Relationship between Presence of Third Molars and Prevalence of Periodontal Pathology of Adjacent Second Molars: a Systematic Review and Meta-analysis

Yang YANG[1#], Yi TIAN[1#], Li Juan SUN[1], Hong Lei QU[1], Fa Ming CHEN[1]

Objective: *To estimate the mean prevalence of periodontal pathology of adjacent second molars (A-M2s) to third molars (M3s) and identify related confounding factors.*
Methods: *Studies published before August 2020 were systematically searched in the Cochrane Library, EMBASE and MEDLINE databases. We included cross-sectional studies that evaluated the periodontal pathology of A-M2s based on clinical or radiographic examinations at the molar level. Studies employing similar periodontal parameters were pooled. Clinical attachment loss ≥ 3 mm, alveolar bone loss ≥ 3 mm or ≥ 20% root length were defined as early periodontal defects, and at least one site with probing depth ≥ 5 mm was considered as deep periodontal pockets around A-M2s in the data synthesis.*
Results: *Nine studies (14,749 M3s) were ultimately included in the meta-analysis. On average, 19% of A-M2s showed distal early periodontal defects with the presence of M3s (95% confidence interval [95% CI] 9%–35%). Subgroup analyses suggested the prevalence was 32% (95% CI 16%–54%) in the mandible, and the prevalence was higher with nonimpacted M3s (25%, 95% CI 12%–47%) than with impacted M3s (19%, 95% CI 10%–35%). Additionally, the pooled prevalence for deep periodontal pockets around A-M2s was 52% (95% CI 39%–64%). Subgroup analyses suggested the prevalence was higher in the mandible (62%, 95% CI 45%–76%) than in the maxilla (43%, 95% CI 31%–56%), and for nonimpacted M3s the prevalence reached 50% (95% CI 36%–64%).*
Conclusion: *The presence of M3s, especially mandibular and nonimpacted M3s, negatively affects the periodontal status of A-M2s.*
Key words: *meta-analysis, periodontal pathology, prevalence, second molars, third molars*
Chin J Dent Res 2022;25(1):45–55; doi: 10.3290/j.cjdr.b2752683

1 State Key Laboratory of Military Stomatology, Department of Periodontology, School of Stomatology, National Clinical Research Centre for Oral Diseases, Fourth Military Medical University, Xi'an, P.R. China.
# These authors contributed equally to this work.

Corresponding author: Dr Fa Ming CHEN, Department of Periodontology, School of Stomatology, National Clinical Research Center for Oral Diseases, Fourth Military Medical University, #145 West Changle Road, Xi'an 710032, P.R. China. Tel/Fax: 86-29-84776096. Email: cfmsunhh@fmmu.edu.cn

This study was partially supported by the National Natural Science Foundation of China (Subproject), grant/award number 81991503.

The eruption of third molars (M3s) is restricted by adjacent tissue and limited space, and M3s often indeed fail to fully erupt[1,2]. Their anatomical features frequently lead to food impaction and plaque accumulation in M3 regions[3]. Insufficient plaque control makes M3s and their neighbours, adjacent second molars (A-M2s), vulnerable to periodontal diseases[4]. Studies have found laboratory evidence of increased levels of periodontal pathogens in M3 regions, even with few clinical symptoms of periodontal diseases[5,6]. Periodontal pathogens in M3 regions develop and the periodontal status of A-M2s is affected by age[7]. As early as the 1960s, Ash et

al[8] reported the periodontal risks related to M3s. Since then, there have been a number of studies examining the relationship between the presence of M3s and the periodontal pathology of A-M2s.

Prevalence is one of the most important pieces of data describing the epidemiological characteristics of the periodontal pathology of A-M2s; however, estimates of the prevalence of periodontal pathology of A-M2s at the molar level vary significantly among studies, ranging from 3.1% to 64.5%[9,10]. Diverse periodontal parameters, including probing depth (PD), alveolar bone loss (ABL) and clinical attachment loss (CAL), accompanied by different examined sites (single or multiple sites around A-M2s), have been employed to evaluate the periodontal status of A-M2s[3,11,12], which may partly account for the statistically significant variance in results. Nevertheless, different characteristics of M3s and patients may also contribute to the high degree of heterogeneity in prevalence[13-15]. Impacted M3s (I-M3s) have been reported to be associated with negative periodontal influences on A-M2s[16-18]. Many studies have compared prevalence among impaction types, but diverse results have been recorded for various I-M3 classifications[9,13,14,19]. In addition, studies on periodontal risks associated with nonimpacted M3s (N-M3s) are limited and controversial[11,14,20]. Characterising the confounding factors that cause heterogeneity is important for evaluating the risks of the presence of M3s for individuals.

Estimating the mean prevalence of periodontal pathology of M2s with neighbouring M3s is the first step towards elucidating the relationship between the presence of M3s and the periodontal status of A-M2s, which contributes to M3 clinical decision making. Thus, this systematic review and meta-analysis aimed to synthesise and calculate the mean prevalence of periodontal pathology of A-M2s at the molar level, and to identify the confounding factors that lead to a high degree of variation in prevalence.

Materials and methods

The meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[20] (Appendix 1, provided on request). The meta-analysis was not registered.

Literature search

The Cochrane Library, EMBASE and MEDLINE databases were searched systematically from inception to August 2020 using specific keywords. The keywords were described by wildcards and MeSH, and the following terms were combined in different databases: "third molar*"; "third-molar*"; "3rd molar*"; "wisdom tooth"; "wisdom teeth" and "second molar*"; "2nd molar*; "adjacent molar*"; "adjacent tooth"; "adjacent teeth" and "periodontitis"; "periodontal disease*"; "periodontal defects"; "periodontal destruction"; "periodontal pathology"; "periodontal inflammation"; "attachment loss"; "alveolar bone loss"; and "periodontal pockets".

