LETTER TO THE EDITOR

Reliability of dental calcification compared to hand-wrist X-ray to evaluate skeletal maturation in growing subjects: a systematic review

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To the Editor,

Skeletal maturation (SM) assessment is used in the common clinical practice of orthodontics, physiatrists, pediatrics, and orthopedics for the diagnosis of skeletal discrepancies to establish an optimal timing for intervention, and to monitor the treatment response in growing subjects (1-3). Moreover, bone maturation stages [prepubertal, peak growth spurt (PGS) or completed skeletal development] might help orthodontists in the choice between extraction or non-extraction, selection of orthodontic retention, and planning orthognathic surgery in case of skeletal malocclusions (4, 5). At the same time, physiatrists and orthopedics should start only from a clear SM evaluation in order to perform an adequate scoliosis screening and to provide a patient-tailored rehabilitative treatment aimed at reducing functional impairments and counteracting the potential disabling sequelae (6-9).

To date, SM is commonly evaluated through the hand wrist maturation (HWM), assessing the morphological changes shown by hand and wrist X-ray (1, 2). Although HWM is considered the gold standard, dental calcification assessment has been proposed as an innovative approach to avoid additional X-ray examinations (3). Dental maturity assessment could be used for evaluation of permanent teeth calcification degree, starting from periapical or panoramic radiographs routinely used for diagnosis in orthodontics (3, 4, 10). However, at the present time, although other SM assessment methods (i.e. cervical vertebral maturation) have been proposed (11), there is still no common agreement regarding the reliability of dental calcification compared to HWM for the assessment of SM (3, 4, 10).

This systematic review aimed to evaluate

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the reliability of dental calcification according to Demirjian compared to HWM to assess SM in growing subjects and provide implications in the clinical management of a wide spectrum of pathological conditions.

Search strategy

This systematic review has been registered with PROSPERO number CRD42020220867 and was performed in accordance with the PRISMA statement. We systematically searched PubMed, Scopus, and Web of Science from inception until February, 1st, 2021 to recognize the papers published in literature, according to each specific thesaurus, adopting the following search strategy: ("hand-wrist") AND ("dental calcification" OR "dental age" OR "lateral cephalogram" OR "orthopantomography" OR "dental X-ray") 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").

Selection criteria

After the removal of duplicates, two reviewers independently screened articles for eligibility. In case of disagreement, a consensus was achieved by the decision of a third reviewer. All observational cross-sectional studies were screened and considered as eligible according to the following PICO model:

1. P) Participants consisted of growing subjects;
2. I) Intervention consisted of Demirjian method for the SM assessment;
3. C) Comparator consisted of HVM methods commonly used in clinical practice for SM assessment (i.e. Grave and Brown and Fishman);
4. O) Outcome measure consisted of the reliability of the Demirjian method compared to HWM for SM assessment.

The exclusion criteria were: studies investigating chronological, skeletal or dental age as primary outcomes; studies with cleft lip/palate patients; papers written in a language different from English; other study designs (e.g. case reports, case series, and reviews); full text unavailable (e.g. posters, conference abstracts, etc.); book chapters; animal studies.

Data extraction

Two reviewers independently extracted data from eligible full-text papers using a customized data extraction form in Microsoft Excel. Key data were extracted from each study relevant to the specific research questions. In case of disagreement, a consensus was achieved by the decision of a further experienced reviewer. The following data were extracted: authors; scientific journal; publication year; Nationality of study participants; population and number of patients; age of subjects; SM assessment methods; main findings.

Data synthesis

All the studies were synthetized describing both extracted data and main characteristics. Each study was then assessed for quality by a 10-item quality scoring according to a previous systematic review performed by our study group (11). The 10 criteria for the quality scoring of the studies included were the following: 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). Thus, the papers were classified as low-quality studies (0–4 points), medium-quality studies (5-7 points) or high-quality studies (8-10 points).

