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LITERATURE REVIEW

Intraoperative neuromonitoring in thyroidectomy: a systematic review and meta-analysis of 10,260 patients

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Abstract

The recurrent laryngeal nerve (RLN) is responsible for vocal cord (VC) movements. Injury of the RLN can be a severe complication of thyroidectomy. Intraoperative neuromonitoring (IONM) has been used to confirm RLN function integrity and facilitate nerve dissection. This study aims to compare the outcomes of visual identification of the RLN *vs*. IONM of the RLN in patients undergoing thyroid surgery. PubMed-MEDLINE and EMBASE were searched until 27 April 2021 to include non-randomized controlled studies that compared both surgical techniques for RLN identification in patients undergoing thyroidectomy, using either IONM or visual identification alone. Permanent and transient VC paralysis rates by group were extracted from each article. The odds ratio (OR) of IONM *vs*. visual identification was obtained from each study to calculate the measurements for transient and permanent VC paralysis by group. Out of 1484 literature studies identified, only seven met our criteria and were included, comprising a total of 10,260 patients. IONM may reduce the incidence of transient and permanent VC paralysis in thyroidectomy.

Keywords: thyroidectomy; intraoperative neuromonitoring; recurrent laryngeal nerve; vocal cord paralysis.

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Introduction

Thyroid surgery is associated with risk of recurrent laryngeal nerve (RLN) injury, which can lead to transient or permanent dysphonia and vocal cord (VC) paralysis – stemming from trauma and thermal injuries[1]. Literature data indicate that the global rate of VC paralysis following total thyroidectomy varies, with estimates ranging from 0 to 4.8%[2]. However, these rates may vary according to the patient's clinical context[3,4]. Notably, VC paralysis post-surgery is a frequent cause of medical lawsuits[5].

Historically, visual identification has been the main technique for RLN identification to prevent nerve injury during thyroidectomy. However, with advancements in medical technology, intraoperative nerve monitoring (IONM) systems) have gained traction. Researchers have increasingly explored their potential to enhance identification accuracy the RLN and reduce the incidence of nerve injury during thyroid surgeries. Additionally, IONM may reduce surgery time (fast RLN identification) and help predict the postoperative function of the VC[6,7].

While IONM has been proposed as an alternative to reduce RLN paralysis, the existing literature on its impact in thyroid surgery presents mixed findings. Some studies have found no difference between the IONM and visual identification methods, whereas others suggest IONM may reduce the incidence of RLN injury[8-10]. Given this conflicting scenario, we conducted a systematic review and meta-analysis to contrast the efficacy of IONM against traditional visual identification of the RLN in patients undergoing thyroidectomy.

Methods

Registration

The study was registered on the PROSPERO platform (ID: CRD42022331546).

Search strategy

We reviewed the literature available on the PubMed-MEDLINE and EMBASE databases until 27 August 2021. The review strategy comprised inclusion and exclusion criteria, study quality assessment, data extraction, and statistical analysis. The search was conducted using the following keywords: thyroidectomy, intraoperative neuromonitoring, recurrent laryngeal nerve, and vocal cord paralysis.

Inclusion and exclusion criteria

Inclusion criteria: (1) evaluated adult participants only (aged ≥18 years); (2) included partial or total thyroidectomy with or without concurrent neck dissection; (3) compared surgical outcomes of thyroidectomy both with and without IONM; (4) were designed as non-randomized controlled trials.

Exclusion criteria: (1) studies that included animals subjects; (2) designed as case reports, letters to editors, or reviews; (3) with participants who had undergone previous neck surgery; (4) evaluating patients with preoperative vocal cord dysfunction; (5) featuring endoscopic or robotic thyroidectomy procedures; (6) included patients with a history of radiotherapy; (7) were not published in English.

Study quality assessment

The quality of all included studies was rigorously assessed by two independent reviewers[11].

Data extraction

Primary data from all included articles, such as study design, study period, country of recruitment, type of surgery, number of nerves at risk, and incidence of transient or permanent VC paralysis by group, were extracted independently by three reviewers.

Statistical analysis

The standardized mean difference (SMD) between IONM and non-IONM (control group) was extracted from the selected studies. An SMD effect is considered "large" at 0.8, "medium" at 0.5, and "small" at 0.2[12,13]. Pooled results were determined using the odds ratio (OR) from each study.

