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Evidence-based mapping of third molar techniques for age estimation applied to Brazilian adolescents – a systematic review

Mapeamento baseado em evidências para técnicas de estimativa de idade por terceiros molares aplicadas a adolescentes brasileiros – uma revisão sistemática

Mapeo basado en evidencia para técnicas de estimación de edad del tercer molar aplicadas a adolescentes brasileños - una revisión sistemática

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Abstract

This study was performed to review the international techniques for third molar dental age estimation applied to Brazilian adolescents. A systematic literature review was structured according to PRISMA. Six primary electronic databases were searched (PubMed, Scopus, LILACS, SciELO, Embase and Web of Science) and two sources of grey literature (Open Grey and Open Thesis) were screened. Only cross-sectional studies were included. The risk of bias was assessed with Joanna Briggs Institute tool for systematic reviews. The initial search found 2284 studies. Ten studies fulfilled the eligibility criteria. The samples varied between 288 and 2097 individuals. The sampled age interval ranged from 5 to 23 years. Seven techniques were found within the eligible studies. All the studies had low risk of bias. Three techniques: Demirjian (DEM), Nicodemo (NIC) and Cameriere (I3M) were included in the quantitative analysis. For each of the developmental stages of the techniques DEM and NIC, as well as for each measuring ratio of I3M, combined age values between studies were reported. In general, the international techniques for dental age estimation based on the radiographic assessment of the third molars were applicable to the Brazilian population.

Keywords: Third molar; Forensic dentistry; Growth and development; Radiology.

Resumo

Este estudo foi realizado para revisar as técnicas internacionais de estimativa de idade dental por terceiros molares aplicadas a adolescentes brasileiros. Uma revisão sistemática da literatura foi estruturada de acordo com o PRISMA. Seis bases de dados eletrônicas primárias foram pesquisadas (PubMed, Scopus, LILACS, SciELO, Embase e Web of Science) e duas fontes de literatura cinza (Open Grey e Open Thesis) foram selecionadas. Apenas estudos transversais foram incluídos. O risco de viés foi avaliado com a ferramenta Joanna Briggs Institute para revisões sistemáticas. A pesquisa inicial encontrou 2.284 estudos. Dez estudos preencheram os critérios de elegibilidade. As amostras variaram entre 288 e 2.097 indivíduos. O intervalo de idade amostrado variou de 5 a 23 anos. Sete técnicas foram encontradas nos estudos elegíveis. Todos os estudos tiveram baixo risco de viés. Três técnicas: Demirjian (DEM), Nicodemo (NIC) e Cameriere (I3M) foram incluídas na análise quantitativa. Para cada um dos estágios de desenvolvimento das técnicas DEM e NIC, bem como para cada razão de medição de I3M, os valores combinados de idade entre os estudos foram relatados. Em geral, as técnicas internacionais de estimativa da idade dentária com base na avaliação radiográfica dos terceiros molares foram aplicáveis à população brasileira.

Palavras-chave: Terceiro molar; Odontologia forense; Crescimento e desenvolvimento; Radiologia.

Resumen

Este estudio se llevó a cabo para revisar las técnicas internacionales de estimación de la edad dentaria de los terceros molares aplicadas a adolescentes brasileños. Se estructuró una revisión sistemática de la literatura según PRISMA. Se realizaron búsquedas en seis bases de datos electrónicas primarias (PubMed, Scopus, LILACS, SciELO, Embase y Web of Science) y se seleccionaron dos fuentes de literatura gris (Open Grey y Open Thesis). Solo se incluyeron estudios transversales. El riesgo de sesgo se evaluó mediante la herramienta del Instituto Joanna Briggs para revisiones sistemáticas. La investigación inicial encontró 2.284 estudios. Diez estudios cumplieron los criterios de elegibilidad. Las muestras variaron entre 288 y 2.097 individuos. El intervalo de edad de la muestra varió de 5 a 23 años. Se encontraron siete técnicas en los estudios elegibles. Todos los estudios tuvieron un bajo riesgo de sesgo. Se incluyeron tres técnicas: Demirjian (DEM), Nicodemo (NIC) y Cameriere (I3M) en el análisis cuantitativo. Para cada uma de las etapas de desarrollo de estas técnicas DEM y NIC, así como para cada razón de medición de I3M, se informaron valores combinados de edad entre los estudios. En general, las técnicas internacionales de estimación de la edad dental basadas en la evaluación radiográfica de los terceros molares fueron aplicables a la población brasileña.

Palabras clave: Tercer molar; Odontología forense; Crecimiento y desarrollo; Radiología.

1. Introduction

In 2020, the Brazilian Statute of the Children and Adolescents completes 30 years of existence (Brazil, 1990). Among other issues, the Statute regulates transitional age thresholds of legal interest, namely the age of 12 to distinguish children from adolescents, and the age of 18 in the interface of the adolescence and the adulthood (age of legal majority) (Brazil, 1990). The specific age of legal majority is corroborated by the Brazilian Constitution of 1988 (Brazil, 1988), as well as the Brazilian Civil (Brazil, 2002) and Criminal Codes (Brazil, 1940). From a forensic perspective, the combination of legal norms plays an important role guiding judicial decisions that require age-related evidences. Asylum seekers and young offenders figure amongst those that may need forensic expertise and age estimation (Schmeling et al., 2006; Sykes et al., 2017; Silva et al., 2013). When it comes to the age

assessment related to legal majority, however, forensic performances become more challenging.

