

Influence of the anesthetic modality on the development of neurological injury after lower third molar extraction: A systematic review of the literature

Fulvia Costantinides^{A,D,E}, Matteo De Nardi^{B,D}, Massimiliano Lenhardt^{B,C}, Giuseppe Perinetti^{C,E}, Lorenzo Bevilacqua^{D-F}, Michele Maglione^{A,F}

Clinical Department of Medical Sciences, Surgery and Health, Unit of Oral Surgery, School of Specialization in Oral Surgery, University of Trieste, Italy

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of the article

Dental and Medical Problems, ISSN 1644-387X (print), ISSN 2300-9020 (online)

Dent Med Probl. 2022;59(2):291–299

Address for correspondence

Lorenzo Bevilacqua
E-mail: l.bevilacqua@fmc.units.it

Funding sources

None declared

Conflict of interest

None declared

Acknowledgements

None declared

Received on May 4, 2021
Reviewed on June 18, 2021
Accepted on June 28, 2021

Published online on June 30, 2022

Abstract

The aim of this study was to determine if the risk of neurological injury to the inferior alveolar nerve (IAN) and the lingual nerve (LN) following the extraction of lower third molars is affected by the anesthetic modality (local anesthesia (LA) vs. general anesthesia (GA)).

A systematic search was performed through the PubMed, Scopus, Cochrane Library, and Web of Science databases; furthermore, a manual search was performed by analyzing the references of full-text articles.

From a total of 309 studies (collected after the removal of duplicates), 6 studies were selected. Of these, 4 reported a correlation between GA and nerve damage, while the other 2 did not show an obvious association. The level of bias in the studies was also calculated. Only 2 studies showed a medium risk of bias, while 4 studies showed a high risk of bias; no study showed a low risk of bias. Four of the 6 studies highlighted a higher incidence of IAN and LN injury following the extractions performed under GA.

Although no scientific evidence is yet available, due to the scarcity and the limited quality of the studies in the literature, considering the risk–benefit ratio, LA should be the first choice in lower third molar surgery.

Keywords: extraction, inferior alveolar nerve, anesthesia, neurological injury, lower third molars

Cite as

Costantinides F, De Nardi M, Lenhardt M, Perinetti G, Bevilacqua L, Maglione M. Influence of the anesthetic modality on the development of neurological injury after lower third molar extraction: A systematic review of the literature. *Dent Med Probl.* 2022;59(2):291–299. doi:10.17219/dmp/139472

DOI

10.17219/dmp/139472

This is an article distributed under the terms of the Creative Commons Attribution 3.0 Unported License (CC BY 3.0) (<https://creativecommons.org/licenses/by/3.0/>).

Introduction

The lower third molar is situated between the second lower molar and the mandibular ramus.

The primary reasons for the impaction of the wisdom tooth are to be searched in the lack of space, malposition, unfavorable eruption angulation, or physical impediments along the pathway of eruption.¹ The etiology of tooth impaction may be associated with abnormalities in tooth development, and it is related to inherent genetic components and specific environmental conditions.²

The impaction of mandibular third molars is a condition associated with a different degree of difficulty during surgery and a higher risk of complications. The mesioangular impaction of third molars is the most frequent situation.³ Most common complications occur when the surgical removal is performed with the altered position of the wisdom tooth, which is generally more difficult, and also in elderly patients.^{3,4}

Complications are usually local, like a hematoma or infections, and temporary, like iatrogenic inferior alveolar nerve (IAN) or lingual nerve (LN) injury.^{5,6} For this reason, the 1979 conference of the American National Institutes of Health (NIH) suggested that third molars should be removed when there is evidence of pathological changes or irreversible pathology.⁷

In ethical terms, it is not advisable to perform a surgical procedure that carries a morbidity risk without valid indications. There are many indications for the extraction of the impacted lower third molar that are derived from the clinical symptomatology with the distinction between 'symptomatic' and 'asymptomatic' teeth. However, the term 'asymptomatic' is ambiguous, since the lack of symptoms should not be confused with the lack of pathology. Some diseases could remain asymptomatic before being diagnosed despite the presence of pathological (clinical or radiographic) signs. It is also important to consider clinical situations where no pathology has been developed yet, but the predisposing factors are present, such as plaque accumulation, common in the case of partially erupted molars or teeth affected by dysodontiasis.