If standard deviations were not reported in some studies, they were estimated based on median, interquartile range, and sample size[12]. The Q test was employed to assess the heterogeneity between studies[14], and the I^2 index was used to quantify the degree of heterogeneity. Both the funnel plot and the Egger's and Begg's tests were applied to estimate publication bias[15,16].

A *p*-value <0.05 was considered statistically significant. All statistical analyses were performed using the Stata 15.0 software (StataCorp LP, College Station, Texas, USA).

Review of literature and results

Study characteristics

The literature review identified 1484 studies, of which seven met the inclusion criteria[17-23] for this meta-analysis (Figure 1). The median MINORS score was 18 (interquartile range (IQR) 16.25–19.57). A total of 10,260 patients were included in the analysis (Table 1). The main outcomes evaluated by each study are detailed in Table 2.

Table 1. Main characteristic of included studies.

Author	Country, Year	Population	Malignant	HT	Goiter	TT	Less than TT
Barczyński et al.[17]	Poland, 2009	1000	162	78	800	794	261
Barczyński et al.[18]	Poland, 2011	302	302	0	0	302	0
Sarı et al.[19]	Turkey, 2010	237	41	36	160	49	188
Zhou et al.[20]	China, 2019	209	0	209	0	191	18
Frattini et al.[21]	Italy, 2010	152	152	0	0	76	76
Mizuno et al.[22]	Japan, 2018	5804	5804	0	0	2292	3512
Vasileiadis et al.[23]	Greece, 2016	2556	848	914	1139	2556	0

Caption: HT = Hyperthyroidism; TT = Total thyroidectomy.

Table 2. Main outcomes of included studies.

Author	IONM	VI	Transient paralysis		Permanent paralysis	
			IONM	VI	IONM	VI
Barczyński et al.[17]	500	500	8	12	19	38
Barczyński et al.[18]	151	151	1	2	2	5
Sarı et al.[19]	123	114	0	0	3	3
Zhou et al.[20]	154	55	0	1	12	6
Frattini et al.[21]	76	76	1	2	2	5
Mizuno et al.[22]	849	4955	21	106	NR	NR
Vasileiadis et al.[23]	1481	1075	4	15	20	51

Caption: IONM = Intraoperative neuromonitoring; VI = Visual identification; NR = Not reported.