Study selection

Two investigators (YY and YT) independently reviewed and screened the searched articles. The selection process involved reading the titles and abstracts, reading the full articles and assessing the inclusion/exclusion of potentially qualified articles. In the event of ambiguities, detailed information was obtained by contacting the authors. Any disagreements were resolved through discussion or through consultation with persisted, a third investigator (LJS) to make the final decision. The inclusion criteria used for the systemic review were as follows:

- cross-sectional studies that evaluated the periodontal status of M2s with neighbouring M3s, regardless of being symptomatic or asymptomatic;
- studies defining the periodontal pathology of A-M2s either through clinical or radiographic examination;
- studies providing explicit information for calculating the prevalence of periodontal pathology of A-M2s at the molar level.

Reviews, case reports, case series, articles with full texts unavailable, studies with a sample size < 200 at the molar level and controversial studies without responses from authors were excluded. Studies involving specific populations such as pregnant women and orthodontic patients were also excluded, as were studies that screened the periodontal status.

Data extraction

The following data were extracted: basic information (first author, year of publication, journal and country), sample characteristics (study design, source of sample, sample number, sample age and sex and periodontal condition of sample), methods (clinical and/or radiographic examination), outcomes (prevalence of periodontal pathology of A-M2s at the molar level) and quality evaluation. CAL, ABL and PD were the most commonly reported parameters for evaluating periodontal status; thus, relevant data at the molar level were

extracted to estimate the prevalence of periodontal pathology of A-M2s clinically and radiographically. Moreover, the prevalence of periodontology of A-M2s under different M3 locations, M3 impaction status, patient sex and patient age was further extracted and listed below the overall prevalence. If one study reported the prevalence of periodontal pathology with more than one parameter, the following priority sequence was followed for data extraction: CAL, ABL and PD. Only the preoperative data from studies that compared the clinical and radiological parameters before and after M3 surgery were extracted and used for statistical analysis. When the explicit prevalence of periodontal pathology was not reported directly, the prevalence was calculated by dividing the number of A-M2s with periodontal pathology by the total number of included A-M2s.

Assessment of study bias

We used the modified Newcastle-Ottawa scale (NOS), which was formulated for cross-sectional studies, to assess the bias of the included studies[21]. For cross-sectional studies, the NOS comprises sample selection, comparability among groups and outcome measurement, and there are detailed evaluation criteria for each item. Once the study met the evaluation criterion, it could be evaluated at one or two points depending on the evaluation standard. The maximum number of points was 10, and a study awarded a score higher than 7 was considered at low risk of bias. Bias was independently assessed by two investigators (YY and YT) and discussion was conducted to reach a consensus on the quality of the studies.

Data synthesis

For internal consistency and high efficiency in the meta-analysis, only studies that reported the prevalence of periodontal pathology for A-M2s with similar periodontal parameters were synthesised. CAL was defined as the distance from the cementoenamel junction to the base of the periodontal pockets greater than 3 mm[22,23], and ABL as the distance from the cementoenamel junction to the alveolar bone greater than 3 mm or 20% root length[24,25]. These general definitions were used to explain the threshold values selected in this meta-analysis (CAL ≥ 3 mm, ABL ≥ 3 mm or 20% root length) for the presence of early periodontal defects. Moreover, at least one site with PD ≥ 5 mm was used to define the deep periodontal pockets around A-M2s[10]. The relevant data were imported into specific software (metafor package, meta package, in R statistical language, version 4.0.2, R Core Team, Vienna, Austria) for meta-analysis. Forest plots were used to describe the estimated effect size and 95% confidence interval (95% CI) for meta-analysis. The heterogeneity of the data was reflected by the Q-statistic and the I^2 test. If heterogeneity was significant ($I^2 > 50\%$ or $P < 0.05$), a random-effects model was used to calculate pooled data. Moreover, subgroup analyses according to different characteristics of M3s (M3 locations and impaction status) and patients (overall periodontal health, sex and age) were conducted to explore possible reasons for heterogeneity. If a sufficient number of studies were included, publication bias and sensitivity were assessed.

Results

In total, 865 records were identified using the search strategies. After removal of duplicates and title/abstract screening, 212 records were included for full-text screening. Based on the inclusion criteria, 193 records were excluded. Consequently, 19 studies were included for qualitative synthesis[3,9-16,19,20,26-33], nine of which (14749 M3s) were used for meta-analysis (Fig 1)[3,10-12,14,15,29,30,33].

Qualitative synthesis

Table 1 presents the main characteristics of all the included studies for qualitative synthesis. Only four of them used the general population as samples[12-14,31]; the others included patients in the analysis. The periodontal status of M2s was confirmed through clinical or radiographic examinations in five prospective studies that recruited participants and conducted data collection at a single time point[3,10,13,30,31]. Fourteen studies retrospectively evaluated the prevalence of periodontal pathology of M2s by collecting radiographic records[9,11,12,14-16,19,20,26-29,32,33]. Only two studies evaluated the overall periodontal health of participants using case definitions from the US Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics (AAP), and most of their participants had mild or moderate periodontitis[12,13]. The periodontal status of A-M2s was evaluated using different periodontal parameters in the included studies. Thirteen studies reported the prevalence of ABL of A-M2s[9,11,14-16,19,20,26-29,32,33] and eight described the specific degree of ABL, including ABL ≥ 1 mm[19], 3 mm[15,29,32], 5 mm[16,32] or 20% root length[11,14]. Five selected studies used PD as a parameter to evaluate the periodontal status of A-M2s[3,10,13,30,31], and in most cases, the measurement of at least one site of PD ≥ 5 mm around A-M2s was emloyed[3,10,30]. Only