Intraoperative pain control is an intrinsic part of a surgical procedure. In most cases, third molar surgery can be performed under local anesthesia (LA), although in particular cases, general anesthesia (GA) is suggested. General anesthesia should be limited to those patients and clinical situations in whom/which LA cannot be used: uncooperative patients; dental phobia; allergy to local anesthetics; acute and extended infections; and extensive dental or maxillofacial surgery. In the literature, there are still no precise indications as to the choice of the anesthetic modality with regard to third molar surgery. On the other hand, considering that many types of risk, e.g., rare and unpredictable death, are associated with GA, this anesthetic choice should be taken into account only if necessary.⁸

Therefore, the aim of this systematic review was to assess the influence of various modalities of anesthesia,

LA vs. GA, used for the extraction of the lower third molar on neurological injury to IAN and/or LN.

Material and methods

The present systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement⁹ and used a previous systematic review as a template.¹⁰

The following PICOS (Population, Intervention, Comparison, Outcome, and Study design) criteria were set:

- Population: patients undergoing lower third molar surgery;
- Intervention: lower third molar extraction under LA;
- Comparison: patients whose surgery had been performed under GA;
- Outcome: neurologic injury to IAN and/or LN; and
- Study design: systematic review.

Search strategy

The review was realized with the use of scientific databases: PubMed; Scopus; Cochrane Library; and the Web of Science, from the inception to the latest research in August 2019. A manual search was also performed among the references of all full-text articles. No language restriction was applied.

The search of PubMed was performed using the following algorithm: (local OR general) AND (anaesthesia OR anesthesia) AND (third OR 3rd OR lower OR mandibular OR wisdom OR impacted) AND (molar OR molars OR tooth OR teeth) AND (extraction OR extractions OR removal OR removals) AND (injury OR injuries OR damage OR lesion OR lesions OR disturbance OR disturbances) AND (lingual nerve OR mandibular nerve OR inferior alveolar nerve). The search strategy applied in Scopus involved the same Boolean string, including the article title, abstract and keywords. In the case of the Cochrane Library search, the "Advanced search" tool was used, choosing all content types. For the Web of Sciences, the "Advanced search" was used, selecting all languages and all document types.

Study selection

The selected studies had to meet the pre-defined eligibility criteria. They had to be randomized clinical trials (RCTs), controlled clinical trials (CCTs), prospective cohort studies (PCSs), or retrospective studies (RSs), with or without a control group.

Studies that considered 2 groups of patients undergoing lower third molar extraction were included, and studies in which 3 groups were considered because of the addition of the LA plus sedation group were also taken into account.

Studies that investigated the risk of developing nerve injury (of IAN and/or LN) in a group of patients treated under GA, in a group of patients treated under LA and in a group of patients treated under LA plus sedation

(if the 3rd type of anesthetic modality was taken in consideration) were collected.

Studies that distinguished temporary and permanent injury after the period of follow-up, with at least 6 months of follow-up were included.

Case report, case series, studies enrolling less than 10 subjects, comments, expert opinions, letters to the editor, reviews, and studies that analyzed the same sample as a pre-existent study were excluded.

Studies that did not evaluate the anesthetic modality as a parameter in the development of neurologic injury and studies that evaluated a single type of anesthetic modality (only a group of patients treated under LA or GA) with regard to nerve injury after lower third molar extraction were excluded.

Studies that did not distinguish temporary and permanent injury after the period of follow-up were excluded.

Redundant studies were excluded.

Data items

The following data was collected: study design; anesthetic modality (LA, GA and LA plus sedation); sample size; gender and age; number of teeth removed; operators' experience; surgical difficulty rated according to different classifications (Winter's classification, Wharfe's score,

and Pell and Gregory's classification); use of a lingual retractor (if used, specifying the type); follow-up; nerve injury classified as temporary or permanent (persisting after 6 months); and clinical implications according to the authors.

Assessment of the risk of bias in individual studies

The risk of bias in individual studies was evaluated according to the modified Downs and Black tool.¹¹ The original Downs and Black tool¹² consists in the calculation performed by evaluating each study across 5 domains, including:

- Reporting (10 items);
- External validity (3 items);
- Internal validity – bias (7 items)
- Internal validity – confounding (6 items); and
- Power (1 item).

The maximum possible score is 32. In the current review, certain modifications were introduced to adhere to the studies dealing with the topic “nerve injury after third molar removal under local or general anesthesia”.