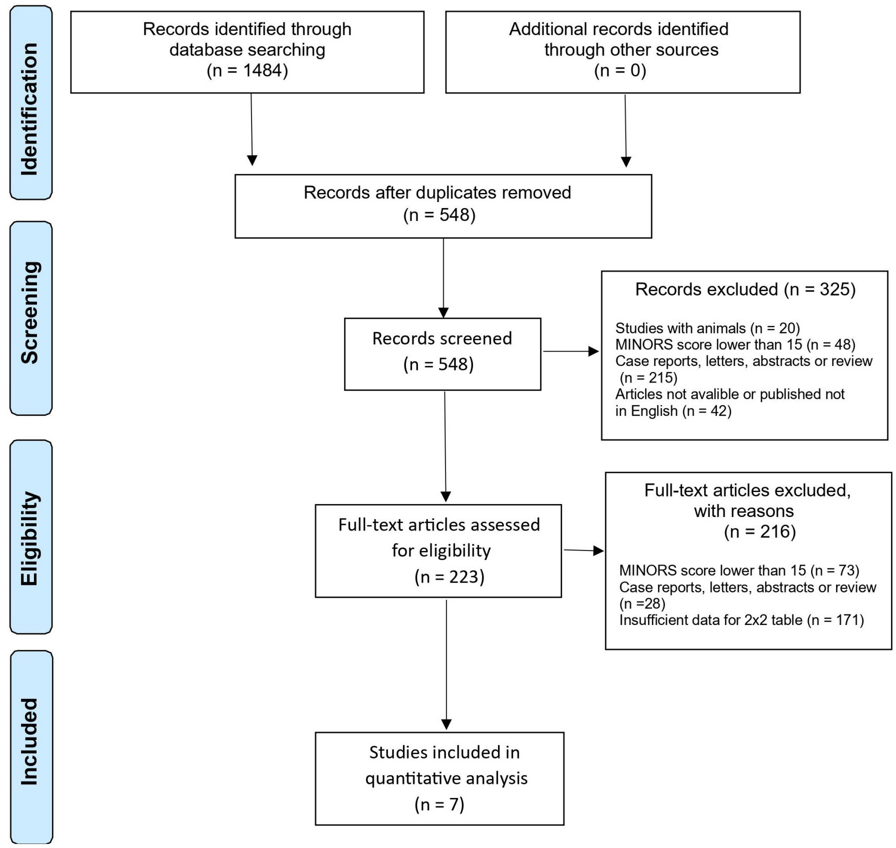

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Recurrent laryngeal nerve injury

The pooled analysis showed a significant difference in transientVC paralysis between the groups, favoring the IONM group (OR, 0.57; 95% CI: 0.40, 0.83; I^2=74.4%; *p*=0.002) (Figure 2A). The comparison of IONM *vs*. visual identification regarding permanent VC paralysis also showed a significant difference in favor of IONM (OR, 0.41; 95% CI: 0.29, 0.57; I^2=0.0%; *p*=0.488) (Figure 2B).

Discussion

Our meta-analysis revealed that IONM is associated with a reduced incidence of both transient and permanent RLN injury after thyroidectomy. Previous meta-analyses found a decrease in overall and transient RLN injury with the use of IONM but did not indicate a significant reduction in the permanent injury rate[24,25]. Lombardi et al.[26] suggested that there is a lack of standardization in defining permanent nerve injury and its measurement across studies, which may have led to these discrepant findings[26].

In our analysis, we standardized the definition of permanent injury (VC paralysis) and its measurement through laryngoscopy, ensuring that these factors did not bias the outcomes. Consequently, the data suggest that the routine use of IONM in thyroidectomy could be beneficial in surgical practice.

