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REVIEW ARTICLE

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Risk factors for root resorption of second molars with impacted third molars: a meta-analysis of CBCT studies

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ABSTRACT

Objective: The aim of this systematic review and meta-analysis is to identify the risk factors of external root resorption (ERR) on second molar (M2) due to presence of impacted third (M3) molar based on cone- beam computerised tomography (CBCT) findings.

Material and methods: Search of PubMed *via* MEDLINE, SCOPUS, and Experta Medical dataBASE (EMBASE) was performed to identify studies assessing the risk factors of ERR in M2 due to the presence of impacted M3.

Results: M2 in close proximity to mesio-angular impacted M3 had 50% higher risk of root resorption than with vertical impacted M3 (RR 0.50 95% CI [0.35, 0.73], $p = .0003$). Presence of the impacted M3 in the lower arch with ERR in M2 was higher (38.3%) than in the upper arch (33.8%). With respect to the inclination of impacted M3, the incidence of ERR was higher with transverse, horizontal and mesio-angular impacted M3 with 54.5%, 47.5% and 44.5% of occurrence, respectively.

Conclusion: ERR in M2 was significantly affected by the contact with impacted M3 and most importantly, the inclination of M3. The presence of mesio-angular, horizontal or transverse impacted M3 in close proximity to apical or middle portion of M2 could possibly be a strong risk factor for ERR in M2.

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Introduction

External root resorption (ERR) is linked to mechanical or inflammatory causes induced by trauma, chronic periodontitis, orthodontic appliance pressure, cysts, benign or malignant tumours, and very commonly, proximity to an impacted tooth [1,2]. The presence of mandibular third molars (M3) has been linked to ERR affecting mandibular second molars (M2) [3]. Even mild to moderate ERR may result in reduced periodontal attachment regeneration after removal of the adjacent M3. Severe ERR may cause significant attachment loss or a pulpal pathology that necessitates tooth extraction [4]. Mild to moderate ERR that does not reach the pulp is typically asymptomatic and cannot be diagnosed clinically. As a result, accurate ERR radiography data would be beneficial for clinical decision-making.

Previous research have relied on the use of panoramic imaging or apical radiography, and reported that the prevalence of ERR of M2 due to pressure of M3 ranged from 0.3% to 24.2% [4–7]. However, overlaps in two-dimensional (2 D) radiography make it difficult to diagnose the degree of ERR on M2. ERR has recently been studied using cone beam computed tomography (CBCT), which enables examination in a three dimensional plane and allows to discover even minor abnormalities [8]. The use of CBCT has revealed that the prevalence rates of ERR of M2 due to pressure of M3 are as high as 49.43% [9].

However, there is currently a lack of data about the clinical features of ERR on M2 induced by the affected M3 that are obtained using CBCT for demonstrating the existence and severity of ERR on M2. These data may aid in the identification of potential risk factors for ERR on M2 caused by impacted M3, as well as the establishment of recommendations for the time of M3 removal to avoid ERR on M2.

The aim of this systematic review and meta-analysis is to identify the risk factors of ERR on M2 due to presence of impacted M3 based on CBCT findings and help clinicians in decision making.

Material and methods

This systematic review and meta-analysis intended to evaluate the risk factors of ERR associated with M2 due to presence of M3. Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) standards were followed to frame this review [10]. The protocol for conducting this study was registered with the International prospective register for systematic reviews (PROSPERO), registration number CRD42021275126.

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Research question

What are the risk factors associated with ERR of M2 based on features of M3 assessed on CBCT?

Search strategy

A rigorous search strategy was devised, which included searching over both digital databases and issues of relevant journals. Electronic search was performed on digital databases such as PubMed *via* MEDLINE, SCOPUS, and Experta Medical dataBASE (EMBASE) using the relevant search keywords. The following search strategy was used across all databases: ((((('Tooth, Impacted') OR 'impacted tooth') OR 'impacted teeth') OR 'impacted third molar') OR 'impacted third molars') AND ((((('tooth resorption') OR 'root resorption') OR 'teeth resorption') OR 'tooth resorptions') OR 'roots resorption') AND ('second molar'). A manual search was also conducted to find issues from inception to the present day of relevant peer-reviewed journals. The most recent search was performed on 30 September 2021. The search was further broadened to include an assessment of possibly relevant papers' bibliographies, as well as prior systematic reviews and meta-analyses.

Study selection

The study selection was carried out by two independent reviewers. The studies identified by the comprehensive search carried out in various databases were compiled into a citation manager and duplicates were removed. After removal of duplicates, a thorough screening was conducted based on the relevancy of title and abstract. Potentially eligible articles were then subjected to full text assessment based on the set eligibility criteria. Articles satisfying the eligibility criteria were included in the meta-analysis.

Eligibility criteria

The inclusion criteria were as follows: (i) studies assessing the risk factors of external root resorption in second molar due to the presence of impacted 3rd molar; (ii) studies employing CBCT as the modality of assessment were included.

The exclusion criteria are as follows: (i) non-English language studies; (ii) Studies not presenting relevant data in terms of identifying various risk factors; iii) Case reports, case series and conference proceedings.

Data extraction

The data extraction was carried out by two independent reviewers. Data from all the included studies were compiled in Microsoft Excel works spreadsheet. The demographic data such as study location, study design, sample size, age and gender of patients, location of M3, and the resorption factor data such as inclination of M3 in relation to M2, and level of M3 in relation to M2, contact between M2 and M3, and type of impaction were collected. In case of any doubt or any missing information, the authors were contacted over email to sought out clarification.

Data analysis

The data was subjected to both qualitative and quantitative analysis. The demographic data and the data which could not be expressed quantitatively were tabulated and summarised in the text. The quantitative analysis was carried out for the possible risk factors using meta-analysis. The outcomes expressed as quantitative variable as numbers, ratios and percentage were pooled using meta-analysis. The association of the risk factors with ERR was computed as Odd's ratio (OR) and the increase or decrease in risk was expressed as Risk Ratio (RR). The meta-analysis was carried out using RevMan 5.4v and Open meta-analyst software, only when at least two or more studies with the similar outcomes were available and pooled OR and RR were derived. The forest plot was constructed using RevMan 5.4v (Cochrane Collaboration, UK). The significance of the effect estimate was set at $p < .05$. A random effect model was used to pool the data of all the included studies considering the heterogeneity of the studies. The heterogeneity between the studies was calculated using I^2 statistics. An I^2 value of less than 40% was considered as low heterogeneity, a value ranging between 40% and 70% was considered moderate, and a value more than 70% was considered high heterogeneity.

