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Review Article

Reliability of cervical vertebral maturation compared to hand-wrist for skeletal maturation assessment in growing subjects: A systematic review

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Abstract.
BACKGROUND: Radiographic methods to assess skeletal maturity (SM) have a key role in adolescent idiopathic scoliosis (AIS) management, allowing to predict risk of spinal curve progression. Cervical vertebral maturation (CVM) has been recently introduced as an alternative tool to assess skeletal maturity; however, its clinical role is still debated.
OBJECTIVE: This systematic review aimed to investigate the reliability of CVM in the SM assessment of growing subjects, comparing it to hand wrist maturation (HVM).
METHODS: PubMed, Scopus, and Web of Science databases were systematically searched from inception until 31st December 2020 to identify observational studies presenting: growing subjects as participants; CVM methods as intervention; HVM methods as comparator; reliability for SM assessment as outcome. A 10-item quality tool has been used to assess study quality.
RESULTS: Out of 205 papers, 12 papers were included in the data synthesis. We classified 10 studies (83.3%) as medium-quality studies and 2 studies (16.7%) as high-quality studies. Eight studies reported a significant correlation between CVM Baccetti and different HWM methods.
CONCLUSION: Taken together, these findings suggested that CVM might be considered as reliable SM assessment method compared to HWM in growing subjects. However, further studies are warranted to confirm these findings.

Keywords: Growth and development, scoliosis, age determination by skeleton, spine, radiology

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1. Introduction

Skeletal maturation (SM) is a physiological sequence of body changes characterized by phenomenon in which timing could vary among growing subjects due to a different biologic clock [1]. As a consequence, both somatic maturity and chronological age have been considered as poor indicators of SM, given the wide variation in the onset of pubertal growth spurt (PGS) [2,3].

The SM assessment is routinely used in the clinical practice of physical and rehabilitation medicine (PRM), orthopedics, pediatrics, and orthodontics to plan an adequate treatment in growing subjects [4–6]. In this context, SM assessment plays a key role in adolescent idiopathic scoliosis (AIS) management, where an optimal evaluation of skeletal discrepancies may allow PRM physicians to assess the risk of curve progression [7], which might lead to a better postural assessment and consequently to an adequate rehabilitation plan [8]. To date, it has been shown that during the PGS, an increase of scoliosis curvature is exponentially correlated with a severe risk of progression [9].

Furthermore, the spinal curve seems to progress more during the first 2 year of puberty, with several implication on therapeutic management [9–12]. The overdiagnosis and overtreatment of scoliosis have been considered as rising problems in recent years, taking into account that there is still no agreement in the literature on the effectiveness of bracing or exercise on the curvature progression in adolescents [13]. However, a Cobb's angle of 20°–25° has been defined as a threshold for bracing, whereas a surgical approach should be proposed for more severe curves [9–12]. In this context, SM assessment has a crucial role in the curve progression risk in growing subjects [14]. Therefore, prescription of bracing or indications for surgery should be based on a precise scoliosis screening and on an adequate SM evaluation to perform a treatment, aimed at reducing functioning impairments and disabling sequelae related to long term clinical complications of the disease [15–17].

In this scenario, the gold standard for assessing SM is the hand wrist maturation (HWM), a method that needs an extra hand and wrist X-ray [18–25]. However, this technique has several limitations, from additional radiation exposure to burden in terms of sanitary costs related to the additional X-rays [26]. Thus, starting from the spine X-ray, among the other SM assessments proposed to overcome this problem, cervical vertebral maturation (CVM) has been started to be frequently used in the common clinical practice [27–29].

In 1972, Lamparski [27] introduced the CVM as a novel SM evaluation method, that was firstly revised by Hassel and Farman [28], which improved the evaluation of the visible lateral profiles of the second, third and fourth cervical vertebrae, and secondly by Baccetti et al. [29], assessing the shape of the inferior border of C2, C3, and C4, thus providing different CVM stages (CVMS). However, to date, there is no agreement on the correlation among CVMS, HWM stages and the PGS.

