# DOES 3-D IMAGING OF THE THIRD MOLAR REDUCE THE RISK OF INFERIOR ALVEOLAR NERVE INJURY DUE TO EXTRACTION? A META-ANALYSIS.

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## ABSTRACT

Background. Panoramic radiographies are generally used to assess the proximity of the lower third molar to the inferior alveolar nerve (IAN). However, when third molar extraction is needed, many clinicians request a computed tomography (CT) to prevent nerve damage.

Types of Studies Reviewed. Two researchers independently searched the MEDLINE (through PubMed), The Cochrane Library, Scopus and Ovid databases. The inclusion criteria were randomized or non-randomized longitudinal studies that compared the number of IAN injuries after third molar removal in patients with preoperative CT versus patients with only panoramic radiographies.

Results. Twenty-six articles were analyzed, from a total of 745 papers initially selected for full-text analysis. Finally, 6 studies were included in the meta-analysis. Four articles had a high risk of bias and only 1 study blinded the patients. No statistically significant differences were observed between groups for the total number of nerve injuries (Risk Ratio: 0.96; 95% confidence interval: 0.50 to 1.85; p=0.91). The prognosis of the injuries was similar for both groups.

Practical Implications. Although having a preoperative CT might provide useful data for the diagnosis and extraction of a lower third molar, it does not reduce the risk of IAN injuries nor affect their prognosis.

Key Words. Third molar, computer tomography, panoramic radiography, mandibular nerve, alveolar nerve.

## INTRODUCTION

Inferior alveolar nerve (IAN) injuries are one of the most important complications after lower third molar (L3M) removal (1-5), causing neurosensory impairment of the lower lip and chin area which clearly affects the quality of life of the patients (1). This complication, which affects from 0.4% to 5.5% (6) of patients, is usually temporary but on occasion can also lead to permanent symptoms. The risk of nerve injury is higher when the neurovascular bundle is exposed during the surgery (3,7).

Some factors related to the surgical technique and the surgeon's experience could have an impact on the risk of IAN injuries (3,7). In addition, some radiographic warnings of risk factors have been described in the literature (2). The most important predictor seems to be the proximity of the L3M roots to the mandibular canal (MC) (1,6).

Traditionally, panoramic radiographies (PANs) have been used to assess the relationship between the L3M roots and the MC. In high-risk cases, when the L3M is in close proximity with the MC, a computed tomography (CT) is usually recommended so that the surgeon can obtain a preoperative three-dimensional view of the area (1). Nevertheless, some recent publications have concluded that the use of 3D imaging does not seem to reduce the number of nerve injuries (1-4,6). In addition, 3D imaging means higher costs (1,6) and higher radiation exposure compared to PANs (1,4). In spite of these facts, some clinicians systematically indicate preoperative CTs before L3M removal to prevent legal issues. Therefore, a meta-analysis of the published data would be of great interest. Consequently, the aim of this study was to determine whether a preoperative CT reduces either the risk or the severity of IAN injuries after L3M removal in comparison to a PAN.

## MATERIAL AND METHODS

This paper adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) declaration (8).

## Study selection criteria

Randomized and non-randomized controlled trials and prospective and retrospective cohort studies that compared the number of IAN injuries after L3M removal in humans with and without preoperative CTs (i.e. only with PANs) were included. No restriction by language or publication date was applied. All the articles that did not meet these criteria were excluded.

The main outcome variable was the number of IAN injuries for each group, defined as a loss of sensation in the lower lip or chin areas, either subjectively reported by the patient or assessed by clinical testing.

The secondary variables were:

- Type of lesion. The lesion was considered persistent if the symptoms lasted longer than 6 months.
- Risk of nerve injury estimated through the previous radiographic assessment. The risk was classified as moderate if there was superimposition of the L3M root and the MC and/or 1 radiographic warning sign according to Rood and Shehab's criteria (9). If more than 1 Rood's sign was present, the procedure was considered to be high risk.

## Search strategy

An electronic search in the Pubmed (MEDLINE), The Cochrane Library (Wiley), Scopus and Ovid databases was conducted up to March 12$^{th}$ 2017.

