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| ORIGINAL

Reproducibility of skeletal and dental maturation parameters

Reprodutibilidade de parâmetros de maturação esqueléticos e dentários

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ABSTRACT

Objective: Amongst other factors, the effectiveness of orthodontic treatment in children and adolescents depends on the identification of most appropriate intervention timing, which has been traditionally based on the identification of maturational stages. There is a wide variety of radiographic methods to identify these phases, either through skeletal parameters, or dental calcification. Considering that the reliability of any given assessment tool is required to enable its safe clinical use, and aiming an appropriate implementation of these parameters in future researches, this study was performed to assess the reproducibility of radiographic growth evaluation methods. **Methods**: Lateral teleradiographs, hand-wrist, and panoramic radiographs of sixty-eight orthodontic patients randomly selected from files of the Orthodontics Graduation Course (Guarulhos University, Guarulhos, SP, Brazil) were evaluated by two examiners to access both intra- and inter-examiner reproducibility of the assessment methods conceived by Baccetti et al.; Fishman; Greulich and Pyle; Nolla and Demirjian et al. **Results**: All methods analyzed showed satisfactory intra- and inter-examiner reliability. Among those that evaluated skeletal maturity, a relatively better performance was observed for Baccetti's method. Fishman's and Greulich's parameters presented similar rates, as did Nolla's and Demirjian's. **Conclusion**: The assessment tools analyzed presented adequate reproducibility and might potentially be used as assessment tools to evaluate children and adolescent's craniofacial growth. Further researches could evaluate the accuracy of radiographic dental calcification parameters for the identification of craniofacial growth stages.

Indexing terms: Diagnostic imaging. Growth and development. Orthodontics. Reproducibility of results.

RESUMO

***Objetivo**: Entre outros fatores, a efetividade do tratamento ortodôntico em crianças e adolescentes depende da identificação do momento de intervenção mais apropriado, que tem sido baseado nos estágios de maturação. Uma variedade de métodos radiográficos identifica essas fases através de parâmetros esqueléticos e da calcificação dentária. Considerando que a confiabilidade de qualquer ferramenta de avaliação é necessária para permitir seu uso clínico e aplicação segura de seus parâmetros em pesquisas*

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futuras, este estudo acessou a reprodutibilidade de métodos radiográficos de avaliação do crescimento. ***Métodos****: Telerradiografias laterais, radiografias carpais e panorâmicas de 68 pacientes ortodônticos randomicamente selecionados dos arquivos do Curso de Graduação em Ortodontia (Universidade de Guarulhos, Guarulhos, SP, Brasil) foram avaliadas por dois examinadores para acessar a reprodutibilidade intra e inter-examinador dos métodos de avaliação concebidos por Baccetti et al.; Fishman; Greulich e Pyle; Nolla e Demirjian et al.* ***Resultados****: Todos os métodos analisados mostraram confiabilidade intra e inter-examinador satisfatória. Dentre os que avaliam maturidade esquelética, um desempenho relativamente melhor foi observado para o método de Baccetti e colaboradores. Os parâmetros de Fishman e de Greulich e Pyle apresentaram valores similares, assim como os de Nolla e de Demirjian e colaboradores.* ***Conclusão****: As ferramentas de avaliação analisadas apresentaram reprodutibilidade adequada e podem ser utilizadas para avaliação do crescimento craniofacial de crianças e adolescentes. Pesquisas futuras poderiam avaliar a acurácia dos parâmetros radiográficos de calcificação dentária para a identificação dos estágios de crescimento craniofacial.*

Termos de indexação: *Diagnóstico por imagem. Crescimento e desenvolvimento. Ortodontia. Reprodutibilidade de resultados.*

INTRODUCTION

The orthopedic/ orthodontic treatment of children and adolescents must consider, amongst other factors, the appropriate timing for the intervention of malocclusions [1,2], which have been traditionally based on growth stages, as assessed by skeletal parameters [3-6]. Alternatively, dental calcification categorization systems have also been explored as a proxy tool to guide the orthodontic intervention, due to its prompt accessibility [7-10]. Different parameters using cervical vertebrae [5,6] and carpal bones [3,4], as well as teeth calcification stages [11,12] - as observed in lateral teleradiographs, hand-wrist and panoramic radiographs, respectively, compose a wide variety of available methods to identify the biological age.