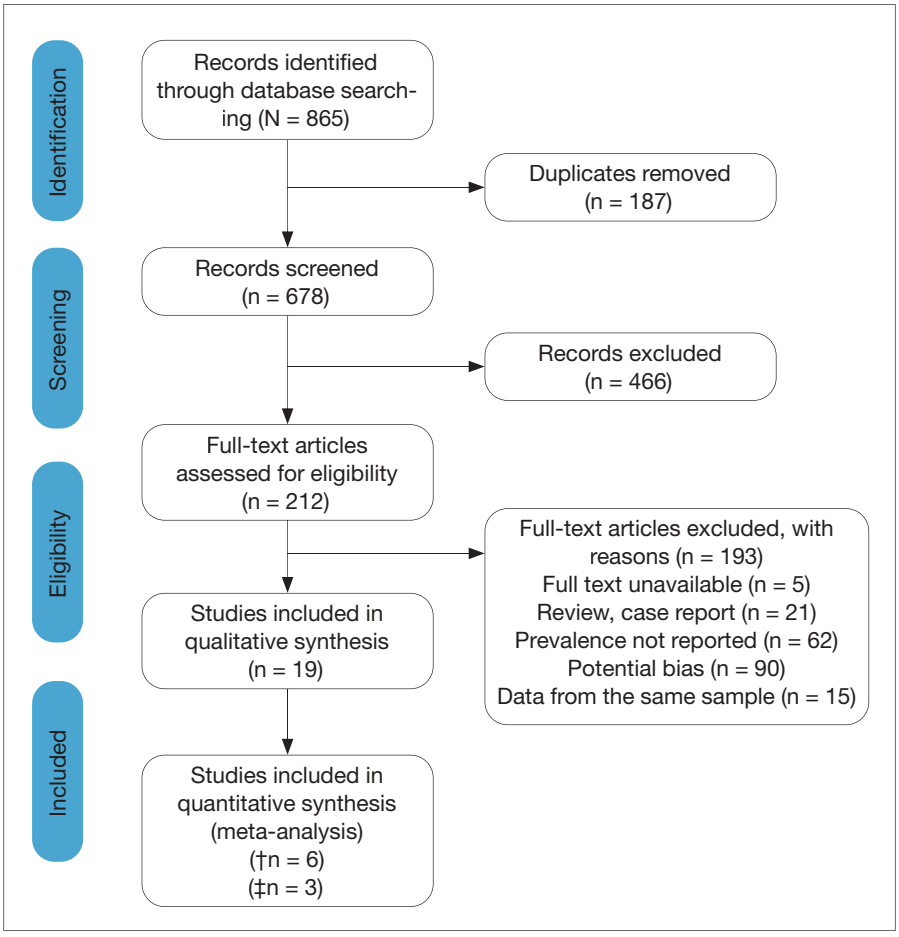

Fig 1 Flow diagram of the screening process. n, number of hits. †Analysis of early periodontal defects: CAL ≥ 3 mm, ABL ≥ 3 mm or ≥ 20% root length on distal sites of second molars with neighbouring third molars; ‡Analysis of deep periodontal pockets: at least one site with PD ≥ 5 mm around second molars with neighbouring third molars.

one study reported the prevalence of CAL on distal sites of A-M2s with depth ≥ 3 mm[12]. The NOS scores for the included studies ranged from 6 to 9, the mean score was 7.16 and the overall risk of bias was low (Appendix 2, provided on request). The main cause of bias was identified as comparability among groups.

Several studies have reported that various characteristics of M3s and patients affect the prevalence of periodontal pathology of A-M2s in different ways. Seven studies compared the difference in prevalence between mandibular and maxillary M3s[3,9-12,30,32], and only one of these found a higher prevalence with maxillary M3s than with mandibular M3s[32]. The impaction status of M3s was analysed in different ways. Four studies reported the difference in periodontal pathology among different angulations of I-M3s according to the Winter classification[9,13,15,19]. Even with different periodontal parameters, mesioangular and horizontal M3s were significantly associated with a higher risk of periodontal pathology than other angulations, and the risk for buccolingual and distal M3s was very low. Another four studies divided M3s into I-M3s (unerupted to the occlusal plane) and N-M3s (erupted to the occlusal plane) without explicit classifications of I-M3s[11,12,14,20], and three of them reported a higher prevalence of periodontal pathology with N-M3s[11,12,20]. Different impaction depths and covered tissues associated with I-M3s were analysed but indicated weak evidence with limited studies[13-15]. Additionally, four studies reported the prevalence of periodontal pathology between different age groups[13,16,28,32]. Older age was associated with a higher risk of periodontal pathology than younger age, especially ≥ 30 years; only one study came to the opposing conclusion[32]. Three studies reported a difference between sexes, but their results were completely different and showed no significant trend that sex influenced individuals' level of vulnerability to periodontal pathology of A-M2s[26,29,32].

Quantitative synthesis

Studies with similar periodontal parameters were included for the data synthesis. Six of those included in the qualitative synthesis evaluated the prevalence of early

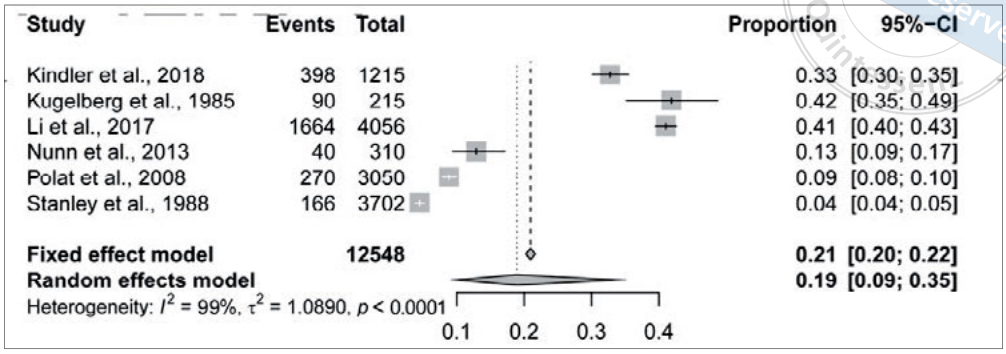

Fig 2 Forest plot of the prevalence of early periodontal defects on distal sites of second molars with neighbouring third molars.