The overall growth velocity is related to SM, which might be determined by hand and wrist X-ray evaluation using methods based on both relative growth velocity and percentage of residual growth remaining, instead of using methods aimed at determining the skeletal age [30]. Thus, SM assessment should be widely used in clinical practice by PRM physicians and orthodontists. However, albeit chronological age could not be considered as a valid predictor of skeletal growth velocity, skeletal age and SM are often wrongly not distinguished in the literature [31–33]. Furthermore, findings of CVM reliability compared to HWM are still controversial in growing subjects [31–33]. In particular, Santiago et al. [31] did not consider CVM method as appropriate for the SM assessment; conversely, Cericato et al. [32] and Szemraj et al. [33] have more recently reported that CVM might be considered as reliable to evaluate SM, although CVM Hassel and Farman method was not investigated [33].

To date, although CVM is a technique commonly used in the clinical practice, there is still a lack of knowledge on its usefulness in assessing SM in growing subjects to have indications useful for the rehabilitative management of AIS. Therefore, the present systematic review aimed to evaluate the available scientific literature on the reliability of CVM methods compared to HWM methods to assess SM in growing subjects.

2. Materials and msethods

2.1. Search strategy

PubMed, Scopus, and Web of Science databases were systematically searched from inception until 31st December 2020 to identify the studies published in the scientific literature, according to each specific thesaurus, adopting the strategies depicted in Table 1.

This systematic review has been performed in accordance with the PRISMA statement [34] and has been registered on PROSPERO with registration number CRD42020220867.

Table 1
Search strategy for the present systematic review

PubMed
("hand-wrist") AND ("cervical vertebral maturation" OR "vertebra" OR "vertebral" OR "cervical vertebral") AND ("skeletal maturation" OR "maturation" OR "skeletal maturity" OR "maturity" OR "growth peak" OR "growth spurt" OR "pubertal growth peak" OR "pubertal growth spurt" OR "ossification") AND ("pubertal stage" OR "growing age" OR "pubertal" OR "growth" OR "children" OR "adolescents")
Scopus
TITLE-ABS-KEY(("hand-wrist") AND ("cervical vertebral maturation" OR "vertebra" OR "vertebral" OR "cervical vertebral") AND ("skeletal maturation" OR "maturation" OR "skeletal maturity" OR "maturity" OR "growth peak" OR "growth spurt" OR "pubertal growth peak" OR "pubertal growth spurt" OR "ossification") AND ("pubertal stage" OR "growing age" OR "pubertal" OR "growth" OR "children" OR "adolescents"))
Web of Science
TS = (("hand-wrist") AND ("cervical vertebral maturation" OR "vertebra" OR "vertebral" OR "cervical vertebral") AND ("skeletal maturation" OR "maturation" OR "skeletal maturity" OR "maturity" OR "growth peak" OR "growth spurt" OR "pubertal growth peak" OR "pubertal growth spurt" OR "ossification") AND ("pubertal stage" OR "growing age" OR "pubertal" OR "growth" OR "children" OR "adolescents"))

2.2. Selection criteria

Two reviewers (MF, CC) independently screened all potential articles for eligibility after duplication removal. Any disagreement has been resolved through discussion or, if necessary, by a consultation of a third reviewer (AdS).

All observational studies were assessed for eligibility according to the following PICO model:

1. P) Participants consisted of growing subjects;
2. I) Intervention consisted of CVM methods commonly used in the clinical practice for the SM assessment;
3. C) Comparator consisted of HVM methods commonly used in the clinical practice for the SM assessment;
4. O) Outcome measure consisted of the reliability of CVM compared to HWM for the SM assessment.

We included observational cross-sectional studies, written in English language, and available in full text. We excluded studies investigating chronological, skeletal or dental age as primary outcomes, book chapters, posters, conference abstracts, and studies involving animals.

2.3. Data extraction

Data extraction was performed by two reviewers independently (MF, CC), assessing eligible full-text papers through a customized data extraction form in Microsoft Excel. Key data were extracted from each study relevant to the specific research questions. We resolved disagreement by a consensus or by the decision of a further experienced reviewer (AdS).

The following data were extracted: 1) authors; 2) scientific journal; 3) publication year; 4) Nationality of study participants; 5) population and number of patients; 6) age of subjects; 7) SM and CVM assessment methods; 8) HWM method; 9) main findings.

