic Accuracy Studies (STARD) (Table 1).[8] When the 2 reviewers were not in agreement, a third investigator was called to succeed in reaching consensus. (MM). The kappa score measuring the extent of agreement was 0.89. Each criterion was assigned a point, if satisfied; no points, if not satisfied. Quality assessment scores ranged from 0 to 12. Articles were classified as "low quality" (score from 0 to 6), "moderate quality" (score from 7 to 10), or "high quality" (score from 11 to 12).

Synthesis Measures and Approach to Synthesis

Due to the heterogeneity between the studies included during this systematic review, particularly within the different methods of evaluating the cervical vertebrae and the lack of specific criteria for random selection, a meta-analysis could not be performed. A narrative summary was performed, illustrating the results of individual studies based on the groups evaluated.

RESULTS

The online database search yielded 1091 potentially relevant titles and abstracts after duplicates were sorted from a complete set of 1284 records. A total of 237 articles were reclaimed for

Table 1. Criteria for assessing quality components in the studies included

		Yes	No
1.	Is the objective clearly formulated?	1	0
2.	Are there key elements of study design early in the paper?	1	0
3.	Was the sample size calculated?	1	0
4.	Does the study report demographic characteristics of the study population?	1	0
5.	Were the sample selection criteria clearly described?	1	0
6.	Does the study describe specifications of material and methods involved including how and when measurements were taken?	1	0
7.	Was there a reliability assessment, with adequate level of agreement intraexaminer or/and interexaminer?	1	0
8.	Were measurements undertaken blindly?	1	0
9.	Does the study give details of methods of assessment (measurements) for each variable of interest?	1	0
10.	Was there a complete and adequate reporting of results, with self-explanatory tables and figures?	1	0
11.	Was there a statistical analysis appropriate for data?	1	0
12.	Was the *P* value stated or confidence intervals provided?	1	0

complete text evaluation, and 43 studies[2,5,9-49] that met the inclusion criteria, were selected from this analysis.

A methodological score was assigned to each study (Table 2). Sixteen articles had low-quality scores, 25 moderate scores and 2 high scores. The characteristics studies of moderate and high-quality scores have been reported (Table 3).

The 27 moderate and high-quality articles were categorized by topics as follows: 16 articles compared the CVM method with the HWM,[2,5,9,13-16,19,21,25-30,32] 2 articles compared the CVM method with chronologic age,[39,40] 1 article compared the CVM method with MP3,[42] 3 articles[46-48] compared the CVM method with dental age, 3 articles compared the CVM method with body height,[43,44,49] 1 article compared the CVM method with both chronologic age and dental age,[37] and finally 1 article compared the CVM method with both HWM and MP3.[24]

Cervical Vertical Maturation Versus Hand-Wrist Maturation

Seventeen moderate and high-quality articles compared the CVM method with the hand-wrist maturation analysis to determine skeletal maturity.[2,5,9,13-16,19,21,24-30,32] Six studies identified a reproducibility of the CVM method between 78% and 98%.[13-15,21,24,25] These studies used the Spearman correlation test or Cohen's Kappa statistic to determine reproducibility values. Thirteen studies described a significant correlation ($.00001 < P < .05$) between the 2 different methods.[2,13,15,16,19,21,24,26,28-30,32,34]

Cervical Vertebral Maturation Versus Chronologic Age

Three moderate-quality studies compared the CVM method with chronologic age.[37,39,40] According to 2 studies there was a statistically significant correlation between age and CVM method ($P < .001$).[37,40] One study, by Litsas et al.,[37] identified a stronger correlation for CVM stage IV for both males ($r = 0.554$) and females ($r = .68$) and a lower correlation for CVM stage III in males ($r = 0.433$; $P < .001$) and for stage II in females ($r = 0.393$; $P < .001$).

Cervical Vertebral Maturation Versus Middle Phalanx of the third finger

Two moderate-quality studies compared the CVM method with the MP3 method.[24,42] All the articles used the Cohen's Kappa statistic to evaluate the agreement between the 2 analyses and established a good relationship between the 6 phases of CVM and the 6 phases of MP3: 0.798 (in females) and 0.794 (in males) respectively.

Cervical Vertebral Maturation Versus Dental Age

Four moderate-quality studies compared the CVM method with dental age.[37,46-48] All articles showed that there was a statistically significant coefficient of correlation ($P < .05$) between dental age and CVM method, greater for males ($r = .703$) than females ($r = 0.499$).