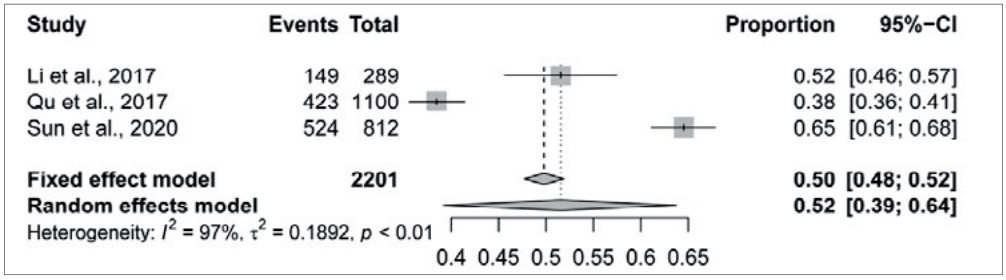

Fig 3 Forest plot of the prevalence of deep periodontal pockets around second molars with neighbouring third molars.

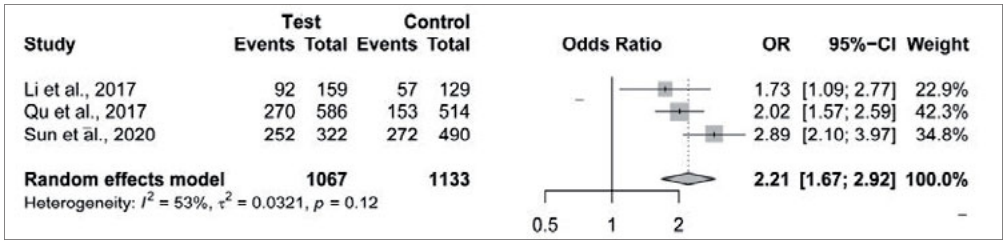

Fig 4 Forest plot of the odds ratio of deep periodontal pockets around second molars with neighbouring mandibular third molars versus maxillary third molars.

periodontal defects on distal sites of A-M2s with CAL ≥ 3 mm, ABL ≥ 3 mm or ≥ 20% root length[11,12,14,15,29,33], and three calculated the prevalence of deep periodontal pockets around A-M2s with at least one site with PD ≥ 5 mm[3,10,30], with subgroup analyses that were pooled and conducted separately. The data for other A-M2 sites and other periodontal parameters were not pooled due to the limited number of studies.

The results showed that the prevalence of early periodontal defects on distal sites of A-M2s was 19% (95% CI 9%–35%, I^2 100%, $P < 0.0001$) (Fig 2) and the prevalence of deep periodontal pockets around A-M2s was 52% (95% CI 39%–64%, I^2 97%, $P < 0.01$) with the random-effects method (Fig 3). Because the number of studies included in the meta-analysis was limited, we did not assess publication bias or conduct a sensitivity analysis.

Subgroup analyses on M3 locations

The prevalence of early periodontal defects on distal sites of A-M2s associated with mandibular M3s was 32% (95% CI 16%– 54%, I^2 99%, $P < 0.01$) (Appendix 3, provided on request). Meanwhile, a higher prevalence of deep periodontal pockets was recorded around A-M2s associated with mandibular M3s (62%, 95% CI 45%–76%, I^2 96%, $P < 0.01$) (Appendix 4, provided on request) than maxillary M3s (43%, 95% CI 31%–56%, I^2 94%, $P < 0.01$) (Appendix 5, provided on request), (odds ratio [OR] 2.21, 95% CI 1.67–2.92, I^2 53%, $P = 0.12$) (Fig 4).

Subgroup analyses on M3 impaction status

No significant difference was found in the prevalence of early periodontal defects on distal sites of A-M2s between I-M3s (19%, 95% CI 10%–35%, I^2 99%, $P < 0.01$) (Appendix 6, provided on request) and N-M3s (25%, 95% CI 12%–47%, I^2 99%, $P < 0.01$) (Appendix 7, provided on request) (OR 1.04, 95% CI 0.71–1.54, I^2 79%, $P < 0.01$) (Fig 5). Additionally, the prevalence of deep periodontal pockets around A-M2s with neighbouring N-M3s was 50% (95% CI 36%–64%, I^2 97%, $P < 0.01$) (Appendix 8, provided on request).

Table 1 Data extraction of the main characteristics of the included studies for final review (cross-sectional studies).