Unlike age estimation techniques dedicated to children, dental age estimation through the assessment of third molars is hampered by the scarce sources of age information (Franco et al., 2013). In particular, only third molars are developing around the age of 18 (Santiago et al., 2018; Liversidge and Marsden, 2010). These teeth are known for their variability among different persons, especially regarding development timing (Johan et al., 2012). Assessing third molar development may be accomplished by means of bi-dimensional and three-dimensional imaging analysis, and also ex vivo from skeletal remains (Franco et al., 2020a). To the present, third molar analysis via panoramic radiographs remains the most feasible in forensic facilities worldwide (especially in growing countries, such as Brazil) and biologically acceptable (cost vs. benefit) approach.

Studies have corroborated the application of international dental age estimation techniques in populations other than the original (Franco et al., 2020b). While for some populations validation studies have confirmed the applicability of international methods (Thevissen et al., 2010), in other populations corrections are recommends to improve the techniques (Prasad and Kala, 2019). Usually, the performance of third molar techniques are investigated country-specific by poling together performances as function of populations (Franco et al., 2020b). Pooling the performance of methods as function of a target population (Franco et al., 2020b), on the other hand, could enable a deeper look into practice.

This study aimed to revisit the scientific literature to detect radiographic techniques for third molar age estimation previously applied to Brazilian adolescents, and to find out method-specific information related to the target Brazilian population.

2. Materials and Methods

Protocol and registration

The present systematic review was registered in the PROSPERO database (http://www.crd.york.ac.uk/PROSPERO, PROTOCOL: CRD42020136170) and was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Moher et al., 2009) (www.prisma-statment.org) and the JBI Manual for Evidence Synthesis (Aromataris and Munn, 2020).

Study design and eligibility criteria

A systematic literature review was designed to answer to the following question: Is there a correlation between the chronological age and third molar age estimated from international radiographic techniques applied in Brazilian adolescents? The question included the following information: population: Brazilian adolescents, exposure: international radiographic techniques for third molar age estimation, comparison: chronological age, outcome: estimated age and its correlation with chronological age.

Only observational (cross-sectional) studies that investigated third molar dental age estimation techniques in Brazilian adolescents were included. Restrictions of date, language and status of publication were not used. The exclusion criteria consisted of studies that sampled patients with radiographically visible bone lesions, and studies that sampled patients with known syndrome and systemic diseases.

Search strategy

The search was performed in May 2020 in PubMed (including Medline), Scopus, LILAC, SciELO, Web of Science and Embase. OpenGrey and OpenThesis databases were searched for grey literature. Reference lists of eligible studies were searched to find articles that eventually were not found through search strategy. These procedures were taken to avoid or minimize publication and selection bias. Medical Subject Headings (MeSH), Health Sciences Descriptors (DeCS) and Embase Subject Headings (Emtree) terms were used combined by Boolean operators "AND" and "OR" (Table 1).

Table 1. Search strategies used in each database.

Database	Search Strategy (May 27th, 2020)
PubMed http://www.ncbi.nlm.nih.gov/pubmed	((“Forensic Odontology” OR “Forensic Dentistry” OR “Forensic Science” OR “Age Estimation” OR “Age Determination” OR “Dental Age” OR “Estimation Techniques” OR “Chronological Age” OR “Age Estimative” OR “Forensic Sciences” OR “Science, Forensic”) AND (“Dentistry” OR “Oral Medicine” OR “Odontology” OR “Dentition” OR “Teeth” OR “Tooth” OR “Stomatognathic System”) AND (“Brazil” OR “Brazilian” OR “Brazilians” OR “Brazilian People” OR “Brazilian Population”))
Scopus http://www.scopus.com/	((“Forensic Odontology” OR “Forensic Dentistry” OR “Forensic Science” OR “Age Estimation” OR “Age Determination” OR “Dental Age” OR “Estimation Techniques” OR “Chronological Age” OR “Age Estimative” OR “Forensic Sciences” OR “Science, Forensic”) AND (“Dentistry” OR “Oral Medicine” OR “Odontology” OR “Dentition” OR “Teeth” OR “Tooth” OR “Stomatognathic System”) AND (“Brazil” OR “Brazilian” OR “Brazilians” OR “Brazilian People” OR “Brazilian Population”))
LILACS http://lilacs.bvsalud.org/	((“Forensic Odontology” OR “Forensic Dentistry” OR “Forensic Science” OR “Age Estimation” OR “Age Determination” OR “Dental Age” OR “Estimation Techniques” OR “Chronological Age” OR “Age Estimative” OR “Forensic Sciences” OR “Science, Forensic”) AND (“Dentistry” OR “Oral Medicine” OR “Odontology” OR “Dentition” OR “Teeth” OR “Tooth” OR “Stomatognathic System”) AND (“Brazil” OR “Brazilian” OR