These were as follows (Table 1):

- Item 19 (Was compliance with the intervention/s reliable?) was not considered, as in the present research, the compliance of the patients was not required to evaluate the results;

Table 1. Modified Downs and Black tool used for the analysis of the risk of bias of non-randomized clinical trials (judgments and scores for each item as follows: no/not applicable (0); yes (1))

Domain	Question
Reporting	1. Is the objective of the study clearly described?
	2. Are the main outcomes to be measured clearly described in the Introduction or Methods section?
	3. Are the characteristics of the patients included in the study clearly described?
	4. Are the interventions of interest clearly described?
	5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?
	6. Are the main findings of the study clearly described?
	7. Does the study provide the estimates of random variability in the data for the main outcomes?
	8. Have all important adverse events that may be a consequence of the intervention been reported?
	9. Have the characteristics of the patients lost to follow-up been described?
	10. Have actual probability values been reported (e.g., 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?
External validity	11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?
	12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?
	13. Were the staff, places and facilities where the patients were treated representative of the treatment the majority of patients receive?
Internal validity – bias	14. Was an attempt made to blind the study subjects to the intervention they received?
	15. Was an attempt made to blind those measuring the main outcomes of the intervention?
	16. If any of the results of the study were based on 'data dredging', was this made clear?
	17. In trials and cohort studies, were the analyses adjusted for different lengths of the follow-up of the patients, or in case-control studies, was the time period between the intervention and the outcome the same for cases and controls?
	18. Were the statistical tests used to assess the main outcomes appropriate?
Internal validity – confounding	19. Were the main outcome measures used accurate (valid and reliable)?
	20. Were the patients in different intervention groups (trials and cohort studies) or were cases and controls (case-control studies) recruited from the same population?
	21. Were the patients in different intervention groups (trials and cohort studies) or were cases and controls (case-control studies) recruited over the same period of time?
	22. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?
	23. Was the loss of patients to follow-up taken into account?
Power	24. Sample size calculation

- Item 23 (Were the study subjects randomized to intervention groups?) and Item 24 (Was the randomized intervention assignment concealed from both patients and healthcare staff until recruitment was complete and irrevocable?) were not considered, as not all of the included studies were randomized; and
- Item 27 (Power) was simplified to “Sample size calculation”.

Thus, the domains of the modified tool were as follows: reporting (10 items); external validity (3 items); internal validity – bias (6 items); internal validity – confounding (4 items); and power (1 item), with a maximum score of 25. The overall risk of bias was defined as follows:

- high: total score ≤ 16 ;
- medium: total score > 16 and < 22 ; and
- low: total score ≥ 22 .

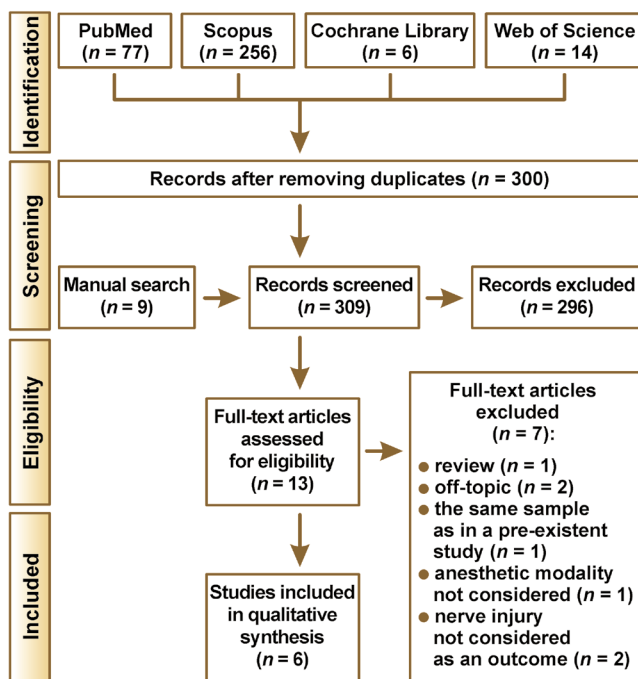


Fig. 1. Flow diagram of the search strategy

Table 2. Studies excluded after full-text consideration with the corresponding main reason for exclusion

Authors	Year	Reference	Main reason for exclusion
Nowak et al.	2014	<i>Dent Med Probl.</i> 2014;51(2):225–230	review
Renton	2013	<i>Br Dent J.</i> 2013;215(8):393–399	anesthetic modality not considered
Gülicher and Gerlach	2000	<i>Oral Maxillofac Surg.</i> 2000;4(2):99–104	the same sample as in a pre-existent study
Loescher et al.	2003	<i>Dent Update.</i> 2003;30(7):375–380,382	off-topic
Edwards et al.	1999	<i>Ann R Coll Surg Eng.</i> 1999;81(2):119–123	paresthesia not considered as an outcome
Edwards et al.	1998	<i>Br J Oral Maxillofac Surg.</i> 1998;36(5):333–340	paresthesia not considered as an outcome
Worrall et al.	1998	<i>Br J Oral Maxillofac Surg.</i> 1998;36(1):14–18	off-topic

Results

Study search

The results of the automatic and manual search are summarized in Fig 1. From a total of 309 articles retrieved, 7 of the 13 full-text articles assessed for eligibility were excluded for the reasons provided in Fig. 1 and Table 2.