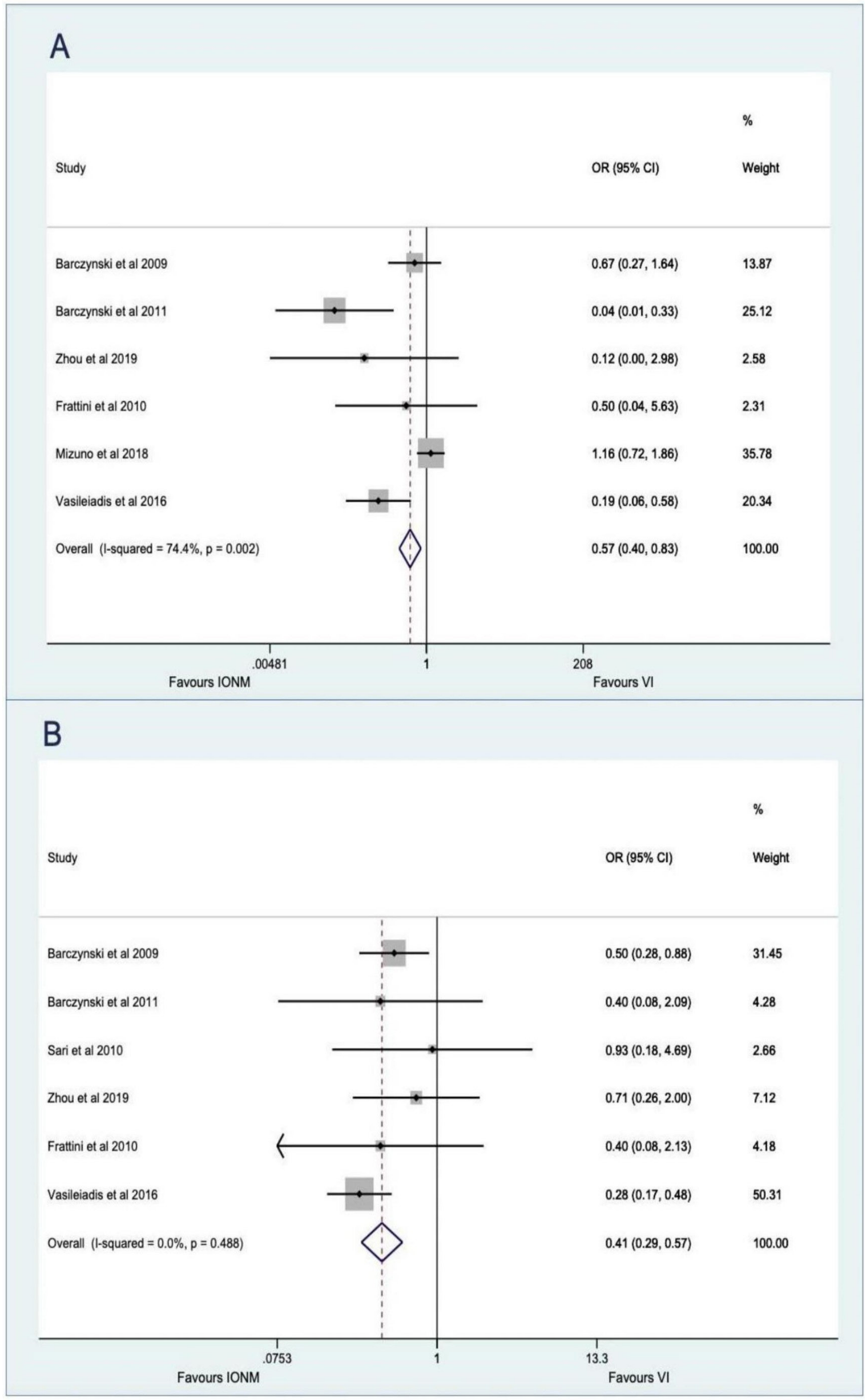

Figure 2A. Forest plot of odds ratio for temporary recurrent laryngeal nerve (RLN) paralysis.
Figure 2B. Forest plot of odds ratio for definitive laryngeal RLN paralysis.

Previous studies have reported an RLN injury rate of 1.2–2.3% in bilateral operations[27,28], which is associated with extensive surgical procedures and prolonged operation times. Our analysis included three newer studies[29-31], revealing a notable decrease in both transient and permanent injuries during malignant-related operations when IONM was utilized. Such surgeries might bear risks because of the potential malignant invasion of the RLN and necessary lymph node dissections. Real-time monitoring through IONM can mitigate these risks.

Reoperation of the thyroid poses higher risks than normal thyroidectomy because of anatomical changes that can result in RLN injury. Factors like Local adhesions can hinder RLN visualization and change its anatomical position. Duong et al. found that IONM reduced the overall injury in the reoperation group.

Operation volume's influence was also emphasized in several studies. A German retrospective multicenter trial indicated that high-volume surgical centers witnessed a lower permanent RLN injury rate and suggested that the use of IONM might be more important in low-volume centers, where less experienced surgeons could avoid hazardous surgical maneuvers around the RLN through real-time nerve identification[28,32].

Our findings associate IONM with a reduction in overall and transient RLN injuries in low-volume surgical centers and a decrease in overall and permanent RLN injury rates in high-volume centers. However, our review presents limitations. Several included studies either omitted outcome metrics or presented inadequately long follow-up data. Potential confounders and inherent heterogeneity could still affect our results. Several studies included cases involving intentional RLN transection, and the influence of concurrent lymph node dissection during the same surgery cannot be ignored. However, we employed sensitivity and subgroup analyses, along with a random-effects model, to address these issues. Additionally, recent studies corroborate the findings of our meta-analysis[33,34].

Nevertheless, another recent systematic review and meta-analysis found different results, identifying no significant differences between IONM and visualization-only methods[35]. These differences could be attributed to the divergence in our research methodologies. First, our study sample was four times larger, thus enhancing the power of analysis. Second, we excluded cases of prior neck surgeries and/or radiotherapy, which, as previously verified[7], could lead to outcome variances that might have biased their results.

Final comments

This meta-analysis indicates that, in thyroidectomies, IONM is associated with a reduced incidence of both transient and permanent RLN injuries compared to conventional visual identification. The specific benefits of IONM in reoperations should be further explored. We anticipate that future large-scale, prospective, randomized clinical trials will assess our findings, ideally applying standardized IONM protocols and outcome measurements.

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