	"Brazilians" OR "Brazilian People" OR "Brazilian Population"))
SciELO http://www.scielo.org/	(("Forensic Odontology" OR "Forensic Dentistry" OR "Forensic Science" OR "Age Estimation" OR "Age Determination" OR "Dental Age" OR "Estimation Techniques" OR "Chronological Age" OR "Age Estimative" OR "Forensic Sciences" OR "Science, Forensic") AND ("Dentistry" OR "Oral Medicine" OR "Odontology" OR "Dentition" OR "Teeth" OR "Tooth" OR "Stomatognathic System") AND ("Brazil" OR "Brazilian" OR "Brazilians" OR "Brazilian People" OR "Brazilian Population"))
Web of Science http://apps.webofknowledge.com/	(("Forensic Odontology" OR "Forensic Dentistry" OR "Forensic Science" OR "Age Estimation" OR "Age Determination" OR "Dental Age" OR "Estimation Techniques" OR "Chronological Age" OR "Age Estimative" OR "Forensic Sciences" OR "Science, Forensic") AND ("Dentistry" OR "Oral Medicine" OR "Odontology" OR "Dentition" OR "Teeth" OR "Tooth" OR "Stomatognathic System") AND ("Brazil" OR "Brazilian" OR "Brazilians" OR "Brazilian People" OR "Brazilian Population"))
Embase https://www.embase.com	('forensic odontology'/exp OR 'forensic odontology' OR 'forensic dentistry'/exp OR 'forensic dentistry' OR 'forensic science'/exp OR 'forensic science' OR 'age estimation'/exp OR 'age estimation' OR 'age determination'/exp OR 'age determination' OR 'dental age'/exp OR 'dental age' OR 'estimation techniques' OR 'chronological age'/exp OR 'chronological age' OR 'age estimative' OR 'forensic sciences'/exp OR 'forensic sciences' OR 'science, forensic') AND ('dentistry'/exp OR 'dentistry' OR 'oral medicine'/exp OR 'oral medicine' OR 'odontology'/exp OR 'odontology' OR 'dentition'/exp OR 'dentition' OR 'teeth'/exp OR 'teeth' OR 'tooth'/exp OR 'tooth' OR 'stomatognathic system'/exp OR 'stomatognathic system') AND ('brazil'/exp OR 'brazil' OR 'brazilian'/exp OR 'brazilian' OR 'brazilians'/exp OR 'brazilians' OR 'brazilian people' OR 'brazilian population')
OpenGrey http://www.opengrey.eu/	("Age determination" OR "Age estimative" OR "Estimation techniques") AND ("Brazil" OR "Brazilian population")
OpenThesis http://www.openthesis.org/	("Age determination" OR "Age estimative" OR "Estimation techniques") AND ("Brazil" OR "Brazilian population")

Source: Elaborated by the authors (2020).

Study selection

Study selection was performed in four steps. The first consisted of the identification of studies after bibliographic search. The studies were imported into EndNote Web™ (Thomson Reuters, Toronto, Canada) software in order to remove the duplicates. The remaining unique studies were listed in Microsoft Word™ 2019 (Microsoft ™ Ltd, Washington, USA) for the manual removal of duplicates. An exercise of study selection was performed to calibrate the examiners on judging the eligibility criteria throughout 20% of the sample. Proper agreement (Kappa ≥ 0.81) led the examiners to the second step.

The second phase consisted of excluding studies based on title reading, separately between examiners and sequentially. Studies were excluded because their titles were evidently not related to the topic of this systematic review. In case of doubt, the studies were kept for phase three. In the third phase, study exclusion was performed based on abstract reading; two examiners were enrolled and proceeded independently. In the fourth phase, exclusion was performed based on eligibility criteria after full-text reading. The reasons for exclusion were recorded and presented for discussion with a third examiner familiar with the topic.

Data extraction

The two examiners enrolled for data extraction underwent a previous calibration exercise to verify their agreement. The initial data extracted from the studies were the authorship, year, language and main country of publication. Sample characteristics also were extracted and consisted of age interval, sample size, patient sex, dental age estimation technique, main outcome, the difference between chronological and estimated ages, ethical criteria involved, the use of checklists for observational study report (e.g. STROBE), and the type of imaging analysis used for dental age estimation.

Risk of bias

The Joanna Briggs Institute Critical Appraisal tools (JBI) for use in systematic reviews of cross-sectional studies (Moola et al., 2020) was used. As recommended by PRISMA (Moher et al., 2009), two examiners assessed each study based on the criteria used to rank the risk of bias. High risk of bias was found when positive answers were ≤49%; moderate risk of bias was considered when the risk of bias was between 50% and 69%; while low risk of bias was detected when positive answers were above 70%.

Summary measures

The obtained outcomes were presented descriptively to clarify the potential heterogeneity of the studies. A meta-analysis of eventually homogeneous studies was planned.