The search strategy used was (((“Tomography, X-Ray Computed"[Mesh]) OR "Cone-Beam Computed Tomography"[Mesh]) AND ("Molar, Third"[Mesh]) OR "Mandibular Nerve/ injuries"[Mesh]) for Pubmed (MEDLINE); (“X Ray Computed Tomography Scanner" OR "Cone Beam Computed Tomography") AND ("Third Molar" OR "Mandibular Nerve”) for The Cochrane Library; (“Computed Tomography, X Ray” OR "Cone Beam Computed Tomography”) AND ("Third Molar” OR "Mandibular Nerve”) for Scopus; and (X Ray computed tomography or Cone Beam computed tomography) and (Third Molar or Mandibular nerve injury) for Ovid.

The search was completed by manual screening of the references cited in the selected articles and reviews.

## Selection of studies

Two researchers (ACO, AST) independently screened the title and abstract of each paper to decide its eligibility. The full-text of the selected articles was then assessed. The studies removed at this stage and the reasons for their exclusion are listed in Figure 1. A third reviewer (OCF) resolved any disagreement. Cohen's kappa was calculated to measure the reviewers' agreement.

When multiple reports on the same patients were identified, only the publication with the longest follow-up was included.

## Data extraction and method of analysis

Two reviewers (ACO and AST) independently extracted the data using data-extraction tables. Whenever possible, the following information was retrieved from the selected papers: author(s), year of publication, country of origin, study design and details of the participants, intervention(s) and outcomes.

The number of IAN injuries was considered to be the primary outcome variable. The secondary outcomes comprised the type of lesion and the preoperative estimation of the risk of nerve injury.

## Risk of bias assessment

The risk of bias was assessed according to the Cochrane Handbook for Systematic Reviews of Interventions version 5.1.0 and the data extraction and meta-analysis were performed with the Review Manager software, version 5.3 (The Cochrane Collaboration, Copenhagen). The Newcastle-Ottawa Scale (NOS) was used to assess cohort studies.

## Statistical analysis

The statistical analysis was carried out with Review Manager software. For dichotomous outcomes, risk ratios (RRs) with 95% confidence intervals (95% CI) were used to estimate the effect of the operation. Parametric and nonparametric tests (Pearson $\chi^2$ and Fisher tests) were used to compare the groups. The level of significance was set at a p-value of less than 0.05.

A meta-analysis was only performed when there were studies comparing similar techniques and reporting the same outcome measures. A subgroup analysis was conducted by preoperative risk groups for IAN damage.

Statistical heterogeneity was estimated by means of $\chi^2$ (Q value) and $I^2$ analyses. A $\chi^2$ p-value of $< 0.10$ and an $I^2$ value of >50% were interpreted as significant heterogeneity (10). A fixed or random-effects model was selected according to these values.

Had there been a sufficient number of meta-analyzed trials (more than 10), publication bias and clinical heterogeneity assessment, as well as sensitivity analyses, would have been performed in accordance with Higgins & Green (11).

## RESULTS

### Study selection and description

As shown in Figure 1, the initial electronic search yielded 745 references. After removal of duplicates, the abstracts of 533 articles were screened. Twenty-six articles were selected for full-text analysis and only 6 papers were included in the meta-analysis. The reviewers' agreement was good, with a Cohen's kappa index of 0.909. The selected studies were 5 randomized controlled trials (RCT) (1-4,12) and a retrospective cohort study (6).

On examining the full text, 20 publications were excluded for the following reasons: the number of IAN injuries in each group was not specified (5,13-15), CTs were performed for all patients (16-28), the study design did not comply with the inclusion criteria (case series (29) and ecological design (30)) and no comparison was made between the CT and the PAN groups (7).

### Risk of bias assessment

Four RCTs were classified as having a high risk of bias due to lack of blinding (1-3,12) and incomplete outcome data (1), as shown in Figure 2.

The cohort study was awarded 4 points in the selection category, 1 in comparability and 3 in outcome, totaling 8 points, and therefore was classified as high quality.