Quality of the included studies

The quality of the included studies was assessed using Newcastle Ottawa (NOS) scale for cohort studies. This scale is made up of eight different components that are divided into three categories: selection, comparability, and outcome. The quality of the study under evaluation was graded using a star scale that ranged from zero to nine. Each included study was given one of three categorical scores: good (three or four scores in the selection domain AND one or two scores in the comparability domain AND two or three scores in the outcome domain), fair (two scores in the selection domain AND one or two scores in the comparability domain AND two or three scores in the outcome domain), or poor (two scores in the selection domain AND one or two scores in the comparability domain AND two or three scores in the outcome domain) (zero or one score in selection domain OR zero score in comparability domain OR zero or one score in outcome domain).

Results

The comprehensive search from all three databases identified a total of 301 reports. After removal of duplicates, 268 reports were screened for identifying the potentially eligible studies based on their title and abstract. Fifteen studies were identified as eligible and were subjected to full text assessment. A total of three studies were excluded for not matching the inclusion and exclusion criteria. Finally, a total of 12

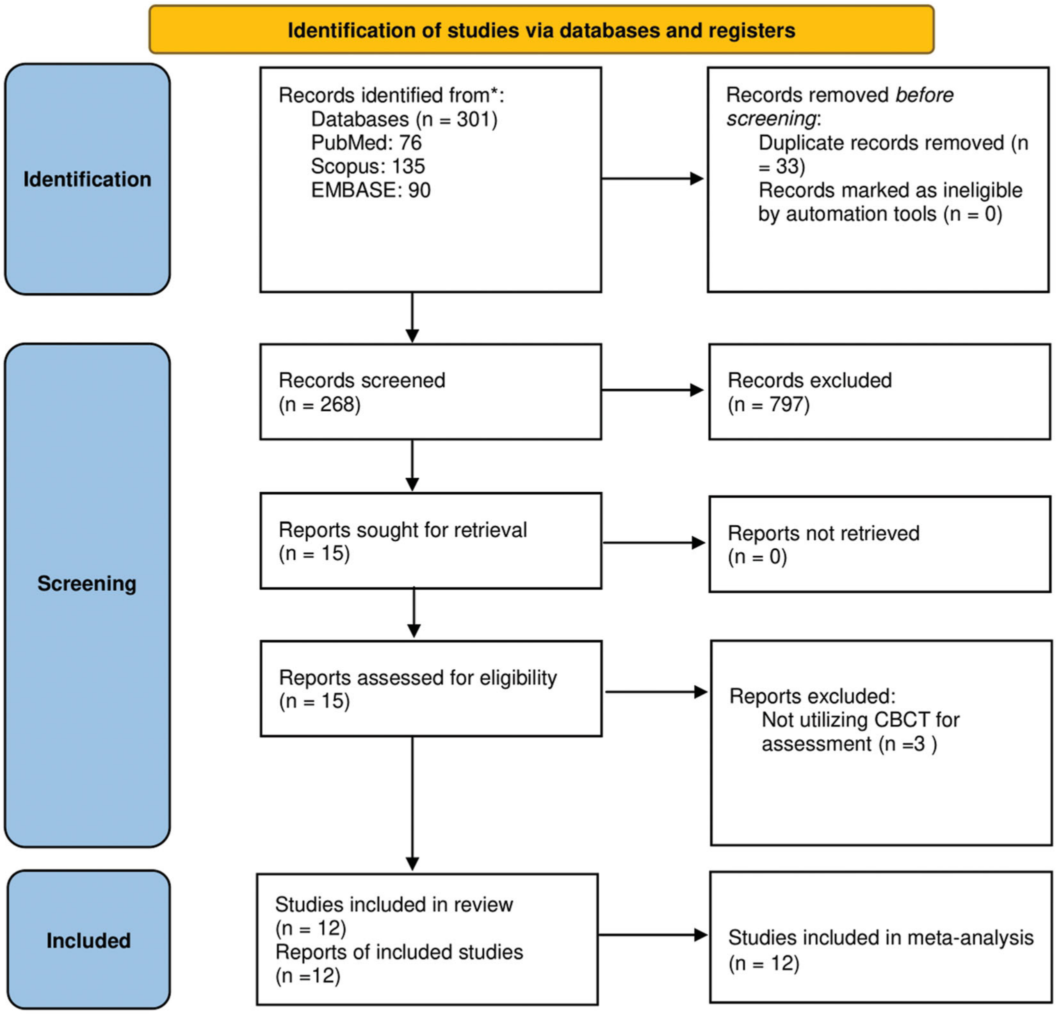

Figure 1. PRISMA flow chart showing study selection process.

studies [3,9,11–20] were included in this systematic review. The detail of the study selection process is provided in Figure 1.

All twelve included studies were retrospective cohort studies. A total of 2378 patients presenting with impacted M3 were included. Out of 2378 patients, 1122 patients were males, and 1256 patients were females. The included patients had an age ranged between 16 and 81 years with a mean age of 26.7 ± 15.2 years. The mean age of patients showing ERR on M2 due to impacted M3 was 28.4 ± 8.8 years and the mean age for patients without ERR was 19.8 ± 6.2 years. This systematic review analysed a total of 3637 impacted M3 in proximity to M2. Out of these teeth, 857 impacted M3 were located in the upper arch and remaining 2780 were located in the lower arch. Only three studies reported the development of root of impacted M3. Completely closed apex was noticed in 55.7% of impacted M3, and open apical foramen was found in 34.6% of cases. The details of the demographic data are provided in Table 1.

The data on resorption factors of M2 due to the presence of impacted M3 was expressed quantitatively as the number of events of resorption with presence of each resorption factor. The quantitative data was then subjected to meta-analysis to pool the estimated odd's ratio or association of particular risk factor with ERR of M2. The detailed data on the resorption factors of M2 identified among the included studies are provided in Table 2.

All the included studies were of good quality according to NOS, achieving a score ranging between 7 and 9 (Table 3).

Meta-analysis

The meta-analysis was carried out in the event of availability of two or more studies evaluating the same resorption factor for M2.

Resorption of M2 due to presence of impacted M3

The association of ERR of M2 with the impacted M3 among the included studies was found to be low with pooled OR of 0.30 95% CI [0.18,0.48], $p < .00001$. However, the data was presented with a significantly high heterogeneity (Figure 2).

Gender as risk factor

Six studies were included to provide data on the incidences of ERR of M2 among male and female patients presenting

Table 1. Demographic characteristics.