Finally, 6 studies were judged eligible according to the inclusion/exclusion criteria (Table 3).

Study design

The 6 selected studies included 1 retrospective observational study (ROS),⁸ 3 prospective studies (PSs),^{13–15} 1 prospective longitudinal study (PLS),¹⁶ and 1 RS.¹⁷ In half of the selected studies, the extractions were performed under LA or GA^{8,14,17}; in the remaining half, the extractions were performed under LA, GA or LA plus sedation.^{13,15,16} The sample size in the selected studies ranged from 387¹³ to 6,803 subjects.¹⁷ All the studies included both males and females. In 3 cases,^{14,16,17} information on gender distribution was not available. The mean age of patients ranged between 24.92 ± 4.67 years¹³ and 41.3 ± 17.8 years⁸; in 2 cases, the mean age of patients was not considered.^{14,17}

The number of teeth extracted under LA was in the range between 105¹⁶ and 631,¹⁵ under GA, it was between 194⁸ and 535,¹³ and the range for LA plus sedation was between 15¹⁵ and 41.¹³ Only Nguyen et al. did not specify how many teeth were extracted under LA or GA.¹⁷

In 4 cases, the extractions were performed by surgeons with different levels of experience^{14–17}; in the study by Brann et al., the operator’s experience was not considered.¹³ Only in 1 study, the extractions were performed by a single surgeon with high experience.⁸

Table 3. Summarized data of the 6 studies included in the review

Study	Type	Anesthetic modality	Sample size <i>n</i>	Gender <i>n</i> and age [years] <i>M</i> ± <i>SD</i>	Number of teeth removed	Operator's experience	Surgical difficulty	Use of a lingual retractor	Follow-up period	Number of cases of nerve injury		Clinical implications
										T	P	
Costantinides et al. ⁹ 2016	ROS	LA	340	M: 283 F: 251 41.3 ± 17.8	340	single surgeon, high experience	P&G: I-A 271 I-B 29 I-C 12 II-A 15 II-B 7 II-C 2 II-A 0 II-B 2 II-C 2 P&G: I-A 58 I-B 19 I-C 10 II-A 35 II-B 45 II-C 7 II-A 3 II-B 2 II-C 15	PRE	6 months	1 IAN 0 LN	1 IAN 0 LN	GA seems to increase the risk of developing IAN and LN lesions
										9 IAN 4 LN	0 IAN 1 LN	
Brann et al. ¹³ 1999	PS	LA	96	M: 250 F: 117	142	NA	WS 8	HR/NA	6 months	5 a	5 b	GA seems to increase the risk of developing nerve injury
		GA LA + sedation	271 20	535 41	WS 8 NA		1 a	0				
Hill et al. ¹⁴ 2001	PS	LA	201	NA	201	4 surgeons, different experience	WS 5.5	HR	6 months	8 a	0	no significant difference in adverse effects between the 2 modalities
		GA	234	430	WS 5.5		16 a	0				
Gülcher and Gerlach ¹⁵ 2001	PS	LA	631	M: 516 F: 590	631	13 surgeons, different experience	WC: H 53 V 350 MA 490 DA 159 Trans 48 O 6	PE	6 months	c 8 LN	d 14 LN	a high risk of nerve injury in procedures under GA
		GA	NA	460	c 14 LN		e					
		LA + sedation	27.3	15	c 1 LN							
Rehman et al. ¹⁶ 2002	PLS	LA	90	NA	105	different surgeons, different experience	WS 5.7	HR/HOR, 45	6 months	5 IAN 4 LN	f 15 IAN 22 LN	no significant relationship between nerve damage and the anesthetic modality
		GA	273	30.00 ± 10.58	474		WS 5.8	HR/HOR, 340	6 months	0		
		LA + sedation	28	35	NA		NA	0				
Nguyen et al. ¹⁷ 2014	RS	LA GA	6,803	NA	11,599	different surgeons, different experience	NA	NA	12 months	4 IAN 1 LN 42 IAN 8 LN	8 IAN 0 LN 15 IAN 6 LN	surgery under GA is a risk factor for permanent IAN injury, no factor increases the risk of LN injury