### Data extraction: qualitative synthesis

Different types of case were included in the selected studies (Table 1). Three studies included high-risk cases (1,6,12). Sanmartí-García et al. (6) selected cases with superimposition of the MC and the L3M roots on the PANs, fully formed roots, and the presence of at least 1 out of 7 radiographic signs of proximity between these structures. Ghaeminia et al. (1) only included cases in which the L3M roots covered more than half of the MC and Korkmaz et al. (12) selected high risk patients with at least one of the signs described by Rood and Shehab's (9). Petersen et al. (4) included cases with contact or overlap between the tooth/root complex and the MC on the PAN. The cases included in this last paper were considered as moderate risk, although the authors did not classify the injury risk of these patients.

Both of the studies by Guerrero et al. (2,3) selected patients with a moderate risk of injury. They excluded cases at "high risk" (with a high probability of harm to the neurovascular bundle) and "low risk" (clearly no radiographic relation between the 3M and the MC).

**<u>Data extraction: quantitative synthesis</u>**

The prevalence of IAN neurosensory disturbance was 9.3% (52/560) for the CT group and 8.3% (44/532) for the PAN group. Persistent neurosensory disturbances were detected in 1.5% of cases (7/477) for the CT group and 0.9% (4/445) for the PAN group. Table 2 shows the prevalence of IAN disturbances according to different preoperative classifications of risk.

No statistically significant differences in the prevalence of IAN injury were found between the CT and PAN groups (RR: 0.96; 95%CI: 0.50 to 1.85; p=0.91), or between studies investigating a moderate (RR: 1.02; 95%CI: 0.27 to 3.86; p=0.97) or high risk (RR: 0.85; 95%CI: 0.33 to 2.23; p=0.75) of potential damage (Figure 3).

Three studies found persistent injuries. Ghaeminia et al. (1) observed 5 lesions in the CT group and 2 in the PAN group that persisted after an 8-months follow-up, while Sanmartí-García et al. (6) and Petersen et al. (4) each classified only one lesion in each group as persistent (at least 12 and 6 months of evolution, respectively). No statistically significant differences in persistent lesions (RR: 1.64; 95%CI: 0.50 to 5.41; p=0.42) were detected in the subgroup analysis of the high risk (RR: 1.82; 95%CI: 0.48 to 6.90; p=0.38) and moderate risk (RR: 1.05; 95%CI: 0.07 to 16.50; p=0.98) subgroups (Figure 4).

**DISCUSSION**

This study failed to find significant differences in the rate of nerve injuries after L3M removal between patients with and without preoperative CT. Unfortunately, there is no consensus on the criteria for preoperative assessment of the IAN injury risk after third molar extraction. Indeed, all the authors establish their own criteria to classify the patients' risk, which makes comparisons difficult. In addition, the time needed to consider a lesion permanent also varies between the published studies. Many authors use the term "permanent" to define a nerve injury that has not recovered by the last follow-up visit. For this reason, the term "persistent" is more appropriate in our opinion, since the evolution after data recording is unknown. In the present meta-analysis, lesions lasting more than 6 months were considered persistent. This time frame was selected since Cheung et al. (31) reported that these lesions had a low recovery probability. Also, Valmaseda-Castellón et al. (32), in their prospective cohort study of 1117 L3M removals, observed that lesions that had not recovered 6 months after surgery were very likely to be permanent.

A drawback of the present report is related to the fact that both the number of studies included and their sample sizes were limited and that 4 of the RCTs included had a high risk of bias. The small number of participants in these trials might have led to a type-2 error (false negative findings). This is clearly related to the low incidence of this complication. Indeed, if IAN injury after L3M is defined as the primary outcome and a 0.5 difference between groups is considered clinically significant, favoring the CT group (as proposed by Petersen et al. (4)), none of the studies had a statistical power greater than 70%. Therefore, the results of this meta-analysis strongly show the need to perform more RCTs with a correct power calculation. These limitations have to been taken into account when considering the results. Even so, the outcomes of this meta-analysis and most of the studies included seem to support the hypothesis that performing a preoperative CT does not appear to lead to a significant decrease in the IAN injury rate after L3M removal.