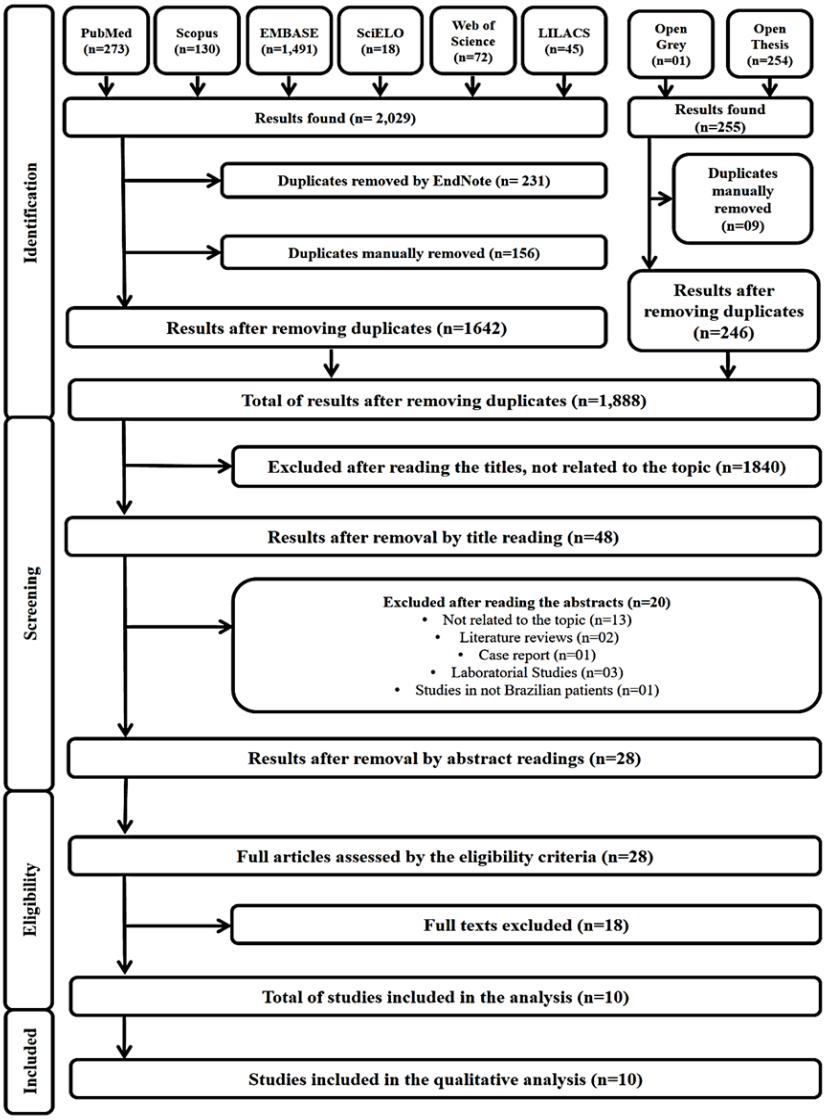
3. Results

Study selection

The initial search resulted in 2284 studies distributed in eight databases, including the grey literature. After the exclusion of duplicates, a total of 1888 studies remained. Title reading led to 1840 exclusions. Twenty of the 48 remaining studies were excluded based on abstract reading. At this point the exclusions were justified based on lack of relation with the Research topic (n = 13); because they were structured as systematic reviews (n = 2), case

report (n = 1), laboratory surveys (n = 3); and because they did not sample Brazilians (n = 1). From the 28 remaining studies, eighteen were excluded during full-text reading, with the following reasons: did not assess third molars (Marcondes et al., 1965; Carvalho et al., 1990; Eid et al., 2002; Kurita et al., 2007; Maia et al., 2010; Fernandes et al., 2011; Cericato et al., 2016; Lavez et al., 2017; Benedicto et al., 2018; Lopes et al., 2018; Machado et al., 2018; Mazzili et al., 2018; Mazzili et al., 2019); did not distinguish third molars analysis from the other teeth (Franco et al., 2013); combine dental and skeletal parameters for age estimation (Azevedo et al., 2018); did not sample Brazilians (Sharma et al., 2018); did not include adolescents (Luz et al., 2019) and not found even after deep search (Rosa, 1969). Ten studies were included in the qualitative analysis (Carneiro et al., 2010; Oliveira et al., 2012; Lopez et al., 2013; Deitos et al., 2015; Soares et al., 2015; Tonin et al., 2016; Ribeiro et al., 2018; Nóbrega et al., 2019; Ramaswami et al., 2020; Sousa et al., 2020). Figure 1 shows the literature review process up to the inclusion and analysis of the eligible studies.

Figure 1. Flowchart depicting the steps of the present systematic literature review and quantification of studies from identification to inclusion.



Source: Elaborated by the authors (2020).

Study characteristics

The studies were published between 2010 and 2020 and were designed with samples from three regions of Brazil, namely the Northeast (n = 4), Southeast (n = 5), and Southeast and Midwest combined (n = 1). All the studies used panoramic radiographs for the analysis of third molars. Demirjian's staging system (DEM) (Demirjian et al., 1973) was the most used (n = 5), followed by Nicodemo' approach (NIC) (Nicodemo et al., 1974) (n = 3), the Third Molar Maturation Index (I3M) (Cameriere et al., 2008) (n = 2), Nolla's (NOL) (Nolla, 1960) (n =1), own Modified Scoring Technique (MST) (Lopez et al., 2013) (n = 1) and the London

Atlas (LON) (AlQahtani et al., 2010) (n = 1). Sample size ranged between 288 and 2097 participants (mean sample n = 711). Studies that reported on sex distribution registered 3126 males and 3985 females. Seven studies analyzed the four third molars, while three studies analyzed only mandibular third molars. Report of ethical criteria was mentioned in nine studies. None of the studies reported the methods and outcomes following the STROBE checklist for observational data (Table 2).

Table 2. Summary of the main characteristics of the eligible studies.