Cervical Vertebral Maturation Versus Body Height

Three moderate-quality studies compared the CVM with body height.[43,44,49] Both articles stated that there was a good statistical correlation coefficient between the 2 methods ($P < .001$) and affirmed that the growth peak occurs between stage III and IV of CVM ($P < .001$), 100% in males and 87% in females.

DISCUSSION

This systematic review, including a comprehensive analysis of 2 high- and 25 moderate-quality studies, found that the CVM method can be considered as an effective method similar to the skeletal analysis of the hand-wrist method. In addition, our initial research question, namely "How effective is the CVM method in terms of predicting the growth spurt?" revealed the answer that the CVM method can be considered an effective tool in determining the growth spurt in growing patients.

The literature search initially uncovered 1284 publications, but only 43 quantitative studies were qualified for evaluation in this review. Such a finding is common when performing systematic reviews, as the initial and deliberate search of the literature was designed to include as many studies as possible in order not

Table 2. Quality assessment of selected studies

Articles	1	2	3	4	5	6	7	8	9	10	11	12	Total	Quality
Hassel and Farman[2]	0	0	0	1	1	1	1	0	0	1	1	1	7	Moderate
Beit et al.[5]	1	1	0	1	1	1	1	1	1	1	1	1	11	High
Mito et al.[9]	1	1	0	0	1	0	1	0	1	1	0	1	7	Moderate
Wong et al.[10]	1	0	0	1	0	0	1	0	1	0	1	1	6	Low
San Romàn et al. [11]	1	0	0	1	0	0	1	0	1	0	1	1	6	Low
Caldas et al.[12]	1	1	0	1	0	0	0	0	1	0	1	1	6	Low
Soegiharto et al.[13]	1	1	0	1	0	0	1	0	1	1	1	1	8	Moderate
Gandini et al.[14]	1	0	0	0	1	1	1	0	1	0	1	1	7	Moderate
Lai et al.[15]	1	1	0	1	0	0	1	1	1	1	1	1	8	Moderate
Pichai et al.[16]	1	1	0	0	0	1	0	0	1	1	1	1	7	Moderate
Kamal et al.[17]	0	0	0	1	0	0	0	0	1	0	1	1	4	Low
Stiehl et al.[18]	1	0	0	0	0	0	1	0	1	1	1	1	6	Low
Soegiharto[19]	1	1	0	1	0	0	1	0	1	1	1	1	8	Moderate
Byun et al.[20]	0	0	0	1	0	0	0	0	0	1	1	1	4	Low
Danaei et al.[21]	1	1	0	0	0	1	1	1	0	1	1	0	7	Moderate
Durka-Zając et al.[22]	1	1	0	0	0	0	0	0	0	0	1	0	2	Low
Carinhena G et al.[23]	1	1	0	0	0	0	1	0	0	1	1	0	5	Low
Pasciuti et al.[24]	1	1	0	0	0	0	1	0	1	1	1	1	7	Moderate
Uysal et al.[25]	1	1	0	1	1	1	1	1	1	1	1	1	11	High
Chatzigianni et al.[26]	1	1	0	0	1	1	1	0	1	1	1	1	9	Moderate
Chang et al.[27]	1	1	0	1	1	1	0	0	1	1	1	1	9	Moderate
Heravi et al.[28]	1	1	0	1	1	1	0	0	1	1	1	1	9	Moderate
Mito et al.[29]	1	1	0	1	1	0	0	0	1	1	1	1	8	Moderate
Turkoz et al.[30]	1	1	0	1	1	0	0	0	0	1	1	1	7	Moderate
Varshosaz et al.[31]	1	1	0	1	0	0	0	0	0	1	1	1	6	Low
Litsas et al.[32]	1	1	0	1	1	0	1	0	1	1	1	1	9	Moderate
Flores-Mir et al.[33]	0	1	0	0	0	0	0	0	0	1	1	1	4	Low
Mahajan et al.[34]	0	0	0	1	0	0	0	0	0	1	0	1	3	Low
Altan et al.[35]	1	1	0	0	0	1	0	0	1	1	1	0	6	Low
Safavi et al.[36]	1	0	0	0	0	0	1	1	0	0	1	1	5	Low
Litsas et al.[37]	1	1	0	1	1	0	1	0	1	1	1	1	9	Moderate
Ramirez-Velásquez[38]	1	1	0	0	0	0	1	0	0	0	1	0	3	Low
Montasser et al.[39]	1	1	0	1	1	0	1	0	1	1	1	1	9	Moderate
Singh et al.[40]	1	1	0	1	1	1	1	0	1	1	1	1	10	Moderate
Prasad et al.[41]	1	0	0	0	0	0	0	0	0	0	1	0	2	Low
Ayach et al.[42]	1	1	0	1	1	0	1	0	0	0	1	1	7	Moderate
Franchi et al.[43]	1	1	0	0	1	0	1	0	1	1	1	1	7	Moderate
Hosni et al.[44]	1	1	0	1	1	1	1	0	1	1	1	1	10	Moderate
Felemban et al.[45]	1	1	0	1	0	0	0	0	0	1	0	0	4	Low
Kocasarac et al.[46]	1	1	0	1	1	1	1	0	1	1	1	1	10	Moderate
Camacho-Basallo et al.[47]	1	1	0	1	1	1	1	0	1	1	1	1	10	Moderate
Cossellu et al.[48]	1	1	0	1	1	1	1	0	1	1	1	1	10	Moderate
Montasser et al.[39]	1	1	0	1	1	1	1	0	1	1	1	1	10	Moderate