#	Author(s)	Year	Country	Type of study	Total patients (M/F)	Mean age (range)	Total teeth (left/right)	Location M3, n (%)		Developmental of M3 roots, n(%)		
								Upper Arch	Lower Arch	Complete, closed apex	Almost complete, open apical foramen	>Two-thirds root developed
1	Yesiltepe et al. [11]	2021	Turkey	Retrospective	121	(18 – 24)	189	189 (100)	0 (0)	NR	NR	NR
2	Schriber et al. [12]	2020	Switzerland	Retrospective	84 (48/36)	34.6 (17 – 77)	84 (37/47)	NR	NR	50 (59.5)	28 (33.3)	6 (7.1)
3	Tunc et al. [13]	2020	Turkey	Retrospective	167 (73/94)	26.08 ± 4 (18 – 40)	250 (127/123)	100 (40)	150 (60)	214 (85.6)	28 (11.2)	8 (3.2)
4	Li et al. [17]	2019	China	Retrospective	276 (124/152)	34 (16 – 81)	507 (266/241)	184 (36.3)	323 (63.7)	NR	NR	NR
5	Smailiene et al. [16]	2019	Lithuania	Retrospective	109 (41/68)	26.4 ± 7.9 (16 – 66)	254	131 (51.6)	123 (48.4)	NR	NR	NR
6	Suter et al. [15]	2019	Switzerland	Retrospective	433 (198/235)	28.2 (15 – 80)	640 (322/318)	0 (0)	640 (100)	279 (43.6)	303 (47.3)	58 (9.1)
7	Tassoker [14]	2019	Turkey	Retrospective	200 (82/118)	27.26 ± 8.6 (18 – 50)	200 (100/100)	78 (39)	122 (61)	NR	NR	NR
8	Matzen et al. [19]	2017	Denmark	Retrospective	379 (168/211)	26 (17 – 73)	379 (180/199)	0(0)	379 (100)	NR	NR	NR
9	Matzen et al. [20]	2017	Denmark	Retrospective	320 (146/174)	26 (17 – 73)	410 (193/217)	0 (0)	410 (100)	NR	NR	NR
10	Wang et al. [18]	2017	China	Retrospective	216 (111/105)	30.45 (16 – 71)	362 (174/188)	0 (0)	362 (100)	NR	NR	NR
11	Oenning et al. [3]	2015	Brazil	Retrospective	116 (46/70)	23.7 (14 – 62)	174	0 (0)	174 (100)	NR	NR	NR
12	Oenning et al. [9]	2014	Brazil	Retrospective	66 (25/41)	22.8 (15 – 76)	188	91 (48.4)	97 (51.6)	NR	NR	NR

Table 2. Risk factors of ERR in M2.

#	Author(s)	Total teeth	M2 resorption and severity, n (%)		Root resorption factors in M2: Sex (%)		M3 (%)				Inclination of M3 (%)						Contact M2/M3 (%)		Location M2/M3 (%)			Type of impaction M3 (%)	
			Yes	No	Female	Male	Left	Right	Upper	Lower	Vertical	Distoan gular	Mesioan gular	Trans verse	Inverted	Hori zontal	Yes	No	Cervical	Middle	Apical	Full bony impaction	Soft tissue coverage
1	Yesiltepe et al. [11]	189	64 (33.9)	125 (66.1)	NR	NR	NR	NR	64/189 (33.9)	0/0 (0)	18/48 (37.5)	22/90 (24.4)	13/30 (43.3)	7/13 (53.8)	0/1 (0)	4/7 (57.1)	NR	NR	NR	NR	NR	51/121 (78.7)	13/68 (21.3)
2	Schriber et al. [12]	84	42 (50.0)	42 (50.0)	18/36 (50)	24/48 (50)	NR	NR	NR	NR	15/35 (42.9)	11/29 (37.9)	9/13 (69.2)	5/5 (100)	1/1 (100)	1/1 (100)	42/80 (52.4)	0/4 (0)	8/28 (28.6)	20/33 (60.6)	14/19 (73.7)	2/4 (50)	40/80 (50)
3	Tunc et al. [13]	250	84 (33.6)	166 (66.4)	57/141 (40.4)	27/109 (24.8)	38/127 (29.9)	46/123 (37.4)	55/100 (55)	29/150 (19.3)	12/63 (19)	12/32 (37.5)	45/109 (41.3)	0/0 (0)	0/0 (0)	8/35 (22.9)	84/209 (40.2)	0/41 (0)	NR	NR	NR	32/96 (33.3)	52/154 (33.8)
4	Li et al. [17]	507	231 (45.6)	276 (54.4)	124/282 (43.9)	107/225 (47.6)	NR	NR	60/184 (32.6)	171/323 (52.9)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	71/135 (52.6)	160/372 (43)
5	Smailiene et al. [16]	254	102 (40.2)	152 (59.8)	NR	NR	NR	NR	44/131 (33.6)	58/123 (47.2)	17/72 (23.6)	2/29 (6.9)	67/134 (50)	0/0 (0)	0/0 (0)	16/19 (84.2)	102/254 (40.2)	0/0 (0)	71/198 (35.9)	31/56 (55.4)		NR	NR
6	Suter et al. [15]	640	204 (31.9)	436 (68.1)	59/235 (25.1)	82/198 (41.4)	NR	NR	NR	NR	35/186 (18.8)	11/135 (8.15)	103/218 (47.2)	0/2 (0)	10/16 (62.5)	45/83 (54.2)	200/444 (45)	4/196 (2)	128/328 (39)	57/98 (58.2)	15/18 (83.3)	3/5 (60)	318/635 (50.1)
7	Tassoker [14]	200	42 (21)	158 (79)	24/118 (20.3)	18/82 (22)	21/100 (21)	21/100 (21)	5/78 (6.4)	37/122 (30.3)	1/21 (4.8)	2/20 (10)	27/124 (21.8)	0/0 (0)	0/0 (0)	12/35 (34.3)	NR	NR	NR	NR	NR	NR	NR
8	Matzen et al. [19]	379	163 (43)	216 (57)	NR	NR	NR	NR	0/0 (0)	163/379 (43)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
9	Matzen et al. [20]	410	167 (40.7)	243 (59.3)	NR	NR	NR	NR	0/0 (0)	167/410 (40.7)	1/36 (2.8)	3/60 (5)	119/218 (54.6)	0/0 (0)		44/93 (47.3)	167/410 (40.7)	0/0 (0)	0/41 (0)	106/192 (55.2)	61/177 (34.5)	NR	NR
10	Wang et al. [18]	362	73 (20.2)	289 (79.8)	40/105 (38.1)	33/111 (29.7)	37/174 (21.3)	36/188 (19.1)	0/0 (0)	73/362 (20.2)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	24/98 (24.5)	49/264 (18.6)
11	Oenning et al. [3]	174	86 (49.4)	88 (50.6)	NR	NR	NR	NR	0/0 (0)	86/174 (49.4)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	19/56 (33.9)	67/118 (56.8)
12	Oenning et al. [9]	188	43 (22.9)	145 (77.1)	NR	NR	NR	NR	13/91 (14.3)	30/97 (30.9)	16/95 (16.8)	1/17 (5.9)	22/65 (33.8)	0/2 (0)	0/0 (0)	4/9 (44.4)	NR	NR	NR	NR	NR	NR	NR

Table 3. Quality of included studies.