Author, year	Region	Sample (n)	Participants	Age (Min – Max) [years]	Average age ± SD (years)	Techniques
Carneiro et al., 2010	Northeast	312	194♀ 118♂	9 - 21	n.r.	Nicodemo
Oliveira et al., 2012	Southeast	407	206♀ 201♂	6 - 25	15.49 ± 5.73	Modified Demirjian
Lopez et al., 2013	Southeast	659	268♀ 391♂	15 - 23	18.89 ± n.r.	Modified Scoring Technique (MST); Demirjian
Deitos et al., 2015	Southeast and Midwest	444	239♀ 205♂	14 - 22	20.14 ± 1.74♀ 19.86 ± 1.57♂	Third Molar Maturation Index (I_{3M})
Soares et al., 2015	Northeast	2097	1,150♀ 947♂	6 - 22	15.0 ± 3.4	Demirjian
Tonin et al., 2016	Southeast	1200	654♀ 546♂	9 - 20	n.r.	Nicodemo
Ribeiro et al., 2018	Northeast	1205	625♀ 580♂	5 - 21	14.67 ± 3.53	Nolla; Demirjian; Nicodemo
Nobrega et al., 2019	Northeast	394	209♀ 185♂	14 - 23	n.r.	Third Molar Maturation Index (I_{3M})
Ramaswami et al., 2020	Southeast	1013	644♀ 369♂	15 - 23	n.r.	Demirjian
Sousa et al., 2020	Southeast	288	155♀ 133♂	5 - 23	n.r.	London Atlas

n: sample size; ♀: females; ♂: males; n.r.: not reported by the author; SD: standard deviation. **Source:** Elaborated by the authors (2020).

Risk of bias

All the eligible studies had low risk of bias – showing high percentage of positive answers to the questions of JBI tool. The only negative answers came from two studies that were not clear enough to report the inclusion and exclusion criteria in question #1 (Table 3).

Table 3. Risk of bias assessed by the Joanna Briggs Institute (JBI) Critical Appraisal Tools for use in JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies (Moola et al., 2020).

Authors	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	% Yes	Risk
Carneiro et al., 2010	√	√	√	√	√	√	√	√	100	Low
Oliveira et al., 2012	--	√	√	√	√	√	√	√	87,5	Low
Lopez et al., 2013	√	√	√	√	√	√	√	√	100	Low
Deitos et al., 2015	√	√	√	√	√	√	√	√	100	Low
Soares et al., 2015	√	√	√	√	√	√	√	√	100	Low
Tonin et al., 2016	--	√	√	√	√	√	√	√	87,5	Low
Ribeiro et al., 2018	√	√	√	√	√	√	√	√	100	Low
Nóbrega et al., 2019	√	√	√	√	√	√	√	√	100	Low
Ramaswami et al., 2020	√	√	√	√	√	√	√	√	100	Low
Sousa et al., 2020	√	√	√	√	√	√	√	√	100	Low

Q1. Were the criteria for inclusion in the sample clearly defined? Q2. Were the study subjects and the setting described in detail? Q3. Was the exposure measured in a valid and reliable way? Q4. Were objective, standard criteria used for measurement of the condition? Q5. Were confounding factors identified? Q6. Were strategies to deal with confounding factors stated? Q7. Were the outcomes measured in a valid and reliable way? Q8. Was appropriate statistical analysis used? √ - Yes; -- - No; U – Unclear; N/A - Not/Applicable.
Source: Elaborated by the authors (2020).

Individual outcomes of the studies

All the studies (n = 10) that were listed for qualitative analysis showed a correlation between chronological age and third molar mineralization stages. Four studies (Soares et al., 2015; Tonin et al., 2016; Nóbrega et al., 2019; Ramaswami et al., 2020) found out that the applied techniques resulted in a positive correlation of within their specific population regardless the sex of the participants. One study (Oliveira et al., 2012) showed that males reached later levels of third molar mineralization before females – statistical significance, however, was not found. A more quantitative study showed mean underestimation of six months for third molar age estimation in Southeast. Other study (Deitos et al., 2015) suggested that supplementary alternatives must be used to aid dental age estimation in Court when specific ages thresholds of legal interest is considered (i.e. the age of 18 as marker for legal majority). The main outcomes of the eligible studies included for qualitative assessment are described in Table 4.

Table 4. Main outcomes of the eligible studies included for qualitative assessment.

Author, year	Main outcomes
Carneiro et al., 2010	There was a correlation between the chronological age and the dental age obtained through the mineralization stages proposed by NIC technique. The development of regional staging tables is recommended to reduce the difference between chronological and estimated ages.
Oliveira et al., 2012	The results indicated a strong correlation between chronological age and mineralization of third molars. The study indicated that more modern Brazilian generations reach an early mineralization of the third molars compared to older generations. Males showed earlier development compared to females.
Lopez et al., 2013	The dental age was underestimated nearly 6 months. The modified Demirjian technique showed greater reproducibility for assessing the age of Brazilians.
Deitos et al., 2015	I3M technique was applicable for age estimation in Brazilians. However, it is suggested the additional use of other tests, analysis and parameters in judicial or criminal situations.
Soares et al., 2015	There was a significant correlation between chronological age and the mineralization stages proposed by DEM technique. It was possible to use the Demirjian technique to estimate age, regardless of sex, or the position of the third molar.
Tonin et al., 2016	The mineralization stages proposed by NIC were applicable for age estimation, regardless of tooth position.
Ribeiro et al., 2018	There was a correlation between chronological age and developmental stages of third molars in the three techniques used (DEM, NOL and NIC). The development of third molars was more advanced in males in most stages, for the three techniques.
Nóbrega et al., 2019	The Cameriere technique allowed to accurately distinguish the age of adolescents in the population studied, with greater precision observed in males.
Ramaswami et al., 2020	The stages of mineralization proposed by DEM technique was useful to assess the development of third molars to estimate age in the evaluated population, with no difference for men or women, above or below 18 years.
Sousa et al., 2020	London Atlas technique must be carefully interpreted when third molars development is the only age parameter.