Table 3. Summary of the main characteristics of the 27 studies of moderate and high quality selected for the systematic review

Author/Year/Study design	Sample Size/Male-Female	Age	CVM Evaluation Method	Standard Method	CVM Reproducibility and Statistical Analysis	CVM Correlation Test Versus Standard Method	CVM and Standard Method Accuracy	Results
Hassel and Farman,[2] 1995, longitudinal study	220 (110 boys, 110 girls)	8-18 years	Hassel and Farman	Fishman (HWM)	Not evaluated	Not evaluated	Not evaluated	By using the lateral profiles of the second, third and fourth cervical vertebrae, it was possible to develop a reliable ranking of patients according to the potential for future adolescent growth potential.
Beit et al.,[5] 2013, cross-sectional study	730 (352 boys, 378 girls)	6-18 years	Not cited	Greulich and Pyle (HWM)	ANOVA	Pearson correlation coefficent	Not evaluated	The agreement between the HWM method and calculated skeletal age was modest and weaker than the agreement between the HWM and chronologic age.
T. Mito et al.,[9] 2002, longitudinal study	176 girls	7-15 years	Hassel and Farman	Tanner–Whitehouse (HWM)	*t*-test	Not evaluated	Not evaluated	Cervical vertebral bone age reflects skeletal maturity because it approximates bone age, which is considered to be the most reliable method for evaluating skeletal maturation.
Soegiharto et al.,[13] 2008, cross-sectional study	2167 (951 boys, 1216 girls)	8-17 years	Baccetti et al.	Fishman (HWM)	Cohen's Kappa	Not evaluated	ROC analysis	The CVM index and the SMI are valid methods to predict the pubertal growth peak.
P. Gandini, et al.,[14] 2006, longitudinal study	30(14 boys, 16 girls)	7-18 years	Baccetti et al.	Bjork Grave and Brown (HWM)	Not evaluated	Cohen Kappa concordant index	Not evaluated	The results show a concordance of 83.3% between the HWM method and the CVM method.
E. Lai et al.,[15] 2008, longitudinal study	709 (379 girls, 330 boys)	8-18 years	Baccetti et al.	NTUH-SMI method (HWM)	Spearman correlation coefficient	Spearman correlation test	Not evaluated	The Spearman's rank correlation (0.910 for males and 0.937 for females) confirmed a strong and significant correlation between CVMS and NTUH-SMI systems ($P < .001$).