2.4. Data synthesis

Each selected study has been synthetized describing both extracted data and studies' characteristics. Then, the study quality was assessed by a 10-item quality scoring adapted by Santiago et al. [31]. The 10 criteria for the quality scoring of the studies included were the following ones: 1. Adequate presentation of study objective; 2. Adequate presentation of study design; 3. Clear description of eligibility criteria of study population; 4. Adequate presentation of methods of assessment; 5. Sample size calculation; 6. Presentation of demographic characteristics of the study population; 7. Adequate reliability assessment; 8. Appropriate statistical analysis; 9. Adequate reporting of results with tables and/or figures; 10. Declared p-values in the results. All of them could be scored as 0 (absence of the criterion) to 1 (presence of the criterion).

Accordingly, two reviewers independently (MF, AdS) provided all studies with a score for the 10 assessment criteria. In case of disagreement, a consensus was achieved involving a further experienced reviewer in the decisional process (MM). Therefore, the studies included were classified as low-quality studies (0–4 points), medium-quality studies (5–7 points) or high-quality studies (8–10 points).

3. Results

Out of 205 search results, 26 duplicates were removed, and 179 studies were considered as eligible for inclusion and screened for title and abstract. Out of these, we included 38 papers for full-text screening. After the exclusion of 26 articles (25 not respecting eligibility criteria and 1 simultaneously published in two different scientific journals), 12 papers [35–46] were in-

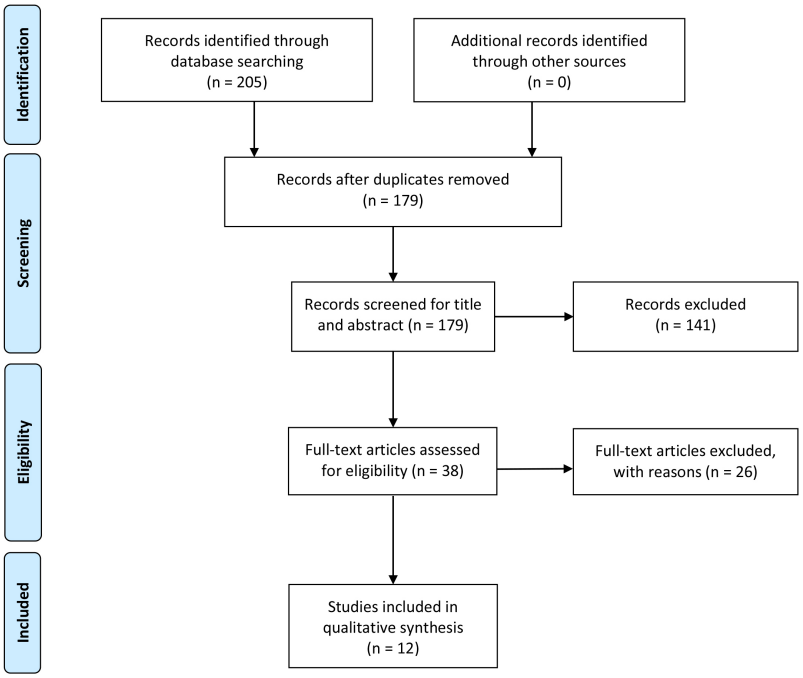

Fig. 1. PRISMA flow diagram.

cluded in the synthesis (see Fig. 1 for the PRISMA flow diagram and Table 2 for further details on the exclusion reasons of 167 articles).

The studies included in the present systematic review [35–46] have been published in the last 19 years (from 2002 to 2017). Most of them (58.3%) were performed in Asia (2 in India [40,46], 2 in Turkey [39,45], 1 in Iran [38], 1 in Hong Kong [41], 1 in Qatar [43]), 4 (33.3%) in Europe (2 in Spain [37], 1 in Italy [36], 1 in Poland [35]), and 1 study (8.3%) from Canada [42].

Considering the study population, all 12 studies [35–46] assessed patients of both sexes, although Pichai et al. [40] did not specify the exact number of males and females included. Study cohorts ranged from 30 [35–37] to 958 [44] subjects, while age of study participants widely varied from 5 [44,45] to 24 [45] years old; information on subjects age was missing in the study of Flores-Mir et al. [42].

Two studies [37,40] assessed more than one SM method and were described in detail, accordingly.