Several risk factors have been identified as predicting IAN injury after L3M removal. Absence of cortication (19,27), dumb-bell shaped MCs (22,27) and a lingual (1,21,28) or interradicular (28) position of the MC are among them. Some authors state that injuries occur more easily in MCs with a narrowed configuration (1). Besides, when the MC is positioned lingually, the IAN may receive unfavorable forces if the surgeon starts his surgical approach by luxating on the buccal side (28). For this reason, it is thought that most IAN injuries are the result of compression and traction movements during L3M surgery (16). In these cases, a CT might provide useful information to the surgeon concerning where to apply the elevator.

A significant proportion (45.5%) of L3Ms have some degree of superimposition over the MC in PANs (7). According to Nakamori et al. (7), this superimposition, darkening of the root and narrowing of the MC on the PAN are correlated with absence of cortication (7) and suggest close contact between the tooth and the nerve. This direct contact, which can be observed in a CT, seems to result in an increased risk of IAN injury (19,23). However, only those cases with a true anatomical relationship between the two are at higher risk of suffering an IAN impairment due to the exposure (25).

Risk factors for IAN injuries are a key issue in the L3M extraction decision-making process, since they allow high-risk patients to be identified. Age, and also, especially, the anatomical proximity of the roots to the MC, are considered the most relevant variables for predicting this complication (16). PAN is still considered the gold-standard exam for L3M extraction. Simple superimposition of the third molar roots over the MC is not considered a sign of close relationship. In fact, the positive predictive value of IAN injury in case of superimposition without additional features is low. Even when more specific images are found, the positive predictive value still remains small, probably due to the low incidence of this complication (28,30). Indeed, only around 15% of the L3M with a PAN suggesting a high risk of IAN injuries will experience a neurosensory impairment (6). Although CTs are more specific in detecting the true anatomical relationships between L3Ms and MCs, their positive predictive value is still low and there are no data suggesting any reduction in the prevalence of IAN impairment when 3D techniques are used, compared to conventional PANs.

According to the results of this meta-analysis, a CT should not be routinely performed before L3M surgery. However, in specific cases, where a close relationship between the MC and the L3M is suspected after observing a PAN, a CT can be recommended (17).

## CONCLUSIONS

According to this meta-analysis, CTs should not be routinely performed before L3M surgery since they do not seem to reduce the incidence or affect the prognosis of IAN injuries in comparison with PANs.