M – mean; *SD* – standard deviation; *T* – temporary; *P* – permanent; *ROS* – retrospective observational study; *PS* – prospective study; *PLS* – prospective longitudinal study; *RS* – retrospective study; *LA* – local anesthesia; *GA* – general anesthesia; *M* – male; *F* – female; *WC* – Winter's classification; *WS* – Wharf's score; *P&G* – Pell and Gregory's classification; *H* – horizontal; *V* – vertical; *MA* – mesioangular; *DA* – distoangular; *Trans* – transversal; *O* – other; *PRE* – Pritchard elevator; *HR* – Howarth retractor; *HOR* – Hovell retractor; *IAN* – inferior alveolar nerve; *LN* – lingual nerve; *a* – merging cases of IAN and LN injury; *b* – merging cases of IAN and LN injury in the LA, GA and LA + sedation groups; *c* – a total of 39 cases of IAN injury by merging the LA, GA and LA + sedation groups; *d* – a total of 10 cases of IAN injury by merging the LA, GA and LA + sedation groups; *e* – a total of 4 cases of LN injury by merging the LA, GA and LA + sedation groups; *f* – a total of 3 cases of IAN injury by merging the LA, GA and LA + sedation groups; *NA* – data not available.

Surgical difficulty was rated according to different classifications. Three studies recorded the degree of surgical difficulty by means of Wharfe's score.^{13,14,16} Hill et al. found a score of 5.5 without differentiating the scores between LA and GA,¹⁴ the other 2 studies found similar Wharfe's scores for the subjects treated under LA and the subjects treated under GA.^{13,16} Winter's classification was used by Glicher and Gerlach to find out the prevalence of the positions of the extracted teeth (horizontal (53), vertical (350), mesioangular (490), distoangular (159), transversal (48), and other (6)) without specifying the anesthetic modality.¹⁵ Costantinides et al. assessed surgical difficulty by using Pell and Gregory's classification, starting from class I-A (271 teeth in the LA group and 58 teeth in the GA group) up to class III-C (2 teeth in the LA group and 15 teeth in the GA group).⁸ In the remaining study, the preliminary staging before the extractions was not clearly described.¹⁷

A lingual retractor was used in 3 cases.^{13,14,16} In 1 case, the Howarth retractor was used in all procedures of extraction¹⁴; the Howarth retractor was also used in the study by Brann et al. for all the teeth requiring bone removal and the retraction of lingual tissues¹³; in another case, the Howarth or Hovell retractors were used based on the choice of the surgeons (in 45 procedures under LA and in 340 procedures under GA).¹⁶ The Prichard elevator was used in 1 study, when necessary, protecting but not retracting the lingual flap.⁸ Glicher and Gerlach used a non-specified periosteal elevator to protect the lingual nerve.¹⁵ Nguyen et al. did not specify the use of a lingual retractor or a periosteal elevator.^{15,17}

The period of follow-up was 6 months.^{8,13–16} Nguyen et al. followed the patients for a period of 12 months.¹⁷

Clinical outcomes

Costantinides et al. did not observe any cases of LN injury (temporary or permanent) after LA.⁸ Only 1 case (0.29%) of temporary IAN injury was observed after a week, which persisted after the period of follow-up and developed into permanent injury. In this single case, the extracted tooth showed a canal between the roots, in which IAN was entrapped. Therefore, the nerve lesion could be ascribed to the complications related to the anatomical conformation of the extracted tooth. Nine cases (4.64%) of temporary IAN injury and 4 cases (2.06%) of temporary LN injury were observed after GA. One case (0.52%) of permanent LN injury was noticed following GA.⁸

Brann et al. found 5 cases (3.52%) of temporary nerve injury after LA, 90 cases (16.82%) after GA and 1 case (2.44%) for LA plus sedation, without distinguishing IAN and LN injury.¹³ Five cases (0.70%) of permanent nerve injury were observed without specifying the anesthetic modality and the nerve involved.¹³

In the study by Hill et al., 8 cases (3.98%) of temporary nerve injury to IAN and LN related to LA, and 16 cases (3.72%) of temporary nerve injury to IAN and LN related to GA were detected.¹⁴ No cases of permanent nerve injury were found either for LA or for GA after the follow-up period.¹⁴

Glicher and Gerlach found 8 cases of temporary injury to LN under LA, 1 case for LA plus sedation and 14 cases under GA.¹⁵ Four cases (0.36%) of permanent LN injury and 10 cases (0.90%) of permanent IAN injury were observed, without specifying the anesthetic modality.¹⁵

Rehman et al. found 9 cases (8.57%) of postoperative temporary nerve injury – 5 (4.76%) to IAN and 4 (3.81%) to LN – following LA, while 37 cases (7.81%) of temporary nerve injury were observed in the GA group (15 (3.16%) to IAN and 22 (4.64%) to LN).¹³ No cases of nerve injury were observed in the group of LA plus sedation. After the follow-up period, no cases of permanent injury to LN were noticed for any anesthetic modality; conversely, a total of 3 cases (0.49%) of nerve injury to IAN were observed, not specifying the anesthetic choice.¹³