Author & Year	Selection				Comparability	Outcome			Total
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest	Basis of the design or analysis	Assessment of outcome	follow-up long enough for outcomes	Adequate follow up	
Yesiltepe et al. [11]	1	1	0	1	1	1	1	1	7
Schriber et al. [12]	1	1	1	1	1	1	1	1	8
Tunc et al. [13]	1	1	1	1	1	1	1	1	8
Li et al. [17]	1	1	1	1	1	1	1	1	8
Smailiene et al. [16]	1	1	1	1	1	1	1	1	8
Suter et al. [15]	1	1	1	1	2	1	1	1	9
Tassoker [14]	1	1	1	1	1	1	1	1	8
Matzen et al. [19]	1	1	1	1	1	1	1	1	8
Matzen et al. [20]	1	1	1	1	2	1	1	1	9
Wang et al. [18]	1	1	1	1	1	1	1	1	8
Oenning et al. [3]	1	1	1	1	1	1	1	1	8
Oenning et al. [9]	1	1	1	1	1	1	1	1	8

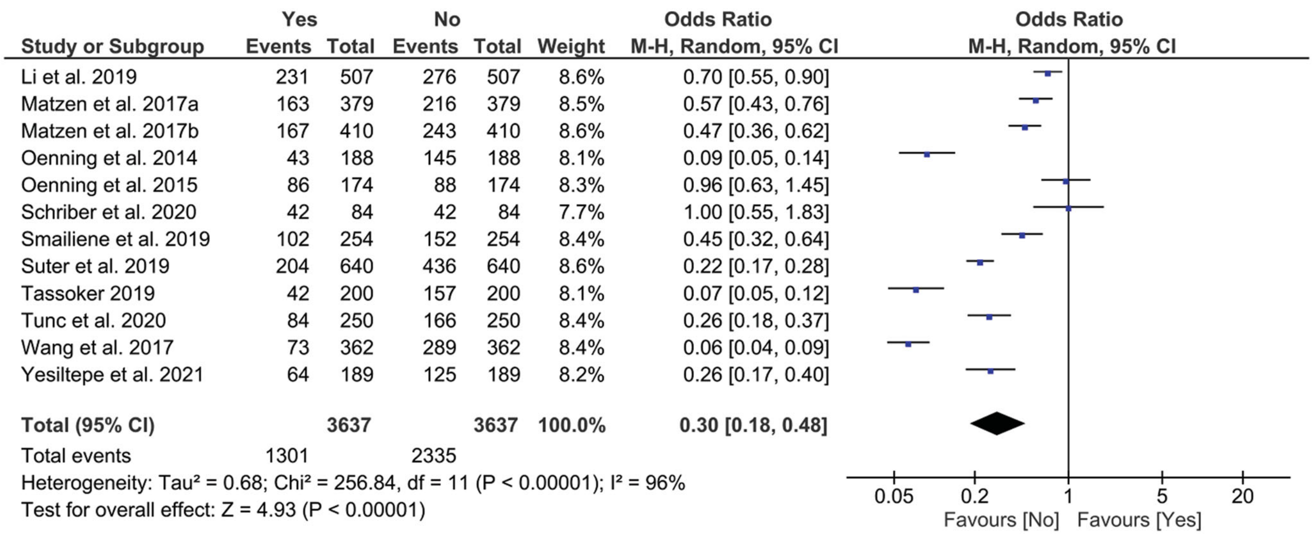

Figure 2. Forest plot showing pooled estimate of association of root resorption of M2 due to presence of impacted M3.

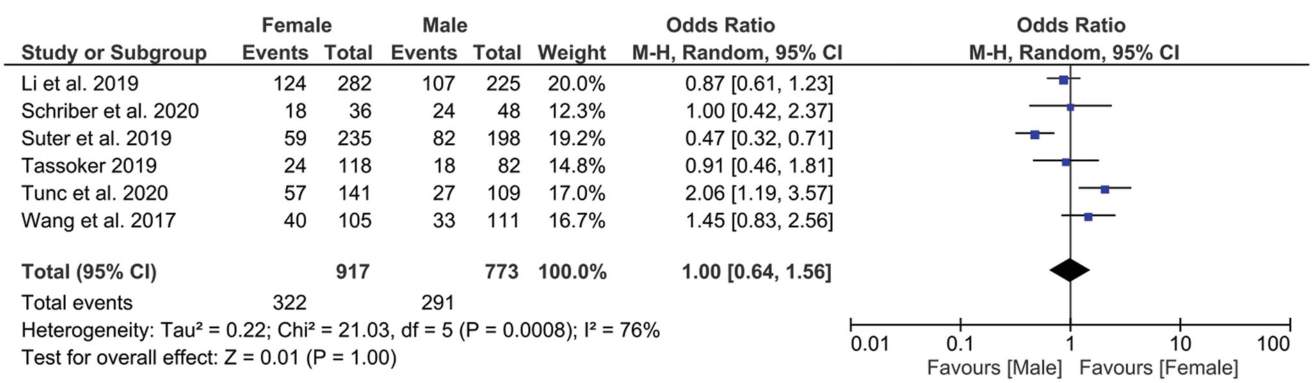

Figure 3. Gender as risk factor for root resorption.

with impacted M3. No difference in association of gender distribution was found, OR 1.00 95%CI [0.64, 1.56], $p = 1.00$ (Figure 3).

Location of impacted M3

Five studies were included to provide data on association of ERR of M2 with the location of impacted M3 in upper or lower arch. No difference in association was found between the presence of impacted M3 in upper or lower arch with OR 0.61 95% CI [0.21,1.74], $p = .36$ (Figure 4).