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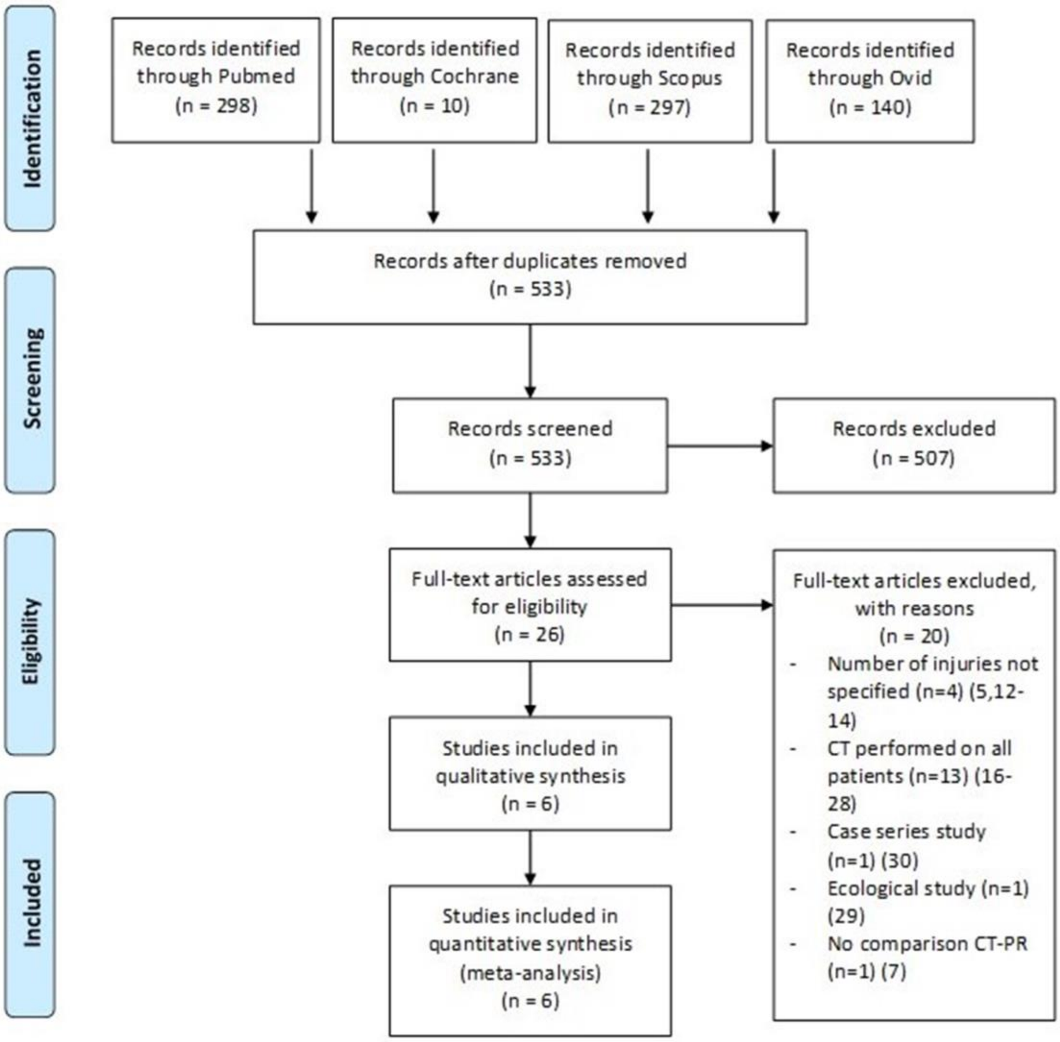
**FIGURE CAPTIONS**