Pichai et al. [40] evaluated CVM Baccetti [29] vs HWM Grave and Brown [23] and CVM Hassel and Farman [28] vs HWM Grave and Brown [23]; Camacho-Basallo et al. [37] evaluated CVM methods compared to different HWM methods: CVM Baccetti [29] vs HWM Grave and Brown [23]; CVM Baccetti [29] vs HWM Fishman [21]; CVM Hassel and Farman [28] vs HWM Grave and Brown [23]; CVM Hassel and Farman [28] vs HWM Fishman [21].

In particular, 10 studies evaluated CVM Baccetti [29], compared with different HWM methods: Bjork [35,36], HWM Grave and Brown [37–40], HWM Fishman [37, 41,42] and HWM Hägg and Taranger [43]. Six papers evaluated CVM with Hassel and Farman, comparing it with HWM Grave and Brown [37,40,44,45] and HWM Fishman [37,46].

According to the abovementioned 10-item quality scoring for the studies included, 2 studies (16.7%) were classified as high-quality studies [44,45] and 10 studies (83.3%) as medium-quality studies [35–43,46]. No low-quality studies were included in the present systematic review (see Table 3 for further details on quality scoring for each assessment criteria). A meta-analysis could not be performed due to the high clinical heterogeneity of the studies included in terms of variability in both SM assessment and study participants characteristics [47]. The main characteristics of the 12 articles included [35–46] are described in detail in Table 4 and in the following paragraphs.

3.1. CVM methods vs HWM methods

3.1.1. CVM Baccetti vs HWM Bjork

Two papers [35,36] compared the CVM Baccetti method [29] with HWM Björk method [20], both show

Table 2
Reasons for article exclusion by the present systematic review

*Articles excluded after title and abstract screening phase ($n = 141$)**	
Not population of interest	14 (9.9%)
Not intervention of interest	37 (26.2%)
Not comparison of interest	29 (20.6%)
Not outcome of interest	79 (56.0%)
Articles excluded after full-text screening phase ($n = 26$)	
Not population of interest	2 (7.7%)
Not intervention of interest	3 (11.5%)
Not comparison of interest	2 (7.7%)
Not outcome of interest	13 (50.0%)
Full-text unavailability	2 (7.7%)
Full-text in a language different than English	3 (11.5%)
Simultaneous publication in two scientific Journals	1 (3.9%)

The exclusion of the articles followed the PICO model defined in the Methods Section. Data are expressed as counts (percentages). $*$ = Papers were excluded also for more than one reason during the title and abstract screening phase.

Table 3
Quality assessment of the studies included in the present systematic review

Articles	Criteria for the quality scoring										Score	Quality level
	1	2	3	4	5	6	7	8	9	10		
Durka-Zając et al. [5]	1	0	1	1	0	0	1	1	0	1	6	Medium quality
Gandini et al. [36]	1	0	0	1	0	0	1	1	1	0	5	Medium quality
Camacho-Basallo et al. [37]	1	0	1	0	0	1	1	1	1	1	7	Medium quality
Hoseini et al. [38]	1	0	1	1	0	0	1	1	1	0	6	Medium quality
Litsas et al. [39]	1	0	1	1	0	0	1	1	1	1	7	Medium quality
Pichai et al. [40]	1	0	1	0	0	0	1	1	1	1	6	Medium quality
Alkhal et al. [41]	1	0	0	1	0	0	1	1	1	0	5	Medium quality
Flores-Mir et al. [42]	1	0	0	0	0	0	1	1	1	1	5	Medium quality
Wong et al. [43]	1	0	0	1	0	0	1	1	1	0	5	Medium quality
San Roman et al. [44]	1	0	1	1	0	1	1	1	1	1	8	High quality
Uysal et al. [45]	1	1	1	1	0	1	1	1	1	1	9	High quality
Mahajan et al. [46]	1	0	0	1	0	0	1	1	1	1	6	Medium quality

Criteria for the quality scoring of the studies included: 1. Adequate presentation of study objective; 2. Adequate presentation of study design; 3. Clear description of eligibility criteria of study population; 4. Adequate presentation of methods of assessment; 5. Sample size calculation; 6. Presentation of demographic characteristics of the study population; 7. Adequate reliability assessment; 8. Appropriate statistical analysis; 9. Adequate reporting of results with tables and/or figures; 10. Declared p-values in the results.

ing consistent results: Durka-Zając et al. [35] reported a strong statistically significant Pearson's correlation between the two methods in both sexes ($r = 0.98$; $p < 0.00001$), while Gandini et al. [36], reducing the stages of growth to five intervals, showed a Cohen k index concordance value of 0.783 ± 0.098 between CVM Baccetti method [29] with Björk HVM method [20].