Study	Country	Journal	Study design	Source of sample	Number of participants	Sex	Number of molars	
Altan et al[19]	Turkey	J Dent Shiraz Univ Med Sci	Retrospective	Patients	954	NR	1598	
Akarslan and Kocabay[26]	Turkey	Oral Surg Oral Med Oral Pathol Oral Radiol	Retrospective	Patients	342	175 M, 167 F	400	
Blakey et al[13]	USA	J Oral Maxillofac Surg	Prospective	General population	329	159 M, 170 F	1289	
Chu et al[16]	China	Hong Kong Med J	Retrospective	Patients	2115	956 M, 1156 F	3178	
Gupta et al[27]	India	J Family Med Prim Care	Retrospective	Patients	400	240 M, 160 F	640	
Jung and Cho[9]	Korea	Imaging Sci Dent	Retrospective	Patients	2048	998 M, 1050 F	4455	
Kindler et al[12]	Germany	J Clin Periodontol	Retrospective	General population	1915	NR	1427	
Kim et al[28]	Korea	J Dent Sci	Retrospective	Patients	630	NR	748	
Kugelberg et al[29]	Sweden	Int J Oral Surg	Retrospective	Patients	144	NR	215	
Li et al[11]	China	J Periodontol	Retrospective	Patients	1958	774 M, 1184 F	4056	
Li et al[30]	China	J Oral Maxillofac Surg	Prospective	Patients	135	59 M, 76 F	289	
Nivedita et al[20]	India	Minerva Stomatol	Retrospective	Patients	749	490 M, 259 F	2342	
Nunn et al[14]	USA	J Dent Res	Retrospective	General population	416	NR	310	
Prahabkar et al[31]	India	Biomed & Phamacol J	Prospective	General population	200	NR	400	
Polat et al[15]	Turkey	Oral Surg Oral Med Oral Pathol Oral Radiol Endod	Retrospective	Patients	1914	828 M, 1086 F	3050	

	Age, y	Periodontitis by AAP/CDC case definition	Diagnostic criteria of periodontal pathology of A-M2s	Prevalence of periodontal pathology of A-M2s Under different M3 locations, M3 impaction status, age of patients and sex of patients (if reported)	Risk of bias
	Range 16–64, mean 26.42 ± 7.60	NR	DPT ABL > 1 mm on distal sites of A-M2s	4.9% Mesial 10.6%, horizontal 9%, vertical 0.2%, others 4.7%	7
	Range 20–25, mean 22.20 ± 1.80	NR	DPT ABL on distal sites of A-M2s	10.8% Male 9%, female 12.5%	7
	Range 14–45	AAP Class I–III	CE PD > 5 mm on distal sites of A-M2s	6.1% At/above OP 6%, below OP 6% Vertical/distal 9.3%, mesial/horizontal 10.2% < 25 y 2.9%, > 25 y 9.3%	8
	Range 17–89, mean 27.9	NR	DPT ABL > 5 mm on distal sites of A-M2s	8.9% < 30 y 5.7%, > 30 y 16.3%	7
	Mean 27 y	NR	DPT ABL on distal sites of A-M2s	39.1%	6
	Range 25–92, mean 50	NR	DPT ABL on distal sites of A-M2s	3.1% Mandibular 4.5%, maxillary 1.2% Mesial 13.5%, horizontal 13.9%, vertical 1.3%, distal 1.1%, inverted 16.1%, buccal 0.0%	7
	Mean 50	None or mild 48.8% Moderate 34.4% Sever 16.8%	Magnetic resonance imaging	32.8% Mandibular 43.5%, maxillary 24.2% I-M3s 27.9%, N-M3s 34.1%	7
	Range 13–74, mean 29.00 ± 10.20	NR	DPT ABL on distal sites of A-M2s	10.8% < 30 years < 3%, > 30 years > 97%	7
	Range 16–53, mean 27.20 ± 6.35	NR	DPT ABL > 3 mm on distal sites of A-M2s	41.9% Male 56.22%, female 26.2%	7
	≥ 19, mean 37.2	NR	DPT ABL ≥ 20% root length on distal sites of A-M2s	41.0% Mandibular 47.6%, maxillary 33.8% I-M3s 40.4%, N-M3s 41.5%	7
	Mean 40.60 ± 11.50	NR	CE PD > 5 mm around A-M2s	51.6% Mandibular 57.9%, maxillary 44.2%	8
	Range 18–83, mean 39.20 ± 12.80	NR	DPT ABL on distal and mesial sites of A-M2s	Distal sites 35.4% I-M3s 2.6%, N-M3s 38.9% Mesial sites 43.2% I-M3s 2.6%, N-M3s 47.6%	8
	Range 28.1–76.2, mean 45.80 ± 7.40	NR	DPT ABL ≥ 20% root length on distal sites of A-M2s	12.9% Soft tissue impaction 28%, bony impaction 16.9%, erupted 9.2%	7
	Range 21–25	NR	CE PD > 4 mm on distal sites of A-M2s	12.0%	7
	Range 18–60, mean 25.91 ± 6.34	NR	DPT ABL > 3 mm on distal sites of A-M2s	Mesial 18.5%, horizontal 16.8%, vertical 0.9%, distal 0.0%, inverted 0% Class A 10.1%, class B 8.8%, class C 3.7%	6

Study	Country	Journal	Study design	Source of sample	Number of participants	Sex	Number of molars	
Qu et al[3]	China	J Oral Maxillofac Surg	Prospective	Patients	572	339 M, 233 F	1100	
Sejfijia et al[28]	Kosovo	Acta Stomatologica Croatica	Retrospective	Patients	710	296 M, 414 F	1297	
Stanley et al[33]	USA	J Oral Pathol	Retrospective	Patients	1756	NR	3702	
Sun et al[10]	China	Oral Dis	Prospective	Patients	371	176 M, 195 F	812	

CE, clinical examination; DPT, dental panoramic tomogram; NR, not reported; OP, occlusal plane.