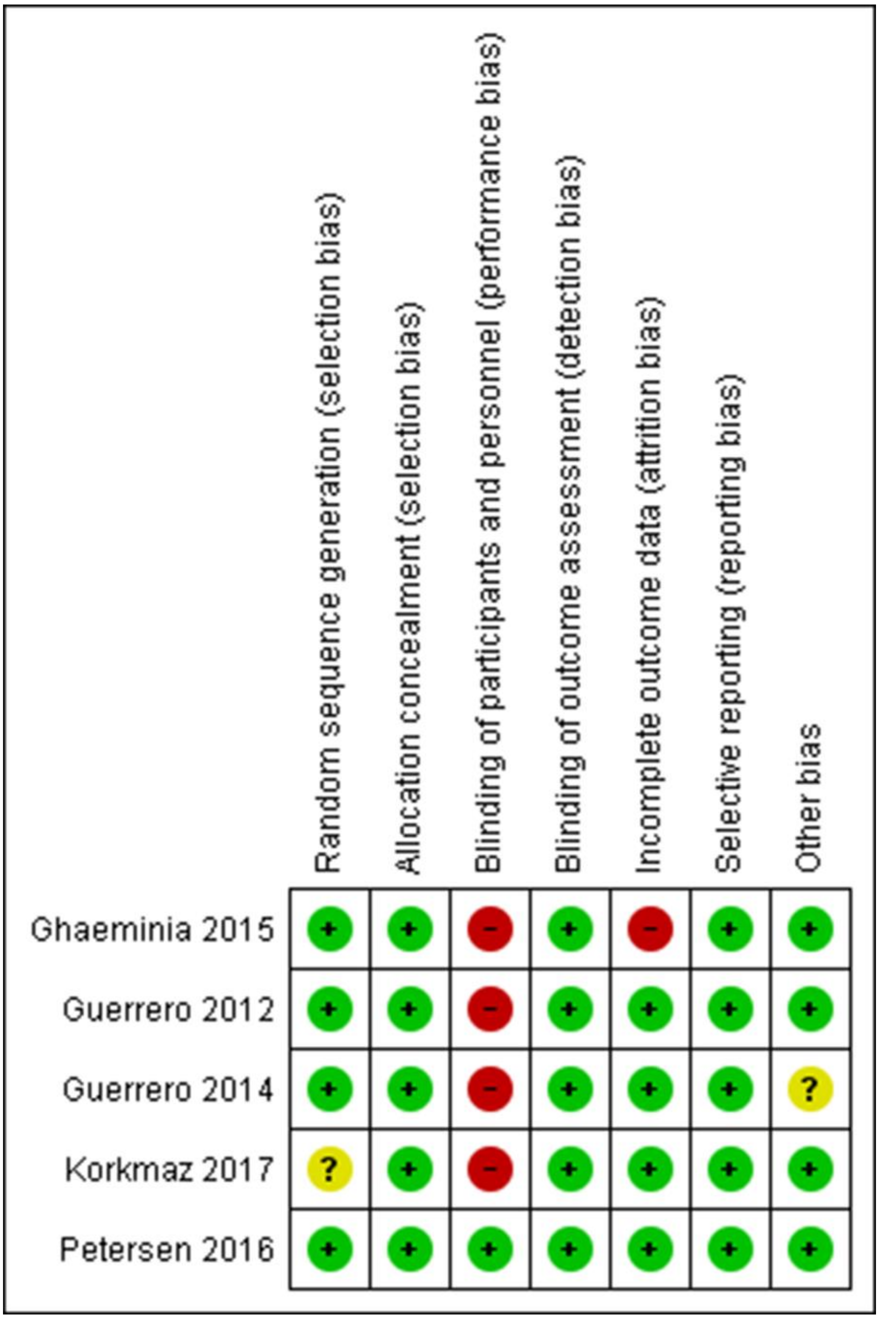
Figure 1. Flow chart of article selection for systematic review and meta-analysis according to PRISMA guidelines. CT: computed tomography; PAN: panoramic radiography.

Figure 2. Risk of bias assessment according to the Cochrane Handbook for Systematic Reviews of Interventions (11). Note: Plus (+) signs indicate no risk of bias and negative (-) signs indicate risk of bias.

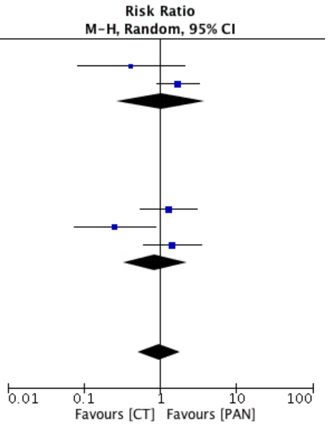
Figure 3. Meta-analysis: inferior alveolar nerve injury after lower third molar removal.

Figure 4. Meta-analysis: persistent inferior alveolar nerve injury after lower third molar removal.

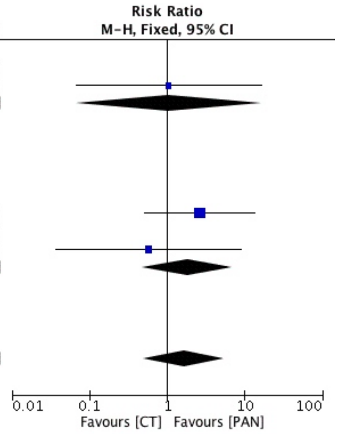

Identification
Screening
Eligibility
Included
Records identified through Pubmed (n = 298)
Records identified through Cochrane (n = 10)
Records identified through Scopus (n = 297)
Records identified through Ovid (n = 140)
Records after duplicates removed (n = 533)
Records screened (n = 533)
Records excluded (n = 507)
Full-text articles assessed for eligibility (n = 26)
Full-text articles excluded, with reasons (n = 20)
- Number of injuries not specified (n=4) (5,12-14)
- CT performed on all patients (n=13) (16-28)
- Case series study (n=1) (30)
- Ecological study (n=1) (29)
- No comparison CT-PR (n=1) (7)
Studies included in qualitative synthesis (n = 6)
Studies included in quantitative synthesis (meta-analysis) (n = 6)