DEM: Demirjian technique; NIC: Nicodemo technique; NOL: Nola technique; I3M: Third molar maturity indec technique.
Source: Elaborated by the authors (2020).

Seven studies were included in the quantitative analysis (Table 5). Studies that used the same techniques for third molar age estimation were analyzed together. Three studies (Oliveira et al., 2012; Lopez et al., 2013; Ramaswami et al., 2020) were combined for the analysis of DEM technique, two studies Carneiro et al., 2010; Tonin et al., 2016) were combined for NIC technique, and two studies (Deitos et al., 2015; Nóbrega et al., 2019) were combined for the I3M technique. During the quantitative analysis, mean chronological age and standard deviation were recorded, as well as sampled sex distribution, third molar position (maxillary, mandibular, right and left) and mineralization stage/ratio depending on the technique.

Table 5. Summary of the main quantitative outcomes of the eligible studies regarding stages of third molar mineralization and chronological age per technique applied for age estimation.

NIC technique											
				Mineralization stages							
	Sex	Position	Side	1	2	3	4	5	6	7	8
Carneiro et al., 2010	M	Maxillary	n.r.	120,60± 9,47	129,00± 6,95	132,00± 16,16	144,61± 21,79	159,25± 19,51	180,75± 17,76	197,88± 16,55	234,42± 19,00
Carneiro et al., 2010	M	Mandibular	n.r.	127,83± 16,04	120,08± 10,43	135,66± 17,75	145,32± 18,86	158,28± 21,98	183,18± 17,08	207,00± 20,46	232,40± 23,11
Carneiro et al., 2010	F	Maxillary	n.r.	114,36± 19,40	126,53± 16,48	132,31± 27,82	140,35± 16,11	161,57± 16,11	184,34± 22,72	214,30± 22,25	237,50± 17,43
Carneiro et al., 2010	F	Mandibular	n.r.	113,00± 16,11	109,85± 10,33	131,00± 18,20	140,30± 14,13	167,34± 23,65	185,03± 18,55	214,92± 22,80	241,20± 15,28
Tonin et al., 2016	M	Maxillary	Right	116,52± 10,68	120,96± 9,00	132,72± 14,64	152,40± 18,72	182,76± 18,96	198,96± 18,24	230,88± 12,36	231,72± 10,92
Tonin et al., 2016	M	Maxillary	Left	113,76± 7,80	122,52± 10,44	132,00± 12,12	153,72± 17,76	182,52± 20,04	199,32± 18,48	220,80± 13,68	229,68± 12,24
Tonin et al., 2016	M	Mandibular	Right	115,32± 9,84	118,56± 10,08	130,92± 13,44	150,36± 16,92	179,28± 19,20	195,00± 18,48	217,68± 12,24	238,20± 9,96
Tonin et al., 2016	M	Mandibular	Left	115,68± 10,20	118,80± 19,12	131,28± 13,56	151,68± 20,04	180,72± 20,40	194,28± 18,60	217,92± 12,84	228,24± 11,16
Tonin et al., 2016	F	Maxillary	Right	114,72± 10,56	121,80± 12,60	134,04± 16,32	160,56± 23,52	182,64± 22,92	200,52± 22,56	219,36± 18,48	230,52± 13,56
Tonin et al., 2016	F	Maxillary	Left	113,52± 9,00	123,84± 12,72	133,92± 15,00	161,16± 24,00	182,64± 20,52	199,20± 22,68	219,00± 18,12	229,44± 13,44
Tonin et al., 2016	F	Mandibular	Right	113,52± 10,08	125,40± 15,36	132,84± 14,28	155,64± 19,44	180,96± 24,48	197,64± 22,44	218,04± 17,76	230,52± 13,44
Tonin et al., 2016	F	Mandibular	Left	115,56± 10,20	122,04± 15,72	131,40± 20,04	159,12± 22,32	180,72± 24,24	199,08± 22,68	218,88± 17,40	230,52± 13,44
DEM technique											
				Mineralization stages							
	Sex	Position	Side	A	B	C	D	E	F	G	H
Oliveira et al., 2012	M	Mandibular	Right	102,00± 12,00	114,00± 18,00	129,60± 18,00	156,00± 19,20	169,20± 21,60	187,20± 13,20	208,80± 16,80	260,40± 26,40
Oliveira et al., 2012	M	Mandibular	Left	102,00± 12,00	114,00± 19,20	130,80± 18,00	154,80± 15,60	176,40± 24,00	190,80± 16,80	207,60± 16,80	260,40± 26,40
Oliveira et al., 2012	F	Mandibular	Right	100,80± 8,40	121,20± 18,00	135,60± 16,80	158,40± 18,00	172,80± 20,40	198,00± 27,60	220,80± 27,60	259,20± 26,40
Oliveira et al., 2012	F	Mandibular	Left	98,40± 12,00	121,20± 18,00	128,40± 19,20	158,40± 19,20	168,00± 21,60	199,20± 28,80	220,80± 27,60	259,20± 26,40