S. Pichai, et al.,[16] 2014, longitudinal study	72	7-16 years	Baccetti et al.	Bjork Grave and Brown (HWM)	Not evaluated	Mann–Whitney test	Not evaluated	There was no significant difference between the HWM analysis and the CVM analysis for assessing skeletal maturation.
Soegiharto, et al.,[19] 2008, cross-sectional study	1422 (648 boys, 774 girls)	8-18 years	Baccetti et al.	Fishman (HWM)	Cohen's Kappa	Bland and Altman's method	ROC analysis	CVM shows a good intra-operator agreement. The K index is 0.85 for males and 0.97 for Indonesian females. The correlation index also shows a good correlation between the 2 methods of analysis.
S. Danaei et al.,[21] 2014, cross-sectional study	178 (90 girls, 88 boys)	8-17 years	Hassel and Farman	Fishman (HWM)	Cohen's Kappa	Not evaluated	Not evaluated	CVM method can be a valuable substitute for hand-wrist radiography in patients with short stature.
Pasciuti, et al.,[24] 2013, longitudinal study	100	6-18 years	Baccetti et al.	Tanner–Whitehouse (HWM) / Rajagopal e Kansal (MP3)	Cohen's Kappa	Not evaluated	Not evaluated	Complete agreement among the 3 methods was observed in 70% of the analyzed samples. The CVM method has the advantage of not necessitating an additional radiograph.
Uysal, et al.,[25] 2006, cross-sectional study	503 (213 boys, 290 girls)	5-24 years	Hassel and Farman	Bjork Grave and Brown (HWM)	Spearman correlation coefficient	Spearman correlation test	Not evaluated	CVM showed high reproducibility. The correlations between CVM and HWM maturation were 0.86 for sexes combined, 0.78 for male, and 0.88 for female subjects. All were significant at $P < .001$.
Chatzigianni, et al.,[26] 2009, longitudinal study	98 (40 boys, 58 girls)	8-17 years	Bookstein	Sempè (HWM)	*t*-test	Not evaluated	Not evaluated	Shape alone could not predict skeletal maturation better than chronologic age. C1 showed lower correlations with hand-wrist maturation.
Chang, et al.,[27] 2001, cross-sectional study	503 (244 boys, 259 girls)	8-18 years	Hassel e Farman	Fishman (HWM)	Wilcoxon test	Spearman correlation test	Not evaluated	The intra-judge and inter-judge reliability test indicated no significant difference for CVM ($P = .500$) and HWM ($P = .500$).

Table 3. Summary of the main characteristics of the 27 studies of moderate and high quality selected for the systematic review (*Continued*)

Author/Year/Study design	Sample Size/Male-Female	Age	CVM Evaluation Method	Standard Method	CVM Reproducibility and Statistical Analysis	CVM Correlation Test Versus Standard Method	CVM and Standard Method Accuracy	Results
Heravi et al.,[28] 2011, cross-sectionalstudy	47 (20 boys, 27 girls)	10-15 years	Hassel and Farman/ San- Roman/ Mito et al.	Tanner–Whitehouse (HWM)	Not evaluated	Pearson correlation test	Not evaluated	There was no significant correlation between CVM and HWM in 10-13-y.o. boys ($P < .05$).
Mito et al.,[29] 2003, cross-sectional study	40 girls	>7 years	Mito et al.	Tanner–Whitehouse (HWM)	*t*-test	Not evaluated	Not evaluated	The study produced a method to predict mandibular growth potential with latero-lateral x-rays only.
Turkoz et al.,[30] 2017, retrospective study	324 (167 girls, 157 boys)	7–17 years	Turkoz C. et al.	Greulich e Pyle (HWM)	Not evaluated	Pearson correlation coefficient	Not evaluated	The study developed a formula for evaluating the skeletal age that is reliable and applicable to both male and female subjects.
Litsas, et al.,[29] 2010, cross-sectional study	393	8–18 years	Hellsing	Chronologic age/Grave and Brown (HWM)	*t*-test	Spearman correlation coefficient	Not evaluated	The correlation coefficient between CVM and chronologic age is $r = 0.73$ for girls and $r = 0.72$ for boys
Litsas, et al.,[37] 2016, cross-sectional study	255 (145 girls, 110 boys)	8-18 years	Baccetti et al.	Chronologic age Demirjian et al. (dental age)	*t*-test	Spearman correlation coefficient	Not evaluated	Chronological and dental age showed a high correlation for both gender ($r = 0.741$ for boys, $r = 0.770$ for girls, $P < .001$). The strongest correlation was for the CVM Stage IV for both males ($r = 0.554$) and females ($r = 0.68$).
Montasser[39], 2017, cross-sectional retrospective study	Not evaluated	7-18 years	Hassel and Farman	Not evaluated	ANOVA	Not evaluated	Not evaluated	Racial differences in CVM II- III-IV-V stages between females and males have been highlighted.
Singh, et al.,[40] 2015, cross-sectional study	80 (40 boys, 40 girls)	10-19 years	Hassel e Farman	Chronologic age	Not cited	Pearson correlation coefficient	Not evaluated	The correlation coefficient CVM and chronologic age is $r = 0.855$ ($P < .001$).
Ayach et al.,[42] 2018, cross-sectional study	50 (21 boys, 29 girls)	8-16 years	Not cited	Perinetti et al. (MP3)	Cohen's Kappa	Spearman correlation coefficient	Not evaluated	The Spearman test reveals a significant correlation between MP3 and the fourth cervical vertebra.