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Ghaeminia 2015 + + − + − + +
Guerrero 2012 + + − + + + +
Guerrero 2014 + + − + + + ?
Korkmaz 2017 ? + − + + + +
Petersen 2016 + + + + + + +

| Study or Subgroup | Computed Tomography Events | Computed Tomography Total | Panoramic radiography Events | Panoramic radiography Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| **1.1.1 Moderate risk of potential damage to the IAN** | | | | | | |
| Guerrero et al. (2014) | 2 | 126 | 5 | 130 | 11.3% | 0.41 [0.08, 2.09] |
| Petersen et al. (2016) | 21 | 111 | 13 | 116 | 27.5% | 1.69 [0.89, 3.20] |
| **Subtotal (95% CI)** | | **237** | | **246** | **38.9%** | **1.02 [0.27, 3.86]** |
| Total events | 23 | | 18 | | | |
| Heterogeneity: $Tau^2 = 0.61$; $Chi^2 = 2.53$, df = 1 (P = 0.11); $I^2 = 60\%$ | | | | | | |
| Test for overall effect: Z = 0.03 (P = 0.97) | | | | | | |
| **1.1.2 High risk of potential damage to the IAN** | | | | | | |
| Ghaeminia et al. (2015) | 11 | 156 | 9 | 164 | 22.9% | 1.28 [0.55, 3.02] |
| Korkmaz et al. (2017) | 3 | 72 | 11 | 67 | 16.1% | 0.25 [0.07, 0.87] |
| Sanmartí-García et al. (2012) | 15 | 95 | 6 | 55 | 22.2% | 1.45 [0.60, 3.51] |
| **Subtotal (95% CI)** | | **323** | | **286** | **61.1%** | **0.85 [0.33, 2.23]** |
| Total events | 29 | | 26 | | | |
| Heterogeneity: $Tau^2 = 0.47$; $Chi^2 = 5.81$, df = 2 (P = 0.05); $I^2 = 66\%$ | | | | | | |
| Test for overall effect: Z = 0.32 (P = 0.75) | | | | | | |
| **Total (95% CI)** | | **560** | | **532** | **100.0%** | **0.96 [0.50, 1.85]** |
| Total events | 52 | | 44 | | | |
| Heterogeneity: $Tau^2 = 0.30$; $Chi^2 = 9.12$, df = 4 (P = 0.06); $I^2 = 56\%$ | | | | | | |
| Test for overall effect: Z = 0.11 (P = 0.91) | | | | | | |
| Test for subgroup differences: $Chi^2 = 0.05$, df = 1 (P = 0.83), $I^2 = 0\%$ | | | | | | |



| Study or Subgroup | Computed Tomography Events | Computed Tomography Total | Panoramic radiography Events | Panoramic radiography Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| **2.1.1 Moderate risk of potential damage to the IAN** | | | | | | |
| Guerrero et al. (2012) | 0 | 43 | 0 | 43 | | Not estimable |
| Petersen et al. (2016) | 1 | 111 | 1 | 116 | 23.3% | 1.05 [0.07, 16.50] |
| **Subtotal (95% CI)** | | **154** | | **159** | **23.3%** | **1.05 [0.07, 16.50]** |
| Total events | 1 | | 1 | | | |
| Heterogeneity: Not applicable | | | | | | |
| Test for overall effect: Z = 0.03 (P = 0.98) | | | | | | |
| **2.1.2 High risk of potential damage to the IAN** | | | | | | |
| Ghaeminia et al. (2015) | 5 | 156 | 2 | 164 | 46.5% | 2.63 [0.52, 13.35] |
| Korkmaz et al. (2017) | 0 | 72 | 0 | 67 | | Not estimable |
| Sanmartí-García et al. (2012) | 1 | 95 | 1 | 55 | 30.2% | 0.58 [0.04, 9.07] |
| **Subtotal (95% CI)** | | **323** | | **286** | **76.7%** | **1.82 [0.48, 6.90]** |
| Total events | 6 | | 3 | | | |
| Heterogeneity: $Chi^2 = 0.86, df = 1 (P = 0.35); I^2 = 0\%$ | | | | | | |
| Test for overall effect: Z = 0.88 (P = 0.38) | | | | | | |
| **Total (95% CI)** | | **477** | | **445** | **100.0%** | **1.64 [0.50, 5.41]** |
| Total events | 7 | | 4 | | | |
| Heterogeneity: $Chi^2 = 0.98, df = 2 (P = 0.61); I^2 = 0\%$ | | | | | | |
| Test for overall effect: Z = 0.81 (P = 0.42) | | | | | | |
| Test for subgroup differences: $Chi^2 = 0.13, df = 1 (P = 0.72), I^2 = 0\%$ | | | | | | |



