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REVIEW ARTICLE

Neuromonitoring in endoscopic and robotic thyroidectomy

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Abstract Intraoperative neuromonitoring (IONM) has proven effective for intraoperative verification of RLN function in the conventional thyroid surgery. However, no studies have performed a systematic evidence-based assessment of this novel health technology in endoscopic and robotic thyroidectomy. Evidence-based criteria were used in a systematic review of relevant literature for