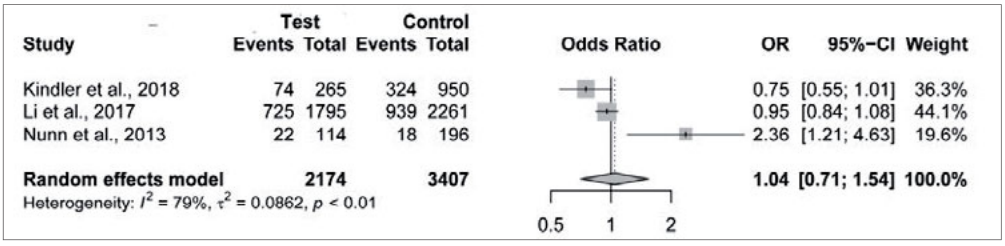

Fig 5 Forest plot of the odds ratio of early periodontal defects on distal sites of second molars with neighbouring impacted third molars versus nonimpacted third molars.

Patient characteristics such as M3 impaction classification, overall periodontal health, sex and age were not fully reported or were not reported with similar periodontal parameters that could be used to conduct a subgroup analysis.

Discussion

Recently, the periodontal impacts of M3s on A-M2s have attracted increasing attention due to great controversy regarding clinical decision making concerning M3s. There is a general consensus that M3s should undergo long-term observation and ultimately removal if symptoms of disease are significant[34,35]. On the other hand, it is not widely agreed that early treatment is necessary to prevent harm to A-M2s and avoid complications after removal in old age[36,37]; however, a wide range of prevalence estimates of periodontal pathology of M2s with neighbouring M3s has been reported across studies due to methodological variations and different sample characteristics, and therefore cannot provide reliable evidence for clinical practice. To better understand the periodontal risks associated with M3s, this systematic review and meta-analysis was conducted. To our knowledge, this is the first meta-analysis on the prevalence of periodontal pathology of A-M2s.

The present meta-analysis appears to indicate that the prevalence of early periodontal defects on distal sites of A-M2s at the molar level was 19%. Periodontal diseases include supporting connective tissue loss and alveolar bone loss[22]. Thus, the presence of early periodontal defects was reflected by a combination of the following parameters: CAL ≥ 3 mm, ABL ≥ 3 mm or ≥ 20% root length, which was a more comprehensive evaluation. M3s are located behind M2s, and periodontal defects distal to A-M2s provide direct evidence for the periodontal risks associated with the presence of M3s and reflect the cumulative effects of periodontal pathology. The high prevalence of deep periodontal pockets around A-M2s (52%) highlights the potential risk of active

	Age, y	Periodontitis by AAP/CDC case definition	Diagnostic criteria of periodontal pathology of A-M2s	Prevalence of periodontal pathology of A-M2s Under different M3 locations, M3 impaction status, age of patients and sex of patients (if reported)	Risk of bias
	Range 19–35, mean 36.80 ± 18.70	NR	CE PD > 5 mm around A-M2s	38.5% Mandibular 46.1%, maxillary 29.8% I-M3s 42.9%, N-M3s 33.9%	9
	Range 18–77, mean 29.30 ± 12.80	NR	DPT ABL > 5 mm on distal sites of A-M2s	5.5% Mandibular 4.9%, maxillary 6.5% < 30 y 6.9%, > 30 y 1.2% Male 4.8%, female 4.9%	7
	Range 20–83, mean 47	NR	DPT ABL > 3 mm on distal sites of A-M2s	4.5%	6
	Mean 35.10 ± 11.90	NR	CE PD > 5 mm around A-M2s	64.5% Mandibular 78.3%, maxillary 55.5%	8

periodontal pathology, and PD ≥ 5 mm has been confirmed to result in high levels of periodontal pathogens and inflammatory mediators in M3 regions[5,38].

In subgroup analyses, a higher prevalence of early periodontal defects was found to be associated with mandibular M3s (32%) than with M3s in general (19%), and the data on maxillary M3s were limited to be synthesised. However, both studies that analysed the difference between M3 locations reported a higher prevalence of early periodontal defects in mandibular than in maxillary molars[11,12]. Moreover, the prevalence of deep periodontal pockets around A-M2s associated with mandibular M3s was significantly greater than that with maxillary M3s (OR 2.21). The higher odds of M3 impaction in mandibular than in maxillary regions could partly explain this difference[1]. Furthermore, subgroup analyses were conducted on M3 impaction status. Intriguingly, a higher prevalence of early periodontal defects was found to be associated with N-M3s (25%) than I-M3s (19%), even with no significant difference (OR 1.04). In the subgroup analysis, two studies reported a higher prevalence of N-M3s without explicit classifications of I-M3s[11,12], while Nunn et al[14] reported that the prevalence of bony impacted and soft tissue impacted M3s was higher than that for N-M3s. The higher prevalence of N-M3s might be caused by the significant difference in the periodontal pathology between different impaction types[19], which affected the overall prevalence associated with I-M3s. In the analysis of deep periodontal pockets around A-M2s, only one study reported separate outcomes for I-M3s and N-M3s[3], which suggested a higher prevalence associated with I-M3s; however, the prevalence of deep periodontal pockets around A-M2s associated with N-M3s reached 50%, which reminds us that the presence of N-M3s is also an important periodontal risk factor for A-M2s. Additionally, some studies have reported other increased pathological parameters around A-M2s with N-M3s, such as Plaque Index and bleeding on probing[3,10].

Our meta-analysis indicated the periodontal risks associated with presence of M3s for A-M2s and highlighted which characteristics of M3s contributed to a higher prevalence of periodontal pathology of A-M2s. Considering the importance of M2s for masticatory function, clinicians need to examine the periodontal condition of A-M2s through clinical or radiographic assessment in regular oral examination, even in the absence of complaints about M3s and irrespective of the impaction status of M3s. The locations and impaction status of M3s should be taken into consideration to determine the best clinical decisions for individuals. It is worth noting that periodontal disease is always asymptomatic until the disease is severe[22], so it is difficult to find periodontal pathology in M3 regions in the early stages of periodontitis. A number of studies have confirmed that asymptomatic M3s are closely related to the periodontal pathology of A-M2s[13,17,30]. More importantly, even with mechanical debridement, it is difficult to reduce the periodontal pathology in M3

regions[4]. Several studies have verified that removal of M3s contributes to improving the periodontal status of A-M2s, regardless of I-M3s or N-M3s, but older age and preoperative deep periodontal pockets lead to an unfavourable prognosis[10,37,39,40].