3.1.2. CVM Baccetti vs HWM grave and brown

Four papers [37–40] compared the CVM Baccetti method [29] with HWM Grave and Brown method [23]; however, there was no agreement on the correlation between the two methods. In particular, Camacho-Basallo et al. [37] showed no significant correlation ($p > 0.05$) between CVM Baccetti method [29] with HWM Grave and Brown method [23]; Hoseini et al. [37] also revealed a low level of agreement between the two methods (Cohen kappa = 0.312). Nevertheless, Litsas et al. [39] reported a significant association between CVM and HVM stages, as well as a 3-stage classification (prepeak/peak/post-peak), in both females ($p < 0.015$) and males ($p = 0.022$). Moreover, Pichai et al. [40] showed that CVM Baccetti method was significantly correlated with HWM Grave and Brown method (Kappa = 0.786; $p < 0.001$).

3.1.3. CVM Baccetti vs HWM fishman

Three papers [37,41,42] compared the CVM Baccetti method [29] with HWM Fishman method [21] showing a significant correlation ($p < 0.05$): Camacho-Basallo

Table 4
Main characteristics of the articles included in the present systematic review

Authors	Journal	Publication year	Nationality	Population (M/F)	Age (years)	CVM assessment methods	HWM assessment method	Main findings
Durka-Zakąc et al. [35]	Pol J Radiol	2013	Poland	30 (15 M/15 F)	10-17	Baccetti [29]	Björk [20]	There was a strong and statistically highly significant ($r = 0.98$; $p < 0.00001$) Pearson's correlation between HWM radiographs using Björk method and CVM using the method by Baccetti et al. in both sexes. The authors concluded that using CVM starting from the routinely taken cephalograms could eliminate the need for additional exposure to X-ray radiation and shorten the duration of examination.
Gandini et al. [36]	Angle Orthod	2006	Italy	30 (14 M/16 F)	7–18	Baccetti [29]	Björk [20]	The authors reduced the stages of growth to five intervals (A–E) to relate the five stages of the CVM Baccetti method to the nine stages of a Björk HVM method. Cohen kappa test index showed a good concordance value (0.783 ± 0.098) between the two methods. The authors affirmed that CVM method can be considered an efficient and repeatable procedure as confirmed by the evaluation carried out on the same radiographs after 6 months.
Camacho-Basallo et al. [37]	Acta Odontol Scand	2017	Spain	202 (104 M/98 F)	11–14	Baccetti [29]	Grave and Brown [23]	No significant correlation was found between CVM Baccetti method and HWM Grave and Brown method ($CC = 0.12$; $p > 0.05$).
Hoseini et al. [38]	Iran J Radiol	2016	Iran	133 (67 M/66 F)	8–18	Baccetti [29]	Grave and Brown [23]	The authors reduced the stages of growth to five intervals (A–E) to relate the five stages of the CVM Baccetti method to the nine stages of a Björk HVM method. Cohen kappa test revealed a low level of agreement between the two methods (0.312), slightly higher in males (0.33) than in females (0.27) between the stages.
Litsas et al. [39]	Eur J Paediatr Dent	2010	Turkey	393 (170 M/223 F)	8–18	Baccetti [29]	Grave and Brown [23]	CVM and HVM stages, as well as a 3-stage classification (prepeak/peak/post-peak) are significantly associated in both females (Chi square $= 8.467$; $p < 0.015$) and males (Chi square $= 7.614$; $p = 0.022$). In males, CVMS I and II belong to pre-peak period, CVMS III to the peak period, and CVMS IV and V to the post-peak period. In females, CVMS I belongs to the prepeak period, CVMS II and III to the peak period, and CVMS IV and V to the post-peak period.