L. Franchi et al.,[43] 2000, longitudinal study	24 (15 girls, 9 boys)	3-18 years	Lamparski	Body height	ANOVA	Not evaluated	Not evaluated	CVM appears to be an appropriate method for the appraisal of mandibular skeletal growth. This provides helpful indications concerning treatment timing of mandibular deficiencies.
S. Hosni et al.,[44] 2018, prospective study	108	8-18 years	Beccetti et al.	Body height	Cohen's Kappa	Not evaluated	Not evaluated	The peak in statural height growth velocity occurred at CVM stage III ($P < .001$). This study suggests that there is a significant relationship between CVM stage and statural height velocity.
Kocasarac et al.,[46] 2016, retrospective cross-sectional study	116 (43 boys, 73 girls)	8-28 years	Lamparski	Demirjian al. (dental age)	Cohen's Kappa	Spearman correlation coefficient	Not evaluated	A strong correlation between the mineralization of the third molar in males (r= 0,723) and weak for females ($r = 0.371$) was evaluated.
Camacho-Basallo et al.,[47] 2016, cross-sectional study	202 (104 boys, 98 girls)	12 years	Hassel e Ferman	Demirjian al. (dental age)	Not cited	Spearman correlation coefficient	Not evaluated	A correlation between the 2 methods of analysis was assessed, regardless of gender.
Cossellu, et al.,[48] 2014, cross-sectional study	500	10-20 years	Hassel e Ferman	Demirjian al. (dental age)	Cohen's Kappa	Spearman correlation coefficient	Not evaluated	A significant correlation between dental age and CVM was assessed (0.081-0.085).
Montasser,[49] 2019, longitudinal study	26 (14 boys, 12 girls)	9-15 years	Not cited	Not cited	*t*-test	Not evaluated	Not evaluated	CVM3 indicates the pubertal growth peak and CVM2 indicates that the peak is not yet reached.

HWM, hand-wrist maturation; CVM, cervical vertebral maturation; CVMS, cervical vertebral maturation stage; SMI, skeletal maturation index; TW3, Tanner–Whitehouse method; NTUH-SMI, National Taiwan University Hospital Skeletal Maturation Index; ROC, indicates Receiver Operating Characteristics; MP3, middle phalanx of the third finger.

to inadvertently miss or overlook any study. The selection was made systematically as illustrated in the Materials and Methods section. Sixteen studies were judged to be of low quality and therefore did not contribute to the evidence.

Only few studies included in our review used rigid parameters regarding the sample selection. Chang et al.[27] stated that the samples analyzed were chosen randomly; however, the specific criteria for random selection have not been described. Only Uysal et al.[25] established rigorous selection criteria, taking under consideration factors like lack of relative medical records, race, systemic diseases, and medical syndromes. Considering the influence of these co-factors on general growth and development, we believe that their strict selection criteria can contribute to the article substantial scientific evidence.

The scientific evidence of our sample was medium/high due to the presence of errors occurring in most of the studies analyzed, such as the lack of standardization in the procedures performed for data collection, the different age groups included in the studies, and the different methods of analysis of the cervical vertebrae. These factors can influence the results of our research. However, this should not be a major issue with regard to the quality of the studies. A detailed analysis of the articles and very selective inclusion criteria lead to a result which is useful internationally as scientific evidence. The study by Heravi et al.[28] showed different levels of correlation between 4 different CVM methods and therefore the same HWM (Tanner–Whitehouse) in a single sample. This result is consistent with several publications that identified different correlations between CVM and HWM using different methods of study of the cervical spine.[25,27] Therefore, the accuracy, correlation and reproducibility of this approach can be influenced by the method of analysis. In fact, there is a good sort of variety of CVM methods, including an easy qualitative analysis of the form and vertebral dimension, quantitative measures of the vertebral shape (some of which are limited to distances and ratios of height and width), depth of the lower concavity, and other more specific measurements.