In their study, performed on 11,599 cases of mandibular third molar removal (6,803 patients), Nguyen et al. found 1 case of temporary LN injury and no cases of permanent LN injury following LA; 4 cases of temporary IAN injury and 8 cases of permanent IAN injury were found for LA.¹⁷ Fifty cases of temporary nerve injury were observed – 8 to LN and 42 to IAN – after GA. Six cases of permanent LN injury and 15 cases of permanent IAN injury were detected after GA.¹⁷

Main reported results and clinical implications

In their conclusions, 3 studies suggested that mandibular third molar surgery under GA seemed to increase the risk of nerve injury as compared to surgery under LA.^{8,13,15}

Nguyen et al. in their conclusions observed an increased risk of permanent IAN injury under GA and concluded that no factor increased the risk of LN injury.¹⁷

In 2 studies, no significant relationships were found between procedures under LA and GA and nerve injury.^{14,16}

Risk of bias in individual studies

According to the risk of bias analysis, only 2 studies were judged to have a medium risk of bias, with an overall score between 16 and 22,^{8,13} and a higher score of 19.⁸

The remaining 4 studies were judged to have a high risk of bias,^{14–17} with a lower score of 12.¹⁷ The internal validity – bias items were related to low scores, with the exception of 2 studies.^{8,14} Full details are summarized in Table 4.

Table 4. Risk of bias in the included studies according to the modified Down and Black tool

Item	Costantinides et al. ⁸	Brann et al. ¹³	Hill et al. ¹⁴	Gülicher and Gerlach ¹⁵	Rehman et al. ¹⁶	Nguyen et al. ¹⁷
1	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)
2	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)
3	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	no
4	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)
5	yes (2)	yes (2)	partial (1)	yes (2)	yes (2)	yes (2)
6	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)
7	no	no	no	no	no	no
8	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)
9	no	no	no	no	no	no
10	yes (1)	yes (1)	no	yes (1)	yes (1)	yes (1)
11	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	unclear
12	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	unclear
13	yes (1)	yes (1)	unclear	unclear	yes (1)	unclear
14	no	no	no	no	no	no
15	yes (1)	unclear	yes (1)	unclear	unclear	unclear
16	no	no	no	no	no	no
17	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)
18	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)
19	yes (1)	unclear	unclear	unclear	unclear	unclear
20	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)
21	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)	yes (1)
22	unclear	unclear	no	unclear	no	no
23	yes (1)	yes (1)	unclear	unclear	unclear	no
24	no	no	no	no	no	no
Total	19	17	14	15	16	12
Overall risk of bias	medium	medium	high	high	high	high

Discussion

The present review examined the potential development of nerve injury after lower third molar extraction performed under LA and the same intervention performed under GA. The number of retrieved studies (6 studies) is still limited, since this aspect has been poorly investigated. Moreover, the heterogeneous designs and recordings of the included studies did not allow any meta-analysis, while the direct comparisons of the obtained results are not fully applicable.

Four of the 6 studies showed an association between GA and nerve injury.^{8,13,15,17} Conversely, 2 of the included studies did not show a significant relationship between nerve damage and the anesthetic modality.^{14,16} Furthermore, the selected studies showed generally a high risk of bias (except 2 studies,^{8,13} which showed a medium risk of bias), limiting the strength of evidence.

An important variable that can constitute a bias is the operator's experience; only in 1 study, the extractions were performed by the same surgeon,⁸ while in most of the remaining ones, the extractions were performed

by different surgeons with different levels of experience; these studies did not specify if the interventions were assigned to the surgeon randomly or if there was a correlation between the surgeon's experience and surgical difficulty.^{14–17} Brann et al. did not give information about the operator's experience.¹³

In 2 studies, the operator's experience was the major factor influencing the frequency of IAN and LN injury during lower third molar extraction.^{13,15} The uncontrolled application of force, low ability in the management of surgical instruments and the lack of experience could cause nerve injury.¹⁸

In 5 of the 6 studies, surgical difficulty was also analyzed with different classifications (Winter's classification, Wharfe's score, and Pell and Gregory's classification).^{8,13–16} Only 3 studies comparing procedures under LA and GA in terms of surgical difficulty showed no substantial differences between the study groups.^{8,13,16} One of these studies did not show a relationship between nerve damage and the anesthetic modality¹⁶; the other 2 studies showed that GA seemed to increase the risk of developing IAN and LN lesions.^{8,13}

In the studies by Glicher and Gerlach¹⁵ and by Nguyen et al.,¹⁷ patients were assigned to surgery under GA based on many factors, including the expected high level of surgical difficulty. In 2 studies, there could be observed a trend to direct patients to surgery under GA rather than LA.^{13,16} In fact, in the UK, dental procedures are frequently performed under GA because of the preference of both surgeons and patients.⁵

A non-homogeneous distribution of surgical difficulty inside experimental groups could be the reason of bias in the evaluation of the influence of LA and GA on the development of nerve injury.⁸ Costantinides et al. supposed that the anesthetic regimen should not be chosen according to the surgeon's preference, but to the patient's choice or clinical characteristics (e.g., dental phobia).⁸ Such an attitude results in a better distribution of surgical variables, and consequently enables a more reliable comparison between groups, with a lower risk of bias.