Table 4, continued

Authors	Journal	Publication year	Nationality	Population (M/F)	Age (years)	CVM assessment methods	HWM assessment method	Main findings
Pichai et al. [40]	J Int Oral Health	2014	India	72 M+F	7–16	Baccetti [29]	Grave and Brown [23]	There was a significant correlation between CVM Baccetti method and HWM Grave and Brown method (Kappa = 0.786; $p < 0.001$).
Camacho-Basallo et al. [37]	Acta Odontol Scand	2017	Spain	202 (104 M/98 F)	11–14	Baccetti [29]	Fishman [21]	CVM Baccetti method was significantly correlated with HVM Fishman method (CC = 0.831; $p < 0.001$).
Alkhal et al. [41]	Angle Orthod	2008	Hong Kong	400 (200 M/200 F)	10–17	Baccetti [29]	Fishman [21]	The authors found a good correlation between CVM and HWM methods, with a linear relationship between the CVM and the HWM in both male and female. CVM resulted significantly correlated with HWM (Spearman's r: males = 0.9206; females = 0.9363). The CVMS3 corresponded to the SMI2 and SMI3 stages in the HWM, which were around the peak of the growth spurt. Thus, the authors concluded that CVM is a valid indicator of skeletal growth during the circumpubertal with a high correlation with the HWM.
Flores-Mir et al. [42]	Angle Orthod	2006	Canada	79 (27 M/52 F)	N/A	Baccetti [29]	Fishman [21]	CVM Baccetti method and HWM Fishman method are significantly correlated ($p < 0.001$) with a Spearman's $r = 0.72$.
Wong et al. [43]	Am J Orthod Dentofacial Orthop	2009	Qatar	400 (200 M/200 F)	10–17	Baccetti [29]	Hägg and Taranger [2]	A linear relationship was found between the CVM Baccetti method and the HWM Hägg and Taranger in both female (Spearman r: 0.9408) and male (Spearman r: 0.9521). In all subjects investigated, the CVMS3 subjects corresponded mainly to the MP3-FG stage (35 male, 21 female), and a few to the MP3-G stage (1 male, 2 female) in the HWM, that were around the PGS.
Camacho-Basallo et al. [37]	Acta Odontol Scand	2017	Spain	202 (104 M/98 F)	11–14	Hassel and Farman [28]	Grave and Brown [23]	No significant correlation was found between CVM Hassel and Farman method and HWM Grave and Brown method (CC = 0.03; $p > 0.05$).
Pichai et al. [40]	J Int Oral Health	2014	India	72 M+F	7–16	Hassel and Farman [28]	Grave and Brown [23]	There was a significant correlation between CVM Hassel and Farman method and HWM Grave and Brown method (Kappa = 0.793; $p < 0.001$).
San Roman et al. [44]	Eur J Orthod	2002	Spain	958 (428 M/530 F)	5–18	Hassel and Farman [28]	Grave and Brown [23]	There was a good correlation between CVM Hassel and Farman method and HWM Grave and Brown method for SM in females and males ($r = 0.84$ and $r = 0.77$, respectively), although it was significantly better for females ($p < 0.01$).

Table 4, continued

Authors	Journal	Publication year	Nationality	Population (M/F)	Age (years)	CVM assessment methods	HWM assessment method	Main findings
Uysal et al. [45]	Am J Orthod Dentofacial Orthop	2006	Turkey	503 (213 M/290 F)	5–24	Hassel and Farman [28]	Grave and Brown [23]	CVM Hassel and Farman method was significantly correlated (p<0.001) with HWM Grave and Brown method, with a Spearman rank-order correlation coefficient of 0.86 (sexes combined); the coefficients for male and female were 0.78 ($p < 0.001$) and 0.88 ($p < 0.001$), respectively.
Camacho-Basallo et al. [37]	Acta Odontol Scand	2017	Spain	202 (104 M/98 F)	11–14	Hassel and Farman [28]	Fishman [21]	CVM Hassel and Farman method was significantly correlated with HWM Fishman method (CC = 0.826, $p < 0.001$).
Mahajan et al. [46]	Indian J Dent Res	2011	India	100 (50 M/50 F)	8–18	Hassel and Farman [28]	Fishman [21]	CVM Hassel and Farman method was significantly correlated with HWM Fishman method (CC = 0.976; $p < 0.0001$).