Inclination of impacted M3

M2 in close proximity to mesio-angular impacted M3 had 50% higher risk of ERR than with vertical impacted M3, with RR 0.50 95% CI [0.35, 0.73], $p = .0003$. Similarly, M2 in close proximity to transverse and horizontal impacted M3 had 55%

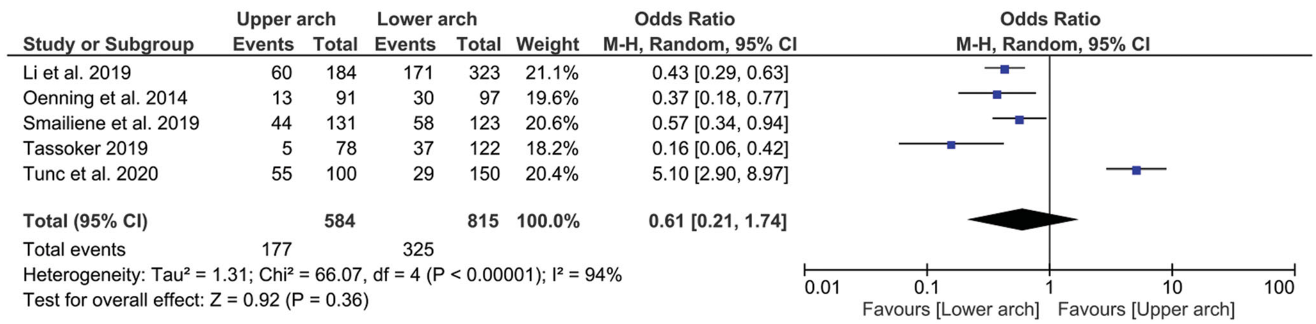

Figure 4. Dental arch as risk factor for root resorption.

and 40% higher risk of ERR respectively, than with vertical impacted M3, with RR 0.55 95% CI [0.39, 0.79], $p = .001$ and RR 40 95% CI [0.27, 0.58], $p < .0001$ (Figure 5). Transverse, horizontal and inverted position of impacted M3 showed higher risk of root resorption in M2 than mesio-angular impacted M3, however, no significant conclusion could be drawn (Figure 6).

Contact between M2 and impacted M3

Three studies were included to find significant association of ERR of M2 due to the presence of contact between M2 and impacted M3 with OR 38.11 95% CI [15.43,94.11], $p < .0001$. There was no heterogeneity between the studies, $i2 = 0\%$ (Figure 7).

Level of impacted M3 in relation to M2

Level of impacted M3 at the middle and apical regions of M2 showed significant association with ERR in M2 as compared to than at cervical region of M2, with OR 0.19 95% CI [0.04, 0.85], $p = .03$ and OR 0.11 95% CI [0.05,0.27], $p < .0001$ (Figure 8).

Estimation of proportion of ERR with respect to different variables

The percentage of occurrence of ERR with respect to different variables like gender, location, arch, contact between M2/M3, inclination of M3, and type of impaction in M3, were pooled across all included studies using Open meta-analyst software and one-arm analysis, estimating untransformed proportion ratio. The estimates of the analysis are provided in Table 4.

The presence of impacted M3 in the lower arch showing ERR in M2 was relatively higher (38.3%) compared to upper arch (33.8%). With respect to the inclination of impacted M3, the prevalence of ERR was higher with transverse, horizontal and mesio-angular impacted M3 with 54.5%, 47.5% and 44.5% of occurrence, respectively.

The prevalence of ERR in M2 was higher in cases of contact between M2/M3 (42.5%) as compared to absence of any contact between both teeth (1.6%). Moreover, the prevalence of ERR in M2 was observed to be 56.4% and 44.8% when the M2/M3 contact level lies at middle and apical level respectively. And the prevalence of ERR was less when at cervical level (34.7%).

No difference was observed in the prevalence of ERR with respect to the type of impaction. The incidence of ERR in M2 was similar with full bony (39.2%) and soft tissue impacted M3 (41.3%).

Discussion

The aim of this systematic review was to identify the risk factors affecting the ERR of M2 due to the presence of impacted M3 among the studies employing CBCT for diagnosis and imaging. Numerous studies confirmed the advantages of CBCT over other imaging modalities due to its higher resolution and imaging quality, sensitivity, reduced artefacts, muti-planar view and also relatively low radiographic dosage exposure. The comparison of diagnostic efficacy of CBCT and peri-apical radiographs to detect ERR clearly showed superior performance, as concluded by a study by Vaz de Souza et al. [21].

Early detection of ERR on M2 or identification of risk factors for ERR is an important clinical consideration for deciding prophylactic removal of impacted M3. ERR on M2 due to impacted M3 remains a clinical difficulty to diagnose and forecast. When ERR is detected, the decision to remove impacted M3 can be difficult for both the patient and the dentist. The identification of risk factors would aid in therapeutic decision-making by giving evidence for estimating the likelihood of ERR on M2 due to the impacted M3. Understanding the risk factors for ERR on M2 might help the clinician decide whether to remove the impacted M3 or to just ‘wait and watch’ [22].

In our study, age, gender, presence of impacted M3 in maxillary or mandibular arch, inclination of impacted M3, contact between M2 and impacted M3, and level of impacted M3 in relation to M2 were identified as considerable risk factors of ERR on M2. The included studies showed that the mean age of the patients with impacted M3 showing ERR on M2 was higher as compared to the patients not showing any signs of ERR on M2. It is evident that the longer the impacted M3 remains in maxillary and mandibular arch, the higher the risk of ERR on M2. ERR is believed to be caused by pressure applied directly on the root surface of an adjacent tooth and associated factors deriving from the follicle that activate clastic cells, triggering resorption [23]. The severity of ERR increases with age because root resorption, induced by mechanical pressure from impacted teeth, may be progressive over time [12].