The use of a lingual retractor is another parameter that can produce a bias. In particular, it regards the Howarth retractor, which is a narrow instrument used for lifting and retracting the surgical flap; it offers poor flap protection and is capable of exerting considerable force on LN, inducing injury, and the alteration or blockage of nerve conduction.^{16,17} The Howarth retractor was used in 3 studies.^{13,14,16}

Retraction has been shown to increase the number of temporary sensory LN injury cases due to neuropraxia.^{18–20} For this reason, many authors suggest avoiding the preparation and retraction of the lingual flap. No cases of permanent LN injury was found when the Howarth retractor was used.^{14,16,18,21}

Rehman et al. observed a total of 3 cases of permanent IAN injury, without distinguishing the anesthetic modality, while no permanent LN injury was observed.¹³ Hill et al. did not observe any permanent nerve injury in their study.¹⁴ Both authors concluded that there was no significant difference between lower third molar surgery performed under LA or GA.^{13,14}

The number of cases of permanent injury after GA is greater in the studies by Glicher and Gerlach¹⁵ and by Nguyen et al.¹⁷ Such data could be a consequence of the high number of extractions performed (1,106 and 11,599 teeth removed, respectively), which could increase the probability of adverse events.^{15,17}

Brann et al. elaborated some theories on a high risk of developing nerve injury after GA and hypothesized that procedures under GA could be complicated by the supine position or by the extent of mucoperiosteal stripping and bone removal.¹³ The same author suggests that the degree of surgical force may be greater under GA and that a conscious patient provides a series of signals to the surgeon, who tends to limit tissue retraction and surgical force, which decreases the risk of nerve injury.¹³

Based on the retrieved data, it is not possible to determine a correlation between the anesthetic modality and

the nerve injury because of different variables that are related to each procedure of extraction and a high risk of bias across the studies.

The only certain indication described in the literature is that the prevalence of complications after dental procedures under GA have induced a reduction in the number of procedures performed with this anesthetic modality.^{13,22}

D'Eramo reported a mortality rate of 1:1,733,055 and a frequency of adverse events of 1:26,698 in patients undergoing GA for oral-maxillofacial surgery.²³ The most commonly observed adverse event is laryngospasm, present in 1 out of 833 patients (0.12%) treated under GA. The same author reported with a lower frequency the following: cardiac arrhythmias; bronchospasm; hypertension; hypotension; congestive heart failure; angina pectoris; myocardial infarction; the nerve and/or cervical lesions associated with changes in the patient's position during anesthesia; phlebitis; insulin shock; and diabetic ketoacidosis.²³

Four of the 6 analyzed studies showed a greater incidence of neurological damage following the extractions performed under GA.

The quality and the number of studies on the topic discussed in the present review is low, and more investigations are necessary with better-quality studies.

Conclusions

In third molar surgery, LA should be preferred when possible because of the increased rate of complications under GA. However, GA remains an appropriate anesthetic modality in case of complex and long procedures, uncooperative patients, dental phobic patients, and patients with allergy to a local anesthetic.

Registration

The present systematic review was registered in the International Prospective Register of Systematic Reviews under No. PROSPERO CRD42021231823.

Ethics approval and consent to participate

Not applicable.

Data availability

All data analyzed during this study is included in this published article.

Consent for publication

Not applicable.

ORCID iDs

Fulvia Costantinides  <https://orcid.org/0000-0001-6044-7531>
 Matteo De Nardi  <https://orcid.org/0000-0002-5168-1534>
 Massimiliano Lenhardt  <https://orcid.org/0000-0003-1765-6199>
 Giuseppe Perinetti  <https://orcid.org/0000-0002-7226-5134>
 Lorenzo Bevilacqua  <https://orcid.org/0000-0002-7245-8358>
 Michele Maglione  <https://orcid.org/0000-0003-0410-1784>