In the literature, there are few studies that systematically analyze the efficacy of the CVM method. However, a review of the literature, similar to the present one, was presented by Santiago et al.[4] in 2012. Opposed to our study, the authors affirmed that the CVM method did not demonstrate a good correlation with the HWM method and its effectiveness could not be proved.

The longitudinal study is the best method to carry out research on craniofacial growth and development since it can provide a continuous comparison with respect to the development of the patient. However, most of the studies included in our review were founded on cross-sectional data that have limitations in terms of growth analysis. In fact, transversal sampling is relatively insensitive to individual variability, contrary to what happens in a longitudinal sample. Unfortunately, according to the study by Soegiharto et al.,[19] the difficulties of obtaining a large sample size tend to preclude this methodology.

Many radiological methods for evaluating skeletal age have been described and evaluated, and of all of them, hand-wrist radiography is believed the gold standard in the scientific literature. However, some authors recommend abstaining from hand-wrist radiography because of the extra x-ray exposition in growing patients.[3,13,14] For this reason, in recent years, the assessment of skeletal age based on vertebral morphology as shown by latero-lateral teleradiography has increasingly established itself in the clinical setting.

Anyhow, the evaluation of skeletal age based on the cervical spine has been critically examined by many authors and its clinical validity has been seriously questioned.[4,5,50] Most studies citing highly reproducible results for the CVM method (> 90%) used cervical vertebrae tracings and not actual radiographs during the spinal analysis steps, thus introducing bias in the results. The authors conducted a study to evaluate the reliability of CVM on a sample of 90 teleradiographs obtaining 62% of intra-observer agreement. This result corresponds to a "moderate" agreement. Nonetheless, the authors interpreted this result as poor proof of reproducibility. On the other hand, numerous articles included in our review reported a reproducibility of the CVM method as between 85% and 98% using actual radiographs of the patients.[13-15,21,24,25]

Several studies have described a significant correlation ($.001 < P < .05$) between HWM and CVM.[15,25,27] Other articles included in our review confirmed that bone age determined by the CVM method is an effective tool for the evaluation of skeletal maturity in the same way as hand-wrist radiograph, which represents the most established method of analysis in literature.[2,43] Thus, these studies showed a high correlation index between the 2 methods. Furthermore, Franchi et al.[43] and Baccetti et al.[3] proved the efficacy of the CVM method in predicting the pubertal growth spurt using hand-wrist radiographs as a concern. Nevertheless, these studies were conducted retrospectively, therefore their validity on the current population could be queried. However, a prospective study was performed recently on a current sample, which demonstrated that the CVM method was an efficient tool to predict the pubertal growth spurt and body growth.[44] Examining the high correlation between the CVM and the HWM methods indicated in the previously cited articles,[2,9,15,25,27,43] it can be inferred that CVM classification has the potential to replace HWM in assessing bone maturation and thus eliminate additional hand and wrist radiography which has been widely contested.[51,52]

According to Beit et al.,[5] chronological age is not a good indicator for assessing a patient's stage of development. In fact, there are many factors that influence a patient's body growth and maturation. These factors include race, genetic conditions, climate, nutrition, hormonal disorders, and environmental influences. For this reason, Montasser et al.[39] recommend taking racial and sex differences into account when using CVM as an indicator of skeletal maturity.

One article included in our review showed that there was a statistically significant correlation between chronological

age and skeletal maturity, determined by the analysis of the cervical vertebrae (r = 0.771).[37] All other studies regarding the correlation between dental age and the CVM method also demonstrated, through the Spearman correlation test, a statistically significant correlation between the 2 methods ($P < .001$).[46-48]

According to the study by Franchi et al.,[43] the accuracy of the CVM method provides useful indications in the identification of the mandibular growth peak, with the additional advantage of decreasing the exposure of patients to x-rays.

Some studies included in our review do not support the use of the CVM method if it is not used concurrently with other skeletal indicators for the precise determination of skeletal maturity.[26,28] However, most of the studies have stated that the CVM method is an effective method for assessing skeletal maturity ($P < .05$).[2,9,13-15,21,24,25,27,29,37,43,44,47,48]

CONCLUSION

With a moderate/high level of evidence:

- The CVM method can be considered as an effective tool to determine the growth spurt in growing patients
- The CVM method can be considered in the same way as the skeletal analysis of the hand-wrist method
- There is no clinical reason for submitting the growing patient to a further radiograph of the hand and wrist since the cervical vertebrae are already recorded on lateral cephalograms.

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