Study or Subgroup	Vertical Events	Vertical Total	Other Events	Other Total	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 Vertical vs Distoangular						
Matzen et al. 2017b	1	36	3	60	1.0%	0.56 [0.06, 5.14]
Oenning et al. 2014	16	95	1	17	1.3%	2.86 [0.41, 20.19]
Schriber et al. 2020	15	35	11	29	4.5%	1.13 [0.62, 2.06]
Smailiene et al. 2019	17	72	2	29	2.1%	3.42 [0.84, 13.89]
Suter et al. 2019	35	186	11	135	4.3%	2.31 [1.22, 4.38]
Tassoker 2019	1	21	2	20	1.0%	0.48 [0.05, 4.85]
Tunc et al. 2020	12	63	12	32	4.2%	0.51 [0.26, 1.00]
Yesiltepe et al. 2021	18	48	22	90	4.8%	1.53 [0.92, 2.57]
Subtotal (95% CI)		**556**		**412**	**23.2%**	**1.29 [0.79, 2.11]**
Total events	115		64			
Heterogeneity: Tau² = 0.22; Chi² = 15.18, df = 7 (P = 0.03); I² = 54%						
Test for overall effect: Z = 1.03 (P = 0.30)						
1.5.2 Vertical vs Mesioangular						
Matzen et al. 2017b	1	36	119	218	1.3%	0.05 [0.01, 0.35]
Oenning et al. 2014	16	95	1	17	1.3%	2.86 [0.41, 20.19]
Schriber et al. 2020	15	35	9	13	4.8%	0.62 [0.37, 1.05]
Smailiene et al. 2019	17	72	67	134	5.1%	0.47 [0.30, 0.74]
Suter et al. 2019	35	186	103	218	5.5%	0.40 [0.29, 0.55]
Tassoker 2019	1	21	27	124	1.3%	0.22 [0.03, 1.52]
Tunc et al. 2020	12	63	45	109	4.7%	0.46 [0.26, 0.80]
Yesiltepe et al. 2021	18	48	13	30	4.7%	0.87 [0.50, 1.50]
Subtotal (95% CI)		**556**		**863**	**28.6%**	**0.50 [0.35, 0.73]**
Total events	115		384			
Heterogeneity: Tau² = 0.14; Chi² = 17.49, df = 7 (P = 0.01); I² = 60%						
Test for overall effect: Z = 3.59 (P = 0.0003)						
1.5.3 Vertical vs Transverse						
Oenning et al. 2014	16	95	0	2	0.8%	1.03 [0.08, 13.45]
Schriber et al. 2020	15	35	5	5	5.1%	0.47 [0.30, 0.73]
Suter et al. 2019	35	186	0	2	0.8%	1.14 [0.09, 14.55]
Yesiltepe et al. 2021	18	48	7	13	4.4%	0.70 [0.37, 1.30]
Subtotal (95% CI)		**364**		**22**	**11.1%**	**0.55 [0.39, 0.79]**
Total events	84		12			
Heterogeneity: Tau² = 0.00; Chi² = 2.18, df = 3 (P = 0.54); I² = 0%						
Test for overall effect: Z = 3.28 (P = 0.001)						
1.5.4 Vertical vs Inverted						
Schriber et al. 2020	15	35	1	1	3.5%	0.57 [0.24, 1.39]
Suter et al. 2019	35	186	10	16	4.9%	0.30 [0.19, 0.49]
Yesiltepe et al. 2021	18	48	0	1	0.9%	1.51 [0.13, 17.11]
Subtotal (95% CI)		**269**		**18**	**9.3%**	**0.41 [0.22, 0.79]**
Total events	68		11			
Heterogeneity: Tau² = 0.12; Chi² = 3.02, df = 2 (P = 0.22); I² = 34%						
Test for overall effect: Z = 2.68 (P = 0.007)						
1.5.5 Vertical vs Horizontal						
Matzen et al. 2017b	1	36	44	93	1.3%	0.06 [0.01, 0.41]
Oenning et al. 2014	16	95	4	9	3.5%	0.38 [0.16, 0.89]
Schriber et al. 2020	15	35	1	1	3.5%	0.57 [0.24, 1.39]
Smailiene et al. 2019	17	72	16	19	5.0%	0.28 [0.18, 0.44]
Suter et al. 2019	35	186	45	83	5.4%	0.35 [0.24, 0.50]
Tassoker 2019	1	21	12	35	1.3%	0.14 [0.02, 0.99]
Tunc et al. 2020	12	63	8	35	3.8%	0.83 [0.38, 1.84]
Yesiltepe et al. 2021	18	48	4	7	4.0%	0.66 [0.31, 1.37]
Subtotal (95% CI)		**556**		**282**	**27.7%**	**0.40 [0.27, 0.58]**
Total events	115		134			
Heterogeneity: Tau² = 0.14; Chi² = 14.54, df = 7 (P = 0.04); I² = 52%						
Test for overall effect: Z = 4.69 (P < 0.00001)						
Total (95% CI)		**2301**		**1597**	**100.0%**	**0.59 [0.46, 0.76]**
Total events	497		605			
Heterogeneity: Tau² = 0.27; Chi² = 97.78, df = 30 (P < 0.00001); I² = 69%						
Test for overall effect: Z = 4.13 (P < 0.0001)						
Test for subgroup differences: Chi² = 15.42, df = 4 (P = 0.004), I² = 74.1%						

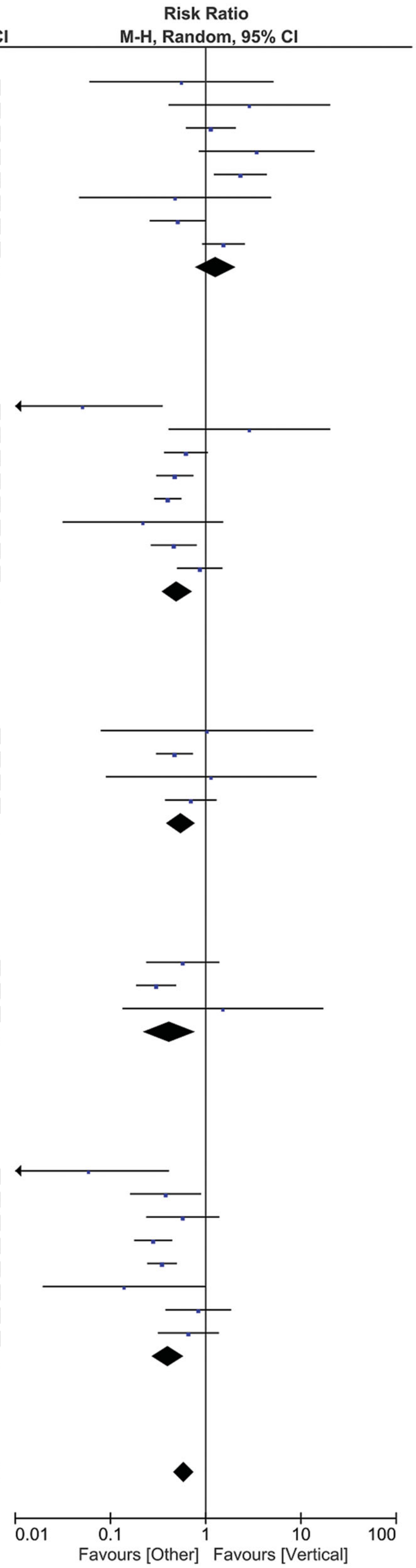

Figure 5. Vertical versus other inclination of M3.