Abbreviations: CC = Correlation coefficient; CVM = cervical vertebral maturation; CVMS = cervical vertebral stage; F = female; HWM = hand–wrist maturation; M = male; N/A = not applicable; SM = skeletal maturation; SMI = skeletal maturation index; PGS = pubertal growth spurt; NB: Two studies [33,36] assessed more than one SM method and were described in more lines, accordingly.

et al. [37] reported a correlation coefficient (CC) = 0.831; Alkhal et al. [41] reported a Spearman's r of 0.9206 in male and 0.9363 in female, while Flores-Mir et al. [42] showed a Spearman's r of 0.72.

3.1.4. CVM Baccetti vs HWM Hägg and Taranger

Only one paper, performed by Wong et al. [43], compared the CVM Baccetti method [29] with HWM Hägg and Taranger method [2] showing a linear relationship between them in both male (Spearman $r = 0.9521$) and female (Spearman $r = 0.9408$).

3.1.5. CVM Hassel and Farman vs HWM Grave and Brown

Four papers [37,40,44,45] compared the CVM Hassel and Farman method [28] with HWM Grave and Brown method [23], reporting different findings: Camacho-Basallo et al. [37] reported no significant correlation between the two methods (CC = 0.03; $p > 0.05$), while Pichai et al. [40] showed a significant correlation between CVM Hassel and Farman method [28] and HWM Grave and Brown method [23] (Kappa = 0.793; $p < 0.001$); San Roman et al. [44] reported an overall good correlation between the two methods, with a more robust correlation in female subjects ($p < 0.01$). Lastly, Uysal et al. [45] showed that CVM Hassel and Farman method [28] was significantly correlated with HWM Grave and Brown [23] method in combined sexes (Spearman rank-order correlation coefficient of 0.86; $p < 0.001$).

3.1.6. CVM Hassel and Farman vs HWM Fishman

Two papers [37,46] showed a significant correlation between the CVM Hassel and Farman method [28] and HWM Fishman method [21]: Camacho-Basallo et al. [37] reported a CC = 0.826 ($p < 0.001$); Mahajan et al. [46] reported a CC = 0.976 ($p < 0.0001$).

4. Discussion

SM assessment is a cornerstone in terms of diagnosis, treatment planning, and monitoring treatments in the PRM clinical practice, including patients affected by AIS, playing a key role to guide physicians in the initiation of bracing, timing and hours of brace wear, and eventually its dismission [3–6,15,48,49]. In this scenario, CVM has been proposed in evaluating the spinal maturity in scoliosis patients representing a tool able to predict spinal growth and curve progression [50,51]. Overall, the present systematic review summarized the level of evidence behind the reliability of CVM, showing significant correlations between these methods compared to HVM in terms of SM assessment in growing subjects.

Interestingly, all papers included might be considered as at least medium-quality studies, according to the abovementioned 10-item quality scoring [31]. However, there were only two high-quality studies [44,45] on the topic investigated and both of them have been published more than 15 years ago: San Román et al. in 2002 [44] and by Uysal et al. in 2006 [45]. These findings testified that further studies with a high-level methodology are warranted for assessing the reliability of CVM compared to HWM to assess SM in growing subjects.

At present, there are only three systematic reviews in literature investigating the reliability of CVM compared to HVM [31–33]. However, Szemraj et al. [33] included only articles investigating CVM Baccetti method [29] as intervention, not providing findings on CVM Hassel and Farman method [28], that is widely used in the common clinical practice and even highly investigated, as shown by this systematic review that included 5 papers comparing the CVM Hassel and Farman method to HWM methods [37,40,44–46].

Furthermore, the three above-mentioned systematic reviews [31–33] did not distinguish skeletal age and skeletal maturation, albeit it is well known that chronological age is not a valid predictor of skeletal growth velocity [30]. On the other hand, we assessed the reliability of CVM compared to HWM to assess SM in growing subjects, taking into account the absence of a common agreement on the reliability of CVM in literature.