References

- Juodzbalsys G, Daugela P. Mandibular third molar impaction: Review of literature and a proposal of a classification. *J Oral Maxillofac Res.* 2013;4(2):e1. doi:10.5037/jomr.2013.4201
- Trybek G, Jaroń A, Grzywacz A. Association of polymorphic and haplotype variants of the *MSX1* gene and the impacted teeth phenomenon. *Genes.* 2021;12(4):577. doi:10.3390/genes12040577
- Jaroń A, Trybek G. The pattern of mandibular third molar impaction and assessment of surgery difficulty: A retrospective study of radiographs in East Baltic population. *Int J Environ Res Public Health.* 2021;18(11):6016. doi:10.3390/ijerph18116016
- Trybek G, Chruściel-Nogalska M, Machnio M, et al. Surgical extraction of impacted teeth in elderly patients. A retrospective analysis of perioperative complications – the experience of a single institution. *Gerodontology.* 2016;33(3):410–415. doi:10.1111/ger.12182
- Susarla SM, Blaeser BF, Magalnick D. Third molar surgery and associated complications. *Oral Maxillofac Surg Clin North Am.* 2003;15(2):177–186. doi:10.1016/S1042-3699(02)00102-4
- Ashfaq MA, Thenmozhi MS. Third molar impaction and its clinical correlation – a systematic review. *Int J Sci Res.* 2016;5(7):80–83. doi:10.21275/v5i6.6061605
- NIH consensus development conference for removal of third molars. *J Oral Surg.* 1980;38:235–236. PMID:6101618.
- Costantinides F, Biasotto M, Maglione M, Di Lenarda R. Local vs general anaesthesia in the development of neurosensory disturbances after mandibular third molars extraction: A retrospective study of 534 cases. *Med Oral Patol Oral Cir Bucal.* 2016;21(6):e724–e730. doi:10.4317/medoral.21238
- Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *J Clin Epidemiol.* 2009;62(10):e1–e34. doi:10.1016/j.jclinepi.2009.06.006
- Martin A, Perinetti G, Costantinides F, Maglione M. Coronectomy as a surgical approach to impacted mandibular third molars: A systematic review. *Head Face Med.* 2015;11:9. doi:10.1186/s13005-015-0068-7
- Centre for Reviews and Dissemination, University of York. Systematic reviews. CRD's guidance for undertaking reviews in health care. York, UK: York Publishing Services; 2009.
- Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health.* 1998;52(6):377–384. doi:10.1136/jech.52.6.377
- Brann CR, Brickley MR, Shepherd JP. Factors influencing nerve damage during lower third molar surgery. *Br Dent J.* 1999;186(10):514–516. doi:10.1038/sj.bdj.4800155
- Hill CM, Mostafa P, Thomas DW, Newcombe RG, Walker RV. Nerve morbidity following wisdom tooth removal under local and general anaesthesia. *Br J Oral Maxillofac Surg.* 2001;39(6):419–422. doi:10.1054/bjom.2001.0723
- Gülicher D, Gerlach KL. Sensory impairment of the lingual and inferior alveolar nerves following removal of impacted mandibular third molars. *Int J Oral Maxillofac Surg.* 2001;30(4):306–312. doi:10.1054/ijom.2001.0057
- Rehman K, Webster K, Dover MS. Links between anaesthetic modality and nerve damage during lower third molar surgery. *Br Dent J.* 2002;193(1):43–45. doi:10.1038/sj.bdj.4801479
- Nguyen E, Grubor D, Chandu A. Risk factors for permanent injury of inferior alveolar and lingual nerves during third molar surgery. *J Oral Maxillofac Surg.* 2014;72(12):2394–2401. doi:10.1016/j.joms.2014.06.451
- Jerjes W, Swinson B, Moles DR, et al. Permanent sensory nerve impairment following third molar surgery: A prospective study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2006;102(4):e1–e7. doi:10.1016/j.tripleo.2006.01.016
- Rood JP. Permanent damage to inferior alveolar and lingual nerves during the removal of impacted mandibular third molars. Comparison of two methods of bone removal. *Br Dent J.* 1992;172(3):108–110. doi:10.1038/sj.bdj.4807777
- Blackburn CW, Bramley PA. Lingual nerve damage associated with the removal of lower third molars. *Br Dent J.* 1989;167(3):103–107. doi:10.1038/sj.bdj.4806922
- Pichler JW, Beirne OR. Lingual flap retraction and prevention of lingual nerve damage associated with third molar surgery: A systematic review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2001;91(4):395–401. doi:10.1067/moe.2001.114154
- Renton T, McGurk M. Evaluation of factors predictive of lingual nerve injury in third molar surgery. *Br J Oral Maxillofac Surg.* 2001;39(6):423–428. doi:10.1054/bjom.2001.0682
- D'Eramo EM. Morbidity and mortality with outpatient anesthesia: The Massachusetts experience. *J Oral Maxillofac Surg.* 1992;50(7):700–704. doi:10.1016/0278-2391(92)90101-5