| Author | Patient | | Intervention | | Outcome | | | Study design |
|---|---|---|---|---|---|---|---|---|
| | Preoperative risk | Assessment criteria | Radiographic technique | Sample size | Nerve lesions (%) | Persistent lesions (n) | Persistent lesion follow-up (months) | |
| Sanmartí-Garcia et al. 2012 | High risk | Superimposition of roots and mandibular canal + any of 7 Rood criteria signs | TC | 95 | 15 (15.8) | 1 | 12 | Cohort (retrospective) |
| | | | PAN | 55 | 6 (10.9) | 1 | | |
| Guerrero et al. 2012 | Moderate risk | Cases without "high risk" (high probability of harm to the neurovascular bundle) or "low risk" (clearly no radiographic relation between the 3M and the canal). | TC | 43 | 1 (2.3) | 0 | NR | RCT (parallel) |
| | | | PAN | 43 | 1 (2.3) | 0 | | |
| Guerrero et al. 2014 | Moderate risk | Cases without "high risk" (high probability of harm to the neurovascular bundle) or "low risk" (clearly no radiographic relation between the 3M and the canal). | TC | 126 | 2 (1.5) | NR | NR | RCT (parallel, multicenter) |
| | | | PAN | 130 | 5 (3.8) | NR | | |
| Ghaeminia et al. 2015 | High risk | Superimposition of roots and mandibular canal covering more than half the MC height | TC | 156 | 11 (7.1) | 5 | 8 | RCT (parallel) |
| | | | PAN | 164 | 9 (5.5) | 2 | | |
| Petersen et al. 2016 | Moderate risk | Superimposition of roots and mandibular canal | TC | 111 | 21 (18.9) | 1 | 6 | RCT (parallel) |
| | | | PAN | 116 | 13 (11.2) | 1 | | |
| Korkmaz et al. 2017 | High risk | Close relationship between the MC and the 3 defined as: presence of at least one of six radiographic markers: interruption of the wh line of the MC, darkening of the roots, narrowing of the MC or roots, dark and bifid roots, deflected roots, diversion of the MC. | TC | 72 | 3 (4.2) | 0 | 6 | RCT (parallel) |
| | | | PAN | 67 | 11 (16.4) | 0 | | |

Table 1. Characteristics of the studies included in the meta-analysis regarding to participants, interventions and outcomes. CT: computed tomography; PAN: panoramic radiography. NR: not reported; RCT: randomized clinical trial.

| | IAN injuries<br>CT | | IAN injuries<br>PAN group | |
|---|---|---|---|---|
| | Overall | Persistent | Overall | Persistent |
| Moderate risk | 9.7% (23/237) | 0.6% (1/154) | 7.3% (18/246) | 0.6% (1/159) |
| High risk | 9.0% (29/323) | 1.9% (6/323) | 9.1% (26/286) | 1.0% (3/286) |
| Overall | 9.3% (52/560) | 1.5% (7/477) | 8.3% (44/532) | 0.9% (4/445) |

Table 2. Percentage of nerve disturbances. IAN: Inferior alveolar nerve; CT: computed tomography; PAN: panoramic radiography.