RESULTS

Out of 108 search results, 37 duplicates were removed, and 71 studies were considered as eligible for inclusion and screened for title and abstract,

of which, 25 papers were included for full-text screening. Sixteen articles not respecting eligibility criteria were excluded by the systematic review. Nine papers (12-20) were included in the synthesis, as depicted by PRISMA Flow Diagram in Fig. 1.

According to the above-mentioned 10-item quality scoring for the studies included, 4 studies (44.4%) were classified as high-quality studies (13-16) and 5 (55.6%) as medium-quality studies (12, 17-20). No low-quality studies were included in the present systematic review (further details about the quality scoring for each assessment criteria are depicted by Table I). A meta-analysis could not be performed due to the high clinical heterogeneity of the articles included in terms of variability of SM assessment and characteristics of study participants. The main characteristics of the 9 papers included (12-20) are shown in detail in Table II and described in the following paragraphs.

DM Demirjian vs HWM Grave and Brown. Three papers (12-14) compared the Demirjian method (3) with the HWM Grave and Brown method (1), reporting contrasting results: Camacho-Basallo et al. (12) showed no significant correlations ($p>0.05$) between the two methods; on the other hand, both Motghare et al. (13) and Uysal et al. (14) demonstrated significant correlations between Demirjian method and HWM Grave and Brown ($p<0.01$) method. More in detail, that the second molar showed the highest relationship (0.865 in female and 0.760 in male, and 0.826 in female and 0.706 in male, respectively). However, it was interesting to notice that canine showed a high significant relationship (0.808 in female and 0.768 in male) in one study (13) and a low significant relationship (0.691 in female; 0.633 in male) in another study (14).

DM Demirjian vs HWM Fishman. Seven papers (12, 15-20) compared the Demirjian method (3) with the HWM Fishman method (2). Günen Yılmaz et al. (15) divided the 11 SM indexes (SMI) of HWM Fishman method into three phases: pre-peak (SMI 1–2–3), peak (SMI 4–5–6–7), and post-peak (SMI 8–9–10–11); they reported a statistically significant correlation ($p<0.01$) between dental calcification and the 3 HWM Fishman groups (prepeak stages: CC=0.478; peak stages: CC=0.605; postpeak stages: CC=0.387).

Another 4 studies (16, 17, 19, 20) reported statistically significant correlations ($p<0.05$) between the Demirjian (3) and HWM Fishman (2) methods. However, the studies showed differences in terms of highest correlation (expressed as CC) with teeth involved: Krailassiri et al. (16) reported second premolars in both sexes (0.69 in female; 0.66 in male);

Table I. *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*		
Camacho-Basallo et al. (2017) [12]	1	0	1	0	0	1	1	1	1	1	7	Medium quality
Motghare et al. (2016) [13]	1	0	1	1	0	1	1	1	1	1	8	High quality
Uysal et al. (2004) [14]	1	1	1	1	0	1	1	1	1	1	9	High quality
Günen Yılmaz et al. (2019) [15]	1	0	1	1	0	1	1	1	1	1	8	High quality
Krailassiri et al. (2002) [16]	1	1	1	1	0	1	1	1	1	1	9	High quality
Lecca-Morales et al. (2017) [17]	1	0	0	0	1	1	1	1	1	1	7	Medium quality
Mustafa et al. (2015) [18]	1	0	1	0	0	0	1	1	1	1	6	Medium quality
Ojha et al. (2018) [19]	0	0	1	1	0	0	1	1	1	1	6	Medium quality
Yadav et al. (2017) [20]	1	0	1	1	0	0	1	1	1	1	7	Medium quality

Criteria for the quality scoring of the studies included performed according to Ferrillo et al. [11] were: 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.