Nevertheless, the early stages of the periodontal pathology of M2s were evaluated in the meta-analysis. Estimates of severe periodontal pathology are available in only a limited number of studies, making it difficult to provide a convincing clinical decision regarding M3s. The periodontal status of M2s is affected by not only the presence of M3s but also other systemic factors, such as the presence of periodontitis, smoking status and diabetes[22]. Considering the postoperative complications of M3 surgery, especially those involving chronic and irrecoverable symptoms such as paresthesia or temporomandibular joint disorder[41], removal of M3s should be conducted after comprehensive assessments, including of patients' age, general health and oral hygiene and willingness to undergo surgery. Only when the benefits of M3 surgery outweigh the risks to individuals is removal of M3s required.

The limitations of the meta-analysis were the small number of studies for data synthesis and the inconsistent definition of early periodontal defects. Some of the studies included in the meta-analysis involved patients with symptomatic M3s; thus, these participants did not effectively reflect the characteristics of the general population and resulted in a higher estimate. In studies using radiographic examination methods, it was difficult to randomly include samples because of ethical concerns, and selection bias may systematically increase the prevalence of periodontal defects; however, we tried to provide the best possible estimates of the prevalence of periodontal pathology of A-M2s through rigorous selection. Large-scale, population-based studies are needed to further demonstrate the adverse periodontal impact of M3s on A-M2s, and confounding factors at the patient level should be discussed. Furthermore, there is a critical need to determine which factors of N-M3s contribute to the periodontal pathology of A-M2s.

Conclusion

This systematic review and meta-analysis indicated that M3s are associated with early periodontal defects on distal sites of A-M2s in 19% of cases and associated with deep periodontal pockets around A-M2s in 52% of cases. In subgroup analyses, mandibular M3s and N-M3s showed a higher prevalence and were identified as risk factors for periodontal pathology of A-M2s. However, these results should be interpreted with caution because of high heterogeneity; thus, comprehensive assessments are imperative in M3 clinical decision making.

Acknowledgements

The authors would like to thank Dr Hari Petsos from Johann Wolfgang Goethe University, Germany, Dr Ahmet Altan from Gaziosmanpaşa University, Turkey, and Dr Martha Nunn from Creighton University School of Dentistry, USA, for providing more explicit data on their articles.

Conflicts of interest

The authors declare no conflicts of interest related to this study.

Author contribution

Dr Yang YANG acquired and interpreted the data and contributed to preparation of the manuscript; Drs Yi TIAN and Li Juan SUN contributed to the study design, data analysis and manuscript revision; Dr Hong Lei QU contributed to the study design.

(Received April 01, 2021; accepted Jun 23, 2021)

References

1. Carter K, Worthington S. Predictors of third molar impaction: A systematic review and meta-analysis. J Dent Res 2016;95:267–276.
2. Kruger E, Thomson WM, Konthasinghe P. Third molar outcomes from age 18 to 26: Findings from a population-based New Zealand longitudinal study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001;92:150–155.
3. Qu HL, Tian BM, Li K, Zhou LN, Li ZB, Chen FM. Effect of asymptomatic visible third molars on periodontal health of adjacent second molars: A cross-sectional study. J Oral Maxillofac Surg 2017;75:2048–2057.
4. Fisher EL, Blakey GH, Offenbacher S, Phillips C, White RP Jr. Mechanical debridement of subgingival biofilm in participants with asymptomatic third molars does not reduce deeper probing depths in the molar regions of the mouth. J Oral Maxillofac Surg 2013;71:467–474.
5. White RP Jr, Madianos PN, Offenbacher S, et al. Microbial complexes detected in the second/third molar region in patients with asymptomatic third molars. J Oral Maxillofac Surg 2002;60:1234–1240.
6. Mansfield JM, Campbell JH, Bhandari AR, Jesionowski AM, Vickerman MM. Molecular analysis of 16S rRNA genes identifies potentially periodontal pathogenic bacteria and archaea in the plaque of partially erupted third molars. J Oral Maxillofac Surg 2012;70:1507–1514.e1-6.
7. Blakey GH, Golden BA, White RP Jr, Offenbacher S, Phillips C, Haug RH. Changes over time in the periodontal status of young adults with no third molar periodontal pathology at enrollment. J Oral Maxillofac Surg 2009;67:2425–2430.