Lopez et al., 2013	M	Maxillary	Right	n.r.	193,00± 0,00	n.r.	205,20± 18,96	214,80± 30,60	217,20± 25,20	222,00± 26,40	230,40± 26,28
Lopez et al., 2013	M	Maxillary	Left	n.r.	193,00± 0,00	193,00± 0,00	204,00± 15,60	213,60± 30,24	216,00± 23,88	224,40± 24,96	230,40± 26,16
Lopez et al., 2013	M	Mandibular	Right	n.r.	n.r.	202,80± 35,04	211,20± 18,12	205,20± 21,00	213,60± 24,72	222,00± 22,80	234,00± 25,44
Lopez et al., 2013	M	Mandibular	Left	n.r.	n.r.	187,20± 5,64	208,80± 14,64	207,60± 25,92	208,80± 21,12	224,40± 23,76	234,00± 24,96
Lopez et al., 2013	F	Maxillary	Right	n.r.	n.r.	218,40± 0,00	208,80± 27,60	220,80± 24,60	223,20± 25,80	229,20± 26,28	235,20± 26,16
Lopez et al., 2013	F	Maxillary	Left	n.r.	n.r.	252,00± 17,76	219,60± 31,32	218,40± 22,56	223,20± 25,08	228,00± 26,16	237,60± 25,20
Lopez et al., 2013	F	Mandibular	Right	n.r.	n.r.	201,60± 28,44	220,80± 25,68	217,20± 26,04	224,40± 26,64	232,80± 26,28	236,40± 25,44
Lopez et al., 2013	F	Mandibular	Left	n.r.	188,40± 0,00	203,40± 23,40	218,40± 21,36	217,20± 24,36	222,00± 26,52	234,00± 27,36	237,60± 24,84
Ramaswami et al., 2020	M	Maxillary	n.r.	n.r.	n.r.	189,60± 2,40	194,40± 14,40	192,00± 9,60	192,48± 10,80	204,00± 10,80	242,40± 19,20
Ramaswami et al., 2020	M	Mandibular	n.r.	n.r.	n.r.	186,00± 3,60	192,00± 12,00	198,00± 15,60	199,20± 9,60	207,60± 13,20	243,60± 19,20
Ramaswami et al., 2020	F	Maxillary	n.r.	n.r.	n.r.	186,00± 2,40	194,40± 12,00	206,40± 19,20	207,60± 20,40	213,60± 19,20	246,00± 18,00
Ramaswami et al., 2020	F	Mandibular	n.r.	n.r.	184,8± 1,2	193,20± 10,80	204,00± 25,20	213,60± 22,80	207,60± 18,00	220,80± 18,00	248,40± 16,80
I3M technique											
				Mineralization ratios (index)							
	Sex	Position	Side	0,0 - 0,04	0,04- 0,08	0,08 - 0,3	0,3 - 0,5	0,5 - 0,7	0,7 - 0,9	0,9 -	N/A
Deitos et al., 2015	M	n.r.	n.r.	238,32± 18,84	216,00± 20,52	197,64± 16,68	180,36± 12,36	168,72± 6,48	183,00± 21,96	171,36± 5,76	N/A
Deitos et al., 2015	F	n.r.	n.r.	241,68± 20,88	224,52± 21,36	209,04± 26,40	192,72± 18,24	191,04± 15,84	188,28± 26,04	183,36± 18,96	N/A
Nobrega et al., 2019	M	n.r.	n.r.	256,68± 24,60	239,88± 28,20	219,72± 27,60	200,40± 27,96	183,12± 13,80	191,16± 32,52	185,40± 5,76	N/A
Nobrega et al., 2019	F	n.r.	n.r.	249,12± 23,88	235,80± 26,16	209,88± 23,16	183,00± 11,88	182,04± 7,20	179,40± 8,16	176,40± 8,88	N/A

NIC: Nicodemo technique; DEM: Demirjian technique; I3M: third molar maturity index; M: males; F: Females.
Source: Elaborated by the authors (2020).

4. Discussion

The scientific literature on dental age estimation faces a new trend of evidence-based research. Over the last decades, the so-called validation studies emerged to test the performance of international methods on a broad spectrum of target populations. Naturally, systematic reviews progressively took place to compile performances pooling together different populations and their estimates from a single method (Santiago et al., 2018). The other way around, systematic reviews also were structured targeting a single specific population and screening the performance of different methods over it (Franco et al., 2020b) The latter, in particular, is only feasible when several methods were previously applied for validation testing in the target population. The advantage of this approach is having a quantified overview of the available methods and even evidences to find out the method with best performance. The present study was designed as a systematic review targeting the Brazilian population in the search for studies that performed dental age estimation via third molars.