Lecca-Morales et al. (17) reported second molars in both sexes (0.792 in female; 0.800 in male); both Ojha et al. (19) and Yadav et al. (20) reported second molars in female (0.882 and 0.845, respectively) and canines in male (0.835 and 0.755, respectively). Nevertheless, Mustafa et al. (18) showed low significant correlations ($p<0.05$) between the DM Demirjian method and HWM Fishman method for male and not statistically significant ($p>0.05$) for female. Lastly, Camacho-Basallo et al. (12) reported significant correlations ($p<0.001$) between the two methods with the exception of the first molars that

Table II. *Main characteristics of the articles included in the present systematic review*

Authors	Journal	Publication year	Nationality	Population (M/F)	Age (years)	Dental calcification assessment method	HWM assessment method	Main findings
Camacho-Basallo et al. [12]	Acta Odontol Scand	2017	Spain	202 (104 M/98 F)	11-14	Demirjian [3]	Grave and Brown [1]	No significant correlations were found between Demirjian method and HWM Grave and Brown method ($p>0.05$).
Motghare et al. [13]	J Forensic Dent Sci	2016	India	300 (150 M/150 F)	7-20	Demirjian [3]	Grave and Brown [1]	All the correlations between Demirjian and HWM Grave and Brown stages were statistically highly significant ($p<0.0001$). The CC indicates that the second molars showed the highest relationship (0.865 in female; 0.760 in male) and the first molars showed the lowest correlation (0.461 in female and 0.480 in male).
Uysal et al. [14]	Angle Orthod	2004	Turkey	500 (215 M/285 F)	7-20	Demirjian [3]	Grave and Brown [1]	All the correlations between Demirjian and HWM Grave and Brown stages were statistically significant ($p<0.01$). The CC indicates that the second molars showed the highest relationship (0.826 in female; 0.706 in male) and the canines showed the lowest correlation (0.691 in female; 0.633 in male).
Günen Yılmaz et al. [15]	Acta Odontol Scand	2019	Turkey	717 (334 M/383 F)	10-15	Demirjian [3]	Fishman [2]	Authors divided the 11 SMI of HWM Fishman method into three phases: pre-peak (SMI 1–2–3), peak (SMI 4–5–6–7), and post-peak (SMI 8–9–10–11). All the correlations between Demirjian and the 3 groups of HWM Fishman method were statistically significant ($p<0.01$) (pre-peak stages: CC=0.478; peak stages: CC=0.605; post-peak stages: CC=0.387).
Krailassiri et al. [16]	Angle Orthod	2002	Thailand	361 (139 M/222 F)	7-19	Demirjian [3]	Fishman [2]	All the correlations between Demirjian method and HWM Fishman method were statistically significant ($p<0.01$). The CC indicates that the second premolar showed the highest correlation (0.69 in female; 0.66 in male) and the third molars showed the lowest correlation (0.31 in female; 0.47 in male).
Lecca-Morales et al. [17]	Dental Press J Orthod	2017	Peru	78 (44 M/34 F)	7-17	Demirjian [3]	Fishman [2]	All the correlations between Demirjian method and HWM Fishman method were statistically significant ($p<0.001$). The strongest correlation between DM stages and HWM stages was with second molars (CC=0.792 in female; 0.800 in male).
Mustafa et al. [18]	Asian Biomed	2015	Saudi Arabia	60 (45 M/15 F)	8-16	Demirjian [3]	Fishman [2]	All correlations between Demirjian method and HWM Fishman method were statistically significant ($p<0.05$) for male and not statistically significant ($p>0.05$) for female. However, the Spearman's CC were low also in male, ranging from 0.44 to 0.51 for the male.
Ojha et al. [19]	J Forensic Dent Sci	2018	India	50 (25 M/25 F)	8-14	Demirjian [3]	Fishman [2]	All correlations between Demirjian method and HWM Fishman method were statistically significant ($p<0.05$). R-value CC ranged from 0.676 to 0.835 for males and from 0.812 to 0.882 for females. Authors concluded that canines reported the highest correlation in male (CC=0.835) and the second molars in female (CC=0.882).
Yadav et al. [20]	Natl J Maxillofac Surg	2017	India	120 (60 M/60 F)	7-13	Demirjian [3]	Fishman [2]	All the correlations between Demirjian method and HWM Fishman method were statistically significant ($p<0.001$). The Spearman's rank CC indicates that the second molars showed the highest correlation in female (CC=0.845) and canines in male (0.755).
Camacho-Basallo et al. [12]	Acta Odontol Scand	2017	Spain	202 (104 M/98 F)	11-14	Demirjian [3]	Fishman [2]	All the correlations between Demirjian method and HWM Fishman method were statistically significant ($p<0.001$), with the exception of the first molars that showed a low significant correlation in female (CC=0.263; $p<0.05$) and not significant correlation in male (CC=0.187; $p>0.05$). The CC indicates that the highest correlation was showed with second molars in female (CC=0.711) and second premolars in male (CC=0.594).