The association of ERR on M2 with the presence of impacted M3 was found be of lesser magnitude among the included studies. A significant heterogeneity was found across the included studies, possibly due to difference in inclusion criteria, recruitment strategies of the patients and sample size. However, the association of ERR on M2 with the presence of impacted M3 was still evident. Understanding the risk factors, therefore, could help clinicians in decision making for timing of extraction of impacted M3. Our systematic review and meta-analysis did not show any significant

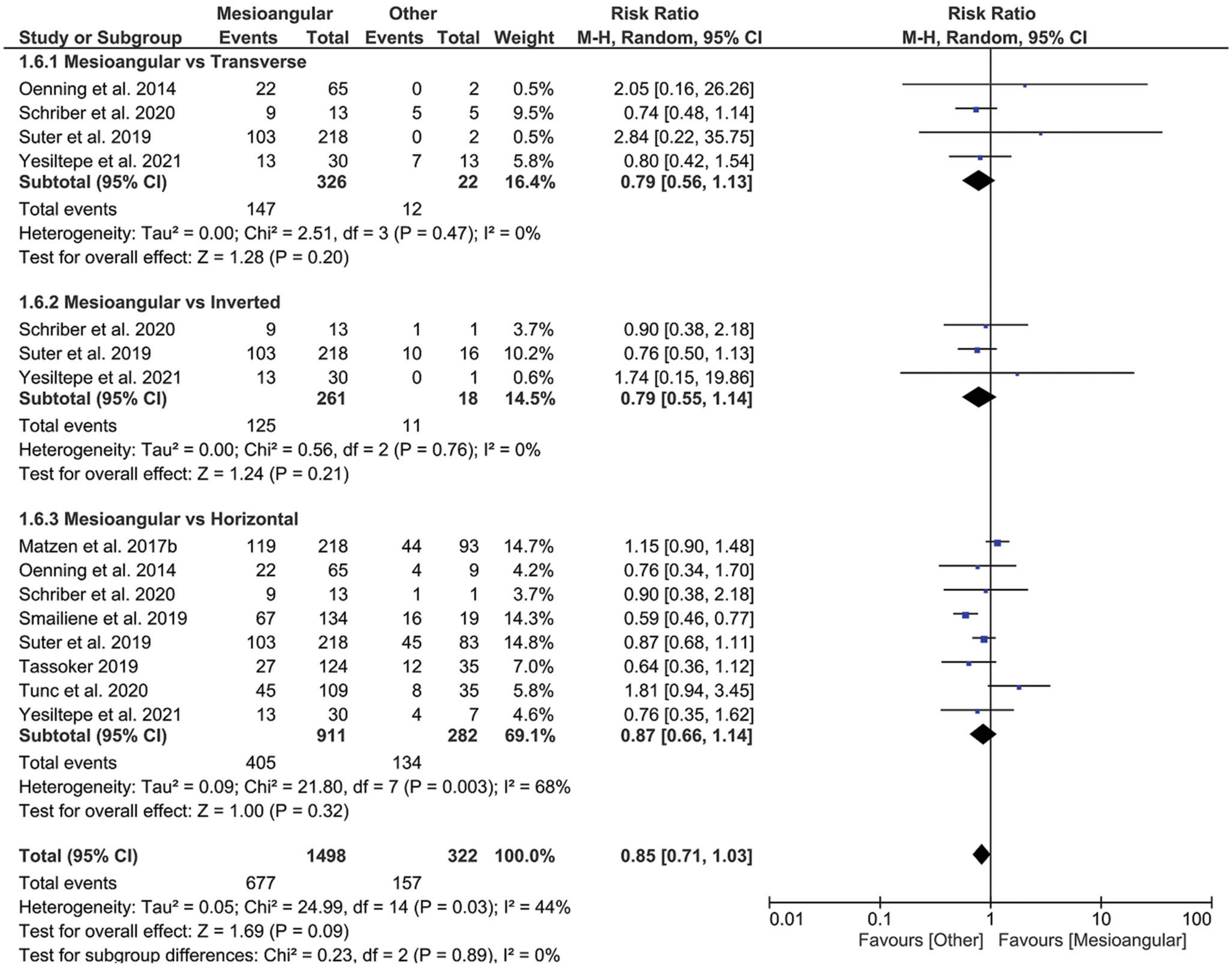

Figure 6. Mesio-angular versus other inclination of M3.

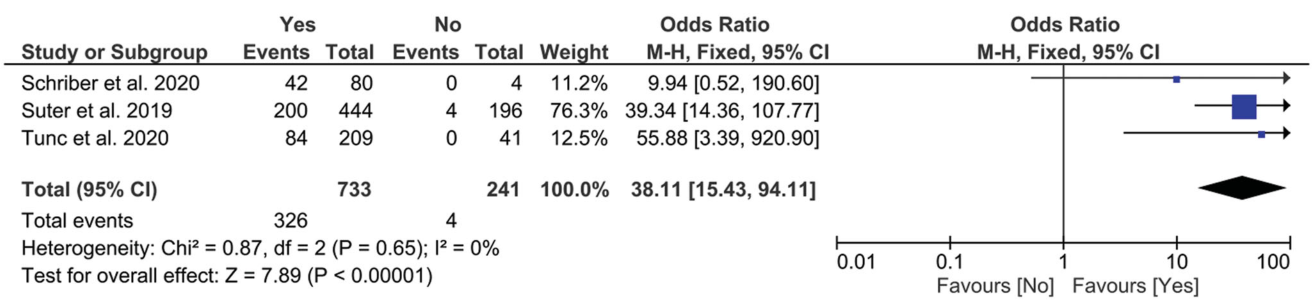

Figure 7. Contact between M2/M3.

association of gender with ERR. Therefore, it could not be considered as a risk factor.

According to the study of de Andrade et al. 2017, the cervical level of contact between the teeth was the most prevalent (51.2%). The apical level, however, was linked to the greatest incidence of ERR (83.3%), followed by the intermediate region (58.2%), and the cervical level (39.0%) [24]. Similar findings were observed in our systematic review, showing that the association of ERR in M2 with the impacted M3 at middle and apical region was significantly higher than at the cervical region.

The position of contact was also strongly linked to the inclination of the teeth. Our findings show that M2 in close proximity to mesio-angular impacted M3 had 50% higher risk of ERR than with vertical, traverse or horizontally impacted M3. Additionally, the prevalence of ERR seems to be higher with transverse, horizontal and mesio-angular impacted M3, with 54.5%, 47.5% and 44.5% of occurrence, respectively. These results are in agreement with the results of Oenning et al. 2015 who reported the incidence of ERR in adjacent second molars in relation to horizontal and mesio-angular impacted mandibular third molars [3]. They observed