The method described by Baccetti et al. [5], which is based on cervical vertebrae maturation, has been widely used by orthodontists because of its simplicity, objectivity, as well as the common routine use of lateral cephalograms [7]. The Greulich's and Pyle's method [3] also provides an important clinical application, as it identifies [18] bone events on hand-wrist radiographs concerning the pubertal growth spurt [13]. Posteriorly, Fishman [4] proposed a different method using the same exam, and it has been mostly recommended, since such assessment tool is able to specify the relative growth speed and the percentage of remaining skeletal development [14].

Nolla [14] was one of the first authors to introduce a biological age estimation method according to teeth calcification, therefore being a time-tested tool [15]. This method has been traditionally taught during professional formation and used in clinical practice [16]. Posteriorly, Demirjian et al [12]. created a simple, practical, and useful classification system for teeth calcification, which is considered as a reference method to predict dental age [15].

The reliability of any given assessment tool is essential to enable its safe clinical use [17]. Additionally, future researches aiming at employing consistent evaluation parameters might benefit from a comprehensive reproducibility analyses. Due to the lack of studies simultaneously evaluating a broad range of skeletal maturation and dental calcification radiographic parameters, with a significant and representative sample, this study was performed to assess the intra- and inter-examiner reproducibility of these examination methods. The null hypothesis was that these assessment tools [3-5,11,12] do not present significant reproducibility.

METHODS

Sample

The Research Ethics Committee of Guarulhos University approved this cross-sectional observational analytical study (#48816415.7.0000.5506). Patients and legal guardians signed an informed consent term authorizing their participation in this research.

Sixty-eight orthodontic patients' records, taken from 2005 to 2015, were randomly selected from files of the Orthodontics Graduation Course (Guarulhos University, Guarulhos, SP, Brazil). In order to be included, patients should

have had their baseline lateral teleradiograph, hand-wrist and panoramic radiographs available and obtained in the same date. Inclusion criteria also comprised Brazilian patients of both genders, with ages ranging from 5 to 21 years, with no syndromes or craniofacial malformations, and no history of hand-wrist or face injuries.

Radiographic evaluation

Radiographic evaluation was performed by two undergraduate students in a dark room, on a negatoscope (Essence Dental VH, Araraquara, SP, Brazil) and with a magnifying glass. One of the examiners conducted two evaluation sessions with at least two weeks apart from each other. The examiners previous training and calibration was conducted after instructions were given by an experienced professional (orthodontist). Afterwards, the initial measurements were supervised and corrected by the same professional until the examiners mastered the evaluation methods. Cervical vertebrae (C2, C3 and C4) were analyzed according to Baccetti's et al. [5] method, in which maturation stages were categorized in five phases (chart 1). An alternative classification method [18], derived from the original [5] was also evaluated. According to this modified classification system, individuals could be categorized as:

Chart 1. Developmental stages of cervical vertebrae, in chronological order, as determined by Baccetti et al. [5].

Stage	Description
CVMS I	Lower border of all analyzed vertebrae (C2, C3 e C4) are flat or border of C2 are slightly concave
	Bodies of C3 e C4 are trapezoidal in shape
CVMS II	Lower border of C2 and C3 are concave
	Bodies of C3 e C4 are trapezoidal or rectangular horizontal in shape
CVMS III	Lower border of C2, C3 and C4 are concave
	Bodies of C3 e C4 are rectangular horizontal in shape
CVMS IV	Lower border of C2, C3 and C4 are sharply concave
	Bodies of C3 e C4 are squared in shape
CVMS V	Lower border of C2, C3 and C4 are sharply concave
	Bodies of C3 e C4 are rectangular vertical in shape

Chart 2. Skeletal maturation stages, in chronological order, as determined by Fishman [4].

Stage	Description
1	Width of epiphysis as width as diaphysis in the proximal phalanx of third finger
2	Width of epiphysis as width as diaphysis in the middle phalanx of third finger
3	Width of epiphysis as width as diaphysis in the middle phalanx of fifth finger
4	Adductor sesamoid ossification of thumb
5	Capping of epiphysis by diaphysis in the distal phalanx of third finger
6	Capping of epiphysis by diaphysis in the middle phalanx of third finger
7	Capping of epiphysis by diaphysis in the middle phalanx of fifth finger
8	Epiphysis and diaphysis fusion in the distal phalanx of third finger
9	Epiphysis and diaphysis fusion in the proximal phalanx of third finger
10	Epiphysis and diaphysis fusion in the middle phalanx of third finger
11	Epiphysis and diaphysis fusion on radius

- undergoing pre-pubertal growth spurt period (CVMS I);
- undergoing pubertal growth spurt period (CVMS II and CVMS III); or
- undergoing post-pubertal growth spurt period (CVMS IV and V).

The hand-wrist radiography was analyzed according to Fishman [4], in which ossification centers were used to identify 11 possible skeletal maturity stages (chart 2). The method proposed by Greulich and Pyle [3] was also used, as detailed in chart 3.

The calcification of mandibular teeth (canine, first premolar, second premolar and second molar) was categorized according to Nolla's [11] (chart 4), as well as Demirjian's et al. [12] method (chart 5).

Chart 3. Skeletal maturation stages, in chronological order, as determined by Greulich and Pyle [3].

Stage	Description
FD	Width of epiphysis as width as diaphysis of distal phalanges
FP	Width of epiphysis as width as diaphysis of proximal phalanges
FM	Width of epiphysis as width as diaphysis of middle phalanges
G1	First evidence of hooky
Psi	Pisiform ossification
FDcap	Capping of epiphysis on distal phalanges
S	Adductor sesamoid ossification
G2	Sharpness of hook
FPcap	Capping of epiphysis on proximal phalanges
FMcap	Capping of epiphysis on middle phalanges
Rcap	Capping of epiphysis on radius
FDui	Epiphyseal union starts on distal phalanges
FPui	Epiphyseal union starts on proximal phalanges
FMui	Epiphyseal union starts on middle phalanges
FDut	Total epiphyseal union on distal phalanges
FPut	Total epiphyseal union on proximal phalanges
FMut	Total epiphyseal union on middle phalanges
Rut	Total epiphyseal union on radius

Chart 4. Dental calcification stages, in chronological order, as determined by Nolla [11].

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Stage	Description
1	Crypt present
2	Inicial calcification
3	Crown one-third complete
4	Crown two-thirds complete
5	Crown almost complete

Chart 4. Dental calcification stages, in chronological order, as determined by Nolla [11].

Stage	Description
6	Crown complete
7	Root one-third complete
8	Root two-thirds complete
9	Root almost complete, apex open
10	Root Apex complete

Chart 5. Dental calcification stages, in chronological order, as determined by Demirjian et al. [12].

Stage	Description
A	Cusp tips are calcified but not fused
B	Calcified cusps are united in a well-defined occlusal surface
C	Enamel formation is complete at the occlusal surface Dentinal deposition has commenced The outlines of the pulp chamber are curved
D	Crown formation is complete to the cementoenamel junction The pulp chamber in the uniradicular teeth is curved, being concave toward the cervical region. In molars the pulp chamber has a trapezoid form The pulp horns are beginning to differentiate Root formation is seen
E	The walls of the pulp chamber are straight and the pulp horns are more differentiated The root length is less than crown height In molars the radicular bifurcation is visible
F	The walls of the pulp chamber form an isosceles triangle The root length is equal to or greater than crown height In molars the bifurcation has developed sufficiently to give the roots a distinct outline with funnel shaped endings
G	The walls of the root canal are parallel and its apical end is still partially open (distal root in molars)
H	The apical end of the root canal is closed (distal root in molars) The periodontal membrane has a uniform width around the root and the apex

Data analysis

Intra- and inter-examiner reproducibility analyses were calculated by kappa (k) coefficient. Kappa value was rated as "low" ($k \leq 0.20$), "fair" ($0.20 < k \leq 0.40$), "moderate" ($0.40 < k \leq 0.60$), "substantial" ($0.60 < k \leq 0.80$) or "nearly perfect" ($0.80 < k \leq 1.00$) [19]. The data were analyzed with SPSS software (version 25 for Windows; SPSS Inc, Chicago, IL, USA) with a 5% ($\alpha \leq 0.05$) significance level.

RESULTS

Sixty-eight patients were included in this study, (females: 53.0%; males: 47.0%). Patients' mean age was 11.1 years (standard deviation: 1.79 years).

The kappa values obtained after intra- and inter-examiner analyses for Baccetti's et al. [5] method were 0.84 (nearly perfect) and 0.78 (substantial), respectively. For the cervical vertebrae simplified classification system [18], intra- and inter-examiner k-values were 0.74 and 0.68, respectively (both substantial). The p-values for all of the above-mentioned analyses were below 0.001.

Intra- and inter-examiner analyses for both hand-wrist classification methods were rated as substantial, displaying satisfactory values (table 1). Intra-examiner kappa values for both methods analyzed on panoramic radiographs were categorized as nearly perfect; and inter-examiner values varied from substantial to nearly perfect (table 2).

The null hypothesis, according to which the evaluation methods [3-5,11,12] investigated here do not present significant reproducibility, was thus rejected.

Table 1. Intra- and inter-examiner reproducibility analyses of hand-wrist radiographic parameters.

	Intra-examiner		Inter-examiner	
	k	p	k	p
Fishman [4]	0.75	< 0.001	0.65	< 0.001
Greulich and Pyle [3]	0.70	< 0.001	0.67	< 0.001

Table 2. Reproducibility intra and inter-examiner of radiographic parameters in panoramic radiography according to each method analyzed.

	Tooth	Intra-examiner		Inter-examiner	
		k	p	k	p
Nolla [11]	33	0.92	< 0.001	0.89	< 0.001
	43	0.90	< 0.001	0.86	< 0.001
	34	0.86	< 0.001	0.79	< 0.001
	44	0.84	< 0.001	0.77	< 0.001
	35	0.91	< 0.001	0.86	< 0.001
	45	0.89	< 0.001	0.82	< 0.001
	37	0.89	< 0.001	0.80	< 0.001
	47	0.91	< 0.001	0.85	< 0.001
Demirjian et al. [12]	33	0.87	< 0.001	0.79	< 0.001
	43	0.91	< 0.001	0.86	< 0.001
	34	0.92	< 0.001	0.85	< 0.001
	44	0.96	< 0.001	0.87	< 0.001
	35	0.88	< 0.001	0.80	< 0.001
	45	0.90	< 0.001	0.81	< 0.001
	37	0.96	< 0.001	0.82	< 0.001
	47	0.91	< 0.001	0.80	< 0.001

DISCUSSION

The reliability of skeletal and dental classification systems [3-6,11,12] must be considered in order to determine its quality as an assessment tool and to guide its potential clinical use. Previous studies have already determined the

reliability of skeletal and dental maturation radiographic parameters [7,8,13,15,18,20-26], although mostly individually. However, in order to compare the available diagnostic methods, this study investigated, in a relatively larger sample, the intra- and inter-examiner reproducibility of a large number of relevant parameters. Considering that reproducibility is one of the essential requirements for a diagnostic assessment tool [17,27], the results provided by this study can guide practitioners towards the selection of a reliable diagnostic test.

In the lateral teleradiographic examination, excellent reproducibility was found for Baccetti's et al. classification method, for both intra and inter-examiner coefficients, which confirms the reliability of this diagnostic tool [6]. Previous studies presented similar kappa values [8,18]. Valizadeh, et al. [8] reported intra-observer kappa of 0.92 for the cervical maturation classification system, which is in accordance with the nearly perfect results observed in the current study. However, in their research, slightly higher values could be explained by the small sample analyzed in comparison with ours (68 subjects).

Contrastingly, a couple of studies reported relatively lower reproducibility values for cervical vertebrae maturation method [20,21]. Both of them used the original CVMS method6 comprising six growth phases, which might explain this difference. In addition, the authors reported that more than two examiners were involved in their analyses; thus, it is speculated that agreement tends to become relatively smaller, as a consequence. According to Nestman, et al. [21], the difficulty in identifying C3 and C4 bodies shape might justify their inferior results.

The merging of Baccetti's method in three growth stages (pre-pubertal, pubertal, and post-pubertal growth spurt periods), as also utilized by Litsas, et al. [18], is intended to simplify the clinical use of this diagnostic tool towards the straightforward identification of orthodontic interventional timing. According to the data presented, this simplified assessment tool provided substantial intra- and inter-examiner k values, indicating high reproducibility and similar results to the previously cited research [18]. Sohrab, et al [23]. found a moderate inter-examiner reproducibility for C3 and C4 shape evaluation – the sole differential sign between stages IV and V, indicating a difficulty of this cervical vertebrae maturation method, even as Nestman, et al. [21]. In relation to that same research, CVMS classification reliability is higher, when concerning to clinical decisions, rather than just a grading system. Therefore, in the simplified method, stages IV and V are grouped into post-pubertal growth spurt period, once both results in the same clinical decision.

Although the method described by Greulich and Pyle [3] has more categories, which could anticipate less agreement, the results of both hand-wrist radiographic methods' reproducibility were very similar, with high k-values for intra- and inter-examiner analyses. Fishman's method presented satisfactory reproducibility in several researches [22,24,26]. Greulich's and Pyle's method had substantial reproducibility values, for both intra and inter-examiner analyses, and another study also found similar results [13]. Nevertheless, as a negative implication, the routine clinical use of hand-wrist radiographic methods involves additional radiation exposure to patients [28,29], while the lateral teleradiograph is readily available to orthodontists [13].

The panoramic radiography, an accessible exam to pediatricians and general dentists, has been alternatively used to determine craniofacial development according to dental calcification as it correlates to the growth pubertal stages [7-10], and it might guide timely patient referral to orthodontist [1,2]. Intra- and inter-examiner reproducibility of Nolla's [11] method was evaluated, and the tooth 33 had relatively larger reproducibility rates. For Demirjian's et al. [12] method, the best performance was observed for the tooth 44. Both methods were rated from substantial to nearly perfect intra- and inter-examiner reliability; and these results are in accordance with previous ones [25] that reported high degree of correlation in intraclass correlation coefficient for Nolla's and Demirjian's scores (0.915 and 0.800, respectively). Al-Balbeesi, et al. [30] stated that these two methodologies were used in their investigation because of their simplicity and reliability.

According to Kumaresan, et al. [15], Nolla's [11] method had a moderate reliability score. However, the authors also observed high values for intraclass correlation coefficient (considering both intra- and inter-examiner reliability analyses), which is analogous to the findings of the present research. In the same study [15], the reliability evaluation was performed with the calculation of the mean absolute error of observations, which might explain this difference in

classification. Yet, Demirjian's et al. [12] method had the lowest reliability rate among those tested [15], even though its intraclass correlation coefficients were satisfactory, which also analogous to results presented here.

In this current investigation, the diagnostic methods did not have their validity evaluated, which can be regarded as a limitation. The characteristics of an ideal assessment tool can only be entirely assessed if its validity is also considered [17]. The findings provided by this study encourage further researches with panoramic radiographs to evaluate craniofacial development through dental calcification staging and its correlation to growth phases, which can enable panoramic radiographic records as a validated tool to be reliably used for timely referrals.

The radiographic evaluation was performed by undergraduate students, which could be perceived as another limitation of this study. However, these examiners were previously trained and calibrated by an experienced professional (orthodontist), which might somehow enable the generalizability potential of the results for trained professionals in clinical situations.

Hand-wrist radiographic evaluation methods result in additional radiographic exposure to the patients. Therefore, considering they did not achieve better results in this study, their use for practical purposes is not recommended.

CONCLUSION

All methods analyzed here obtained satisfactory intra- and inter-examiner reproducibility performances. Fishman's [4] and Greulich's and Pyle's [3] methods had similar values, as did Nolla's [11] and Demirjian's et al. [12]. Among the methods that evaluated skeletal maturity, relatively better reproducibility rates were observed for Baccetti's et al. [5] method, as compared to others.

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Collaborators

VL Paschoini contributed to conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, resources, software, supervision, validation, visualization, writing-original draft, and writing-review & editing. SV Grillo performed the data curation, investigation, and methodology. ACR Nahás-Scocate contributed to conceptualization, data curation, investigation, and methodology. MFN Feres performed the conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing-original draft, and writing-review & editing.

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