Abbreviations: CC: Correlation coefficient; F: female; HWM: hand–wrist maturation; M: male; SM: skeletal maturation; SMI: skeletal maturation index. The paper by Camacho-Basallo et al. [12] assessed more two HWM methods and was described in two lines, accordingly.

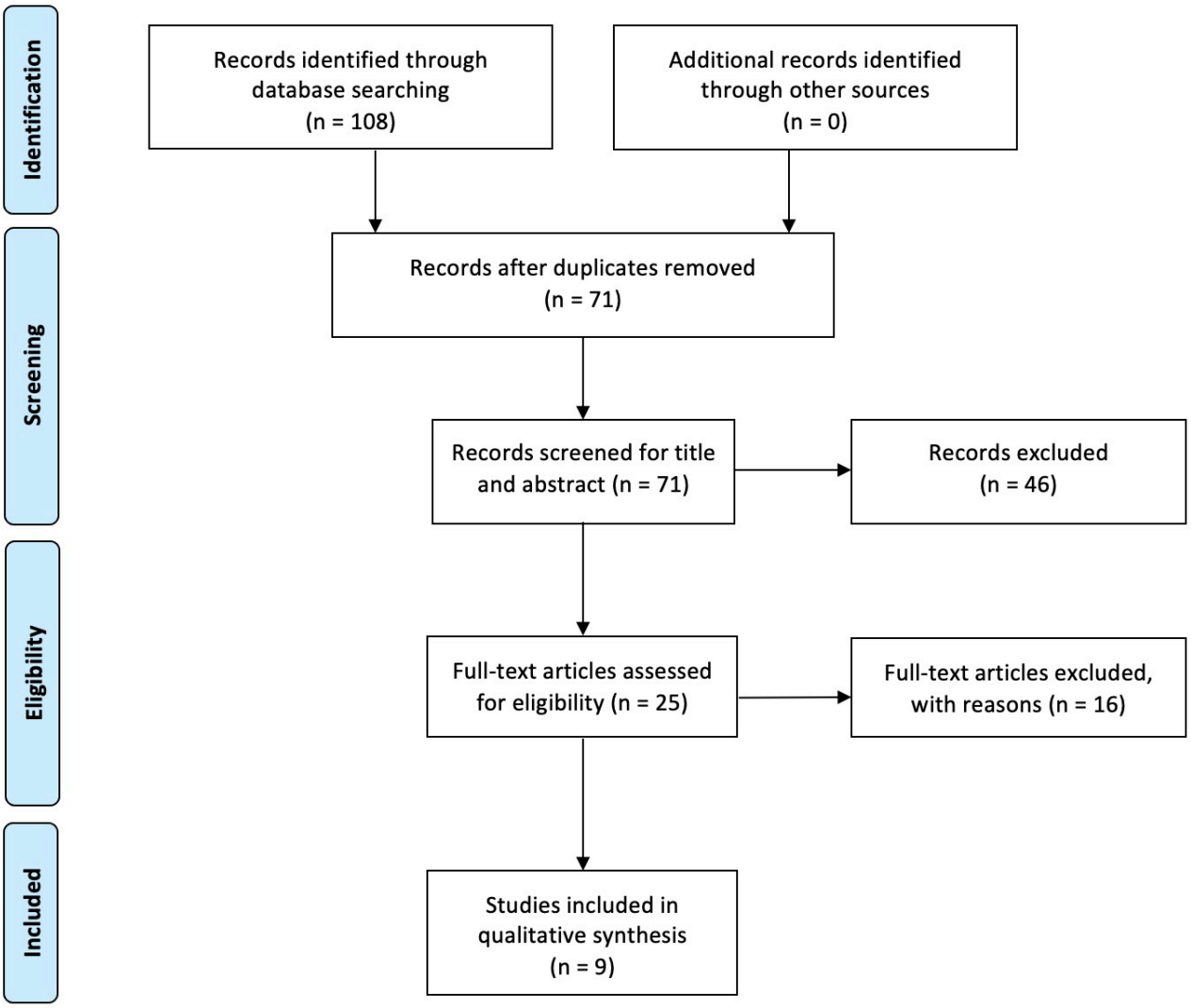

Fig. 1. *PRISMA 2009 Flow diagram*

showed a low significant correlation in female (CC=0.263; $p<0.05$) and not significant correlation in male (CC=0.187; $p>0.05$).

DISCUSSION

The present systematic review summarized the level of evidence behind the reliability of DM, showing substantial correlations between this method compared to HWM for the SM assessment in growing subjects. All nine studies (12-20) showed a statistically significant correlation between Demirjian (3) and HWM methods (1-2). However, two studies (12, 18) reported that Demirjian (3) was not significantly correlated with HWM Grave and Brown (in both sexes) (12) and HWM Fishman (in female) (18). Günen Yılmaz et al. (15) compared Demirjian to HWM Fishman stages, showing that mandibular second molar was categorized according to the different peak phases. Moreover, Lecca-Morales et al. (17) confirmed that the PGS was found in approximately the stage G in the mandibular second molar. Similarly, Motghare et al. (13) found that the second molar stage G for both sexes was indicative of a very high rate of growth acceleration. These findings were confirmed by Krailassiri et al.

(16), reporting that the mandibular second molar development was highly concentrated in stage G, during the stage at middle phalanx of the third finger when the epiphysis caps its diaphysis (MP3cap). According to the previous results about mandibular molars, an interesting remark was that two papers included in this systematic review (19, 20) reported a high correlation between Demirjian and HWM in the canines in male (0.835 and 0.755, respectively). Indeed, Ojha et al. (19). showed that the canine stage F had shown the highest percentage distribution in male (92%), during the stage of middle phalanx of the third finger, when the epiphysis equals its diaphysis (MP3 stage), suggesting the onset of a period of accelerating growth in the MP3 stage. Also, Yadav et al. (20) concluded that canine stage G and H could represent the peak of the PGS in male. Accordingly, a recent longitudinal study (4) confirmed that Demirjian applied to mandibular second molars could be considered as a plausible predictor of the occurrence of the distance to growth peak according to their findings; they stated that developmental stages of the mandibular second molar most closely observed to the PGS onset were stage F for female and stage G for male.

This review had some limitations, as the absence of a meta-analysis that could not be performed due to the high clinical heterogeneity, and the inclusion of only cross-sectional studies hindering to obtain data on growth analysis. However, this is the first systematic review that assessed the reliability of the Demirjian method compared to HWM methods to evaluate SM in growing subjects, from inception to February 2021 in the main scientific databases.

Taken together, the findings of this systematic review showed the reliability of the Demirjian dental calcification method compared to HWM in growing subjects, highlighting the potential role of the mandibular second molar calcification as a plausible indicator of SM to monitor conservative intervention in orthodontics clinical practice.

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