8. Ash MM, Costich ER, Hayward JR. A study of periodontal hazards of third molars. J Periodontol 1962;33:209–219.
9. Jung YH, Cho BH. Prevalence of missing and impacted third molars in adults aged 25 years and above. Imaging Sci Dent 2013;43: 219–225.
10. Sun LJ, Qu HL, Tian Y, Bi CS, Zhang SY, Chen FM. Impacts of non-impacted third molar removal on the periodontal condition of adjacent second molars. Oral Dis 2020;26:1010–1019.
11. Li ZB, Qu HL, Zhou LN, Tian BM, Chen FM. Influence of non-impacted third molars on pathologies of adjacent second molars: A retrospective study. J Periodontol 2017;88:450–456.
12. Kindler S, Holtfreter B, Koppe T, et al. Third molars and periodontal damage of second molars in the general population. J Clin Periodontol 2018;45:1365–1374.
13. Blakey GH, Marciani RD, Haug RH, et al. Periodontal pathology associated with asymptomatic third molars. J Oral Maxillofac Surg 2002;60:1227–1233.
14. Nunn ME, Fish MD, Garcia RI, et al. Retained asymptomatic third molars and risk for second molar pathology. J Dent Res 2013;92: 1095–1099.
15. Polat HB, Ozan F, Kara I, Ozdemir H, Ay S. Prevalence of commonly found pathoses associated with mandibular impacted third molars based on panoramic radiographs in Turkish population. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;105:e41–e47.
16. Chu FC, Li TK, Lui VK, Newsome PR, Chow RL, Cheung LK. Prevalence of impacted teeth and associated pathologies--A radiographic study of the Hong Kong Chinese population. Hong Kong Med J 2003;9:158–163.
17. Petsos H, Korte J, Eickholz P, Hoffmann T, Borchard R. Surgical removal of third molars and periodontal tissues of adjacent second molars. J Clin Periodontol 2016;43:453–460.
18. Petsos H, Korte J, Eickholz P, Hoffmann T, Borchard R. Effect of the surgeon's dominant hand on postoperative periodontal status of adjacent molars after removal of lower third molars. J Oral Maxillofac Surg 2019;77:912–919.
19. Altan A, Akbulut N. Does the angulation of an impacted mandibular third molar affect the prevalence of preoperative pathoses? J Dent (Shiraz) 2019;20:48–52.
20. Nivedita S, John ER, Acharya S, D'costa VG. Prophylactic extraction of non-impacted third molars: Is it necessary? Minerva Stomatol 2019;68:297–302.
21. Herzog R, Álvarez-Pasquin MJ, Díaz C, Del Barrio JL, Estrada JM, Gil Á. Are healthcare workers' intentions to vaccinate related to their knowledge, beliefs and attitudes? A systematic review. BMC Public Health 2013;13:154.
22. Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. Lancet 2005;366:1809–1820.
23. Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. J Periodontol 2007;78:1387–1399.
24. Haffajee AD, Socransky SS, Goodson JM, Lindhe J. Intraclass correlations of periodontal measurements. J Clin Periodontol 1985;12: 216–224.
25. Schei O, Waerhaug J, Lovdal A, Arno A. Alveolar bone loss as related to oral hygiene and age. J Periodontol 1959;30:7–16.
26. Akarslan ZZ, Kocabay C. Assessment of the associated symptoms, pathologies, positions and angulations of bilateral occurring mandibular third molars: Is there any similarity? Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:e26–e32.
27. Gupta P, Naik SR, Ashok L, Khaitan T, Shukla AK. Prevalence of periodontitis and caries on the distal aspect of mandibular second molar adjacent to impacted mandibular third molar: A guide for oral health promotion. J Family Med Prim Care 2020;9:2370–2374.
28. Kim JY, Jee HG, Song HC, Kim SJ, Kim MR. Clinical and pathologic features related to the impacted third molars in patients of different ages: A retrospective study in the Korean population. J Dent Sci 2017;12:354–359.
29. Kugelberg CF, Ahlström U, Ericson S, Hugoson A. Periodontal healing after impacted lower third molar surgery. A retrospective study. Int J Oral Surg 1985;14:29–40.
30. Li ZB, Qu HL, Zhou LN, Tian BM, Gao LN, Chen FM. Nonimpacted third molars affect the periodontal status of adjacent teeth: A cross-sectional study. J Oral Maxillofac Surg 2017;75:1344–1350.
31. Prabhakar P, Bhuvaneshwarri J, Paddmanabhan P. Evaluation of the Impact of Impacted Mandibular Third Molars on Surrounding Structures: A Clinical and Radiographic Analysis in Students of Tagore Dental College and Hospital. Biomed Pharmacol J 2015;8SE: 241–243.
32. Sejfija Z, Koçani F, Macan D. Prevalence of pathologies associated with impacted third molars in Kosovar population: An orthopantomography study. Acta Stomatol Croat 2019;53:72–81.
33. Stanley HR, Alattar M, Collett WK, Stringfellow HR Jr, Spiegel EH. Pathological sequelae of "neglected" impacted third molars. J Oral Pathol 1988;17:113–117.
34. Hill CM. Removal of asymptomatic third molars: An opposing view. J Oral Maxillofac Surg 2006;64:1816–1820.
35. Dodson TB. The management of the asymptomatic, disease-free wisdom tooth: Removal versus retention. Atlas Oral Maxillofac Surg Clin North Am 2012;20:169–176.
36. Ventä I. How often do asymptomatic, disease-free third molars need to be removed? J Oral Maxillofac Surg 2012;70(9 suppl 1):S41–S47.
37. Petsos H, Fleige J, Korte J, Eickholz P, Hofmann T, Borchard R. Five-years periodontal outcomes of early removal of unerupted third molars referred for orthodontic purposes. J Oral Maxillofac Surg 2021;79:520–531.
38. White RP Jr, Offenbacher S, Phillips C, Haug RH, Blakey GH, Marciani RD. Inflammatory mediators and periodontitis in patients with asymptomatic third molars. J Oral Maxillofac Surg 2002;60: 1241–1245.
39. Passarelli PC, Lajolo C, Pasquantonio G, et al. Influence of mandibular third molar surgical extraction on the periodontal status of adjacent second molars. J Periodontol 2019;90:847–855.
40. Tian Y, Sun L, Qu H, Yang Y, Chen F. Removal of nonimpacted third molars alters the periodontal condition of their neighbors clinically, immunologically, and microbiologically. Int J Oral Sci 2021;13:5.
41. Huang GJ, Cunha-Cruz J, Rothen M, et al. A prospective study of clinical outcomes related to third molar removal or retention. Am J Public Health 2014;104:728–34.