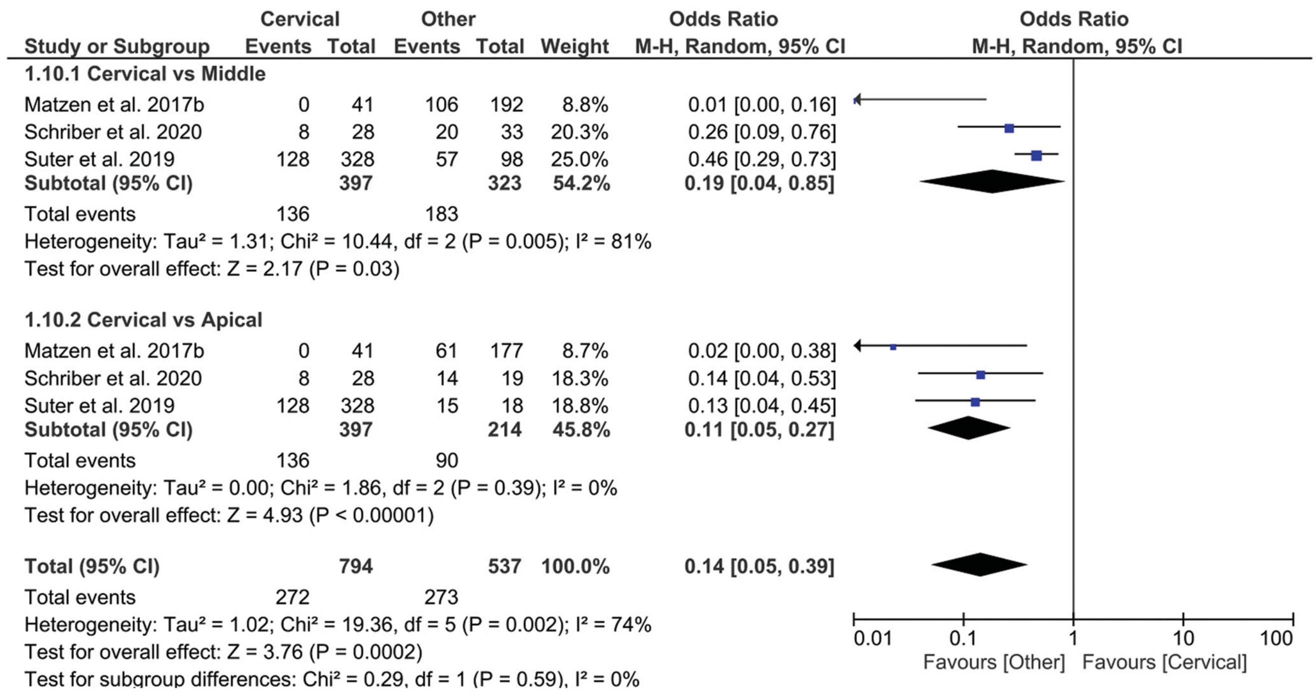

Figure 8. Level of impacted M3 in relation to M2.

Table 4. Prevalence of ERR in M2 with respect to different risk factors of impacted M3.

#	Risk factors	Estimate of proportion	Upper 95% CI	Lower 95% CI	ERR (%)
1	Gender (Suppl. Figure 1)				
	Male	0.356	0.263	0.449	291/777 (37.4%)
	Female	0.355	0.264	0.446	322/917 (35.1%)
2	Location of impacted M3 (Suppl. Figure 2)				
	Left side	0.238	0.183	0.292	96/401 (23.9%)
	Right side	0.255	0.148	0.362	103/411 (25.06%)
3	Arch location of impacted M3 (Suppl. Figure 3)				
	Upper	0.317	0.163	0.470	241/713 (33.8%)
	Lower	0.378	0.282	0.474	784/2043 (38.3%)
4	Inclination of impacted M3 (Suppl. Figure 4)				
	Vertical	0.193	0.112	0.275	115/556 (20.6%)
	Mesio-angular	0.438	0.344	0.532	405/911 (44.5%)
	Disto-angular	0.148	0.076	0.219	64/412 (15.5%)
	Transverse	0.496	0.229	0.762	12/22 (54.5%)
	Horizontal	0.499	0.356	0.641	134/282 (47.5%)
5	Contact between M2/M3 (Suppl. Figure 5)				
	Yes	0.426	0.394	0.459	595/1397 (42.5%)
	No	0.019	0.002	0.036	4/241 (1.6%)
6	Level of contact (Suppl. Figure 6)				
	Cervical	0.260	0.026	0.495	207/595 (34.7%)
	Middle	0.565	0.515	0.615	214/379 (56.4%)
	Apical	0.607	0.373	0.841	121/270 (44.8%)
7	Type of impaction (Suppl. Figure 7)				
	Full bony impaction	0.387	0.293	0.482	202/515 (39.2%)
	Soft tissue impaction	0.387	0.271	0.502	699/1691 (41.3%)

that mesially inclined third molars (mesio-angular and horizontal) are more likely to be linked to second molar ERR. Furthermore, mesio-angularly inclined M3 are more likely to come into direct contact with M2, which may explain higher incidence of ERR in these patients.

There was no difference in association between having impacted M3 in the maxillary or mandibular arch. However, there was a small but substantial correlation with the mandibular arch. When compared to the upper arch (33.8%), the presence of impacted M3 in the lower arch demonstrating ERR in M2 was substantially higher (38.3%). The difference in ERR prevalence between maxillary and mandibular M2s may be explained by the fact that disto-angular and vertical impaction was the most common impaction type in maxillary M3s, whereas mesio-angular and horizontal impaction was the most common impaction type in mandibular M3s [25]. The frequency of ERR in impacted M3s in maxillary and mandibular M2s was 32.6% in maxillary and 52.9% in mandibular M2, which was consistent with prior CBCT findings (from 20.2 to 54.9%)

The main strength of our systematic review is the inclusion of studies which employed CBCT for evaluation of ERR, which is more reliable imaging technique for diagnosis than two-dimensional imaging techniques. However, this study has its own limitations. The included studies in this systematic review were retrospective cohorts, which could introduce the potential bias of sample selection. A longitudinal study is therefore warranted to address this limitation. Another limitation is that there were insufficient clinical or histological validations, such as direct viewing or histological investigation in the included studies to validate the CBCT findings. All the diagnoses were based on the radiographic findings alone. However, the diagnosis of ERR could only be validated after extraction of the affected M2 or by any histopathological examination, which is not feasible.

Conclusion

Within the limitations of this review, it can be concluded that ERR in M2 was highly associated with their contact with impacted M3 and most importantly, with the inclination of M3. The presence of mesio-angular impacted M3 in close proximity to apical or middle portion of M2 was associated with the increased risk of ERR in M2. Moreover, the presence of M2 in close association with mesio-angular impacted M3 in the mandibular arch was associated with high prevalence of ERR. The clinicians must be taking into consideration all the risk factors identified in this review for better decision making.

Author contribution

YM conceived and designed the study; YM and DM were involved in literature search and data collection; YM and DM analysed the data; XL wrote the paper; and XL reviewed and edited the manuscript. All authors read and approved the final manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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