Indeed, Santiago et al. [31] concluded that the CVM was not appropriate for the SM assessment, underlining the low-quality evidence of the papers included. On the other hand, the systematic reviews performed by Cericato et al. [32] and Szemraj et al. [33] reported a high level of correlation between CVM and HWM, concluding that CVM was reliable to evaluate SM and might replace HWM in the next future in the common clinical practice.

Findings highlighted by the present systematic review are in agreement with the last two systematic reviews [32,33]. We showed that 8 studies [35–37,39–43] showed a high correlation between CVM Baccetti and different HWM methods, and 5 studies [37,40,44–46], comparing CVM Hassel and Farman with different HWM methods, highlighted a significant correlation between these different techniques. However, we should

report that 3 studies showed no significant correlation between CVM methods and HWM Grave and Brown: two [37,38] assessing CVM Baccetti and one [37] evaluating CVM Hassel and Farman.

Moreover, compared to the aforementioned systematic reviews [31–33], we found a few differences in terms of correlation between CVM and HWM methods. This aspect might be due to the well-known difference in the PGS onset between male and females [1], which has not been adequately assessed by 7 papers included [35–38,40,44,46]. In this context, Wong et al. [43], considering the crucial difference in the onset of the circumpubertal periods between sexes, stratified their analysis using different age ranges (female: 10–15 years; male: 12–17 years), showing a highly significant correlation between CVM and HWM (Spearman r was 0.9408 in male and 0.9521 in female). Furthermore, it should be noted that CVM showed a low sensitivity for SM assessment in subjects away from the circumpubertal period [43]. This aspect is poorly considered in literature and could generate a major bias (e.g. Uysal et al. [45] included subjects aged from 5 to 24 years).

Furthermore, it was interesting to highlight the findings reported by Litsas et al. [39] suggesting the importance that the gender differentiation might play during the circumpubertal period. The Authors showed that CVMS I and II belong to pre-peak period and CVMS III to the peak period in male; at the same time, the Authors showed that CVMS I belongs to the pre-peak period and CVMS II and III to the peak period in female. CVMS IV and V represent the post-peak period in both sexes.

Taken together, these findings reported that CVM has a significant reliability in the SM assessment and might be considered a valid alternative to HWM in providing an adequate assessment of the growth curve progression. Indeed, in 2020, Zhang et al. [51] firstly showed that CVM could be used as an alternative to Risser sign in determining peak height velocity, reporting a strong correlation between CVM stages and the Risser sign ($r = 0.85$, $P < 0.01$). In this context, starting from an adequate diagnosis, AIS might counteract AIS by a prescription of physical exercise and bracing [52–54], taking into account also the need an adequate assessment of aesthetic perception, satisfaction with management, and health-related quality of life in these young subjects [55].

Nevertheless, the present systematic review could not be considered as free from limitations: first of all, the high clinical heterogeneity of the studies included in terms of variability in both study population characteristics and the SM assessment methods used that did not consent to perform a meta-analysis; moreover, all papers included had a cross-sectional design that hinders to obtain data on growth analysis; lastly, the literature screening has been limited to articles published in English language, albeit a comprehensive search of the literature was performed. However, the present systematic review firstly evaluated the reliability of CVM methods (both Baccetti and Hassel and Farman) compared to HWM methods to assess the only skeletal maturation (not the skeletal age) in growing subjects, based on the data of studies searched in the main scientific databases from inception until 31st December 2020.

5. Conclusions

Taken together, the findings of this systematic review demonstrated that both CVM Baccetti and Hassel and Farman methods might be considered reliable SM assessment methods compared to HWM in growing subjects. However, further studies with a Level of Evidence 2 according to the OCEBM 2011 [56] are warranted to elucidate the role of CVM in SM assessment, which is a crucial indicator for physicians to plan an appropriate management of AIS in the PRM clinical practice.

Author contributions

Study design and conceptualization: MF and AdS.
Databases search: AdS.
Data screening: MF, CC, AdS.
Data extraction: MF, CC, AdS.
Data synthesis and interpretation: MF, MM, AdS.
Manuscript drafting: MF and AdS.
Critical revision: AR, MM, MI.
Study supervision: AdS.
Study submission: AdS. All authors read and approved the final version of the manuscript.

Conflict of interest

None of the authors declare any conflict of interests, funding sources or consultant relationships with any organizations involved in this research.

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