Geographically, Brazil has 27 federative units (26 States and a federal district) divided into five main regions: North (n = 7), Northeast (n = 9), Midwest (n = 4), Southeast (n = 4) and South (n = 3). The North has the largest territory, but the lowest number of habitants. Southeast and Northeast regions figure as those tanked first and second in population (IBGE, 2020) Brazil has not only a continental size and a large nation (n = nearly 210 million), but also (at least on of) the largest community of active dentists worldwide (n = nearly 330 thousand) (CFO, 2020). Is estimated that almost 30% of the Brazilian dentists are located in the State of São Paulo, in the Southeast (CFO, 2020). This scenario justifies the predominance (60%) of populations sampled from the Southeast region across the eligible studies. Other regions, for instance, were scarce of studies dedicated to third molar age estimation (i.e. Midwest region), or even lacked samples (i.e. South region). This systematic literature review corroborates the need for studies with populations from the Midwest and South in order to build-up a better panorama of third molar populations in Brazil.

When it comes to third molar dental age estimation, the target sample is generally found within the interval between 16 and 23 years – a category of individuals in which third molars are the only teeth developing (Franco et al., 2013). In particular, at the age of 16, it is expected at least initial root formation of third molars (Franco et al., 2020a). In the present systematic review, only 40% of the eligible studies sampled individuals exclusively aged within or close to the age category of adolescents. The remaining studies analyzed third

molars from early development (down to the minimum age of five years old). This approach is justified to understand the chronology of third molar development in the childhood, but in practice it may have a restricted use. In the childhood, several teeth develop simultaneously and the combination of developing information leads to more accurate age estimates Franco et al., 2013). Specific methods (Demirjian et al., 1973; Nicodemo et al., 1974; Willems et al., 2001) exist for the purpose of age estimation of children and they are encouraged instead of third molar techniques.

Another aspect to be considered in the eligible studies is the sample distribution, which was evidently not balanced based on sex for all the studies. The current knowledge of dental age estimation corroborates the importance of distinguishing males and females because of their different development timing (Jung and Cho, 2014). Hence, having samples with balanced (homogeneous) distribution based on sex could reduce the bias. While some samples had sex distribution close to a 1:1 ratio (Oliveira et al., 2012), other studies (Ramaswami et al., 2020) reached the discrepant ratio of 1:1.74. It is the duty of the present systematic review to recommend standard sampling strategies that could minimize as much as possible sex bias in dental age estimation. To this end, it is suggested that the ratio of males and females should not be close to 1:1 only for the general sample, but for each age category (of one year, for instance) within the sample. Ideally, in this context, a sample of 800 individuals between 16 and 23 years, should have 400 females and 400 males homogeneously distributed on sex every interval of one year (i.e. 50 males and 50 females between 16 and 16.99 years and so on).

Sampling aspects apart, this study focused on understanding the techniques used for third molar age estimation in Brazil and how they behave when tested in different regions. Interestingly, the technique (DEM) (Demirjian et al., 1973) used more often in the eligible studies was not a technique originally designed for forensic purposes even less for third molar staging. DEM technique proposes the analysis of the seven mandibular left permanent teeth in order to estimate the age of young individuals. Since the technique depends on remaining development of the permanent teeth (except third molars), it not much of use for application in adolescents. With the popularization of DEM technique, adapted staging systems appeared in the scientific literature for specific application in third molars (Mincer et al., 1993; Solari and Abramovitch, 2002). The present systematic literature review recommends application of methods in practice as they were originally designed. Hence, DEM should be preferably used for children, while the subsequent adaptations should be used for adolescents (third molars). Ideally, authors should pay attention to techniques that were originally established for

forensic applications and for third molar assessment. This is the case of I3M approach (Cameriere et al., 2008). Despite the need for metric analysis the I3M is dedicated to quantify third molar morphometric ratios in face of cut-off values for forensic applications. Consequently, this technique represents an alternative specifically for third molar age estimation. It must be noted, however, that evidence-based outcomes found in the scientific literature point toward a better age prediction from staging techniques compared to metric (ratios and measurements) analyses (Thevissen et al., 2011). In other words, dental age estimation performances could benefit more from third molar staging (using original third molar systems, preferably designed for forensic purposes).

Another technique used in Brazil for third molar age estimation was expected because of its inherent Brazilian origin (Nicodemo et al., 1974), NIC technique was used in three eligible studies. This technique, not usually applied in foreign populations, is the combination of three separate studies with different tooth positions that was consecutively used over the time since it was first published in 1974. The main limitation of the technique is the small sample of origin and the large age interval between ordinal stages. Despite the known limitations of the method, it remains popular in medico-legal institutes of Brazil. The present systematic literature review highlights the need of using other existing methods (I3M, London Atlas, Modified DEM) hereby confirmed as applicable for Brazilian adolescents. This is an evidence-based call to having the attention of Brazilian forensic dentists about the available international methods that may be of use for practice.

The low risk of bias of the eligible studies and the general applicability of international methods corroborated for third molar age estimation suggest that the Brazilian forensic practice has a potential variety of tools scientifically tested for third molar age estimation. An overview of the methods translated for interpretation and application in practice was presented in Table 5 as a palpable visualization of the three main methods studied in the country. Transferring the knowledge from academy to practice is a challenging task that must be promoted. Systematic literature reviews must focus on bridging the existing gap to deliver evidence-based tools to forensic dentists that seek for scientifically reliable performances.

5. Conclusion

A broad spectrum of techniques for third molar age estimation was tested within Brazilian adolescents. DEM, NIC and I3M techniques were the most common and all showed proper applicability. Forensic dentists are encouraged to use in practice techniques as they

were originally designed or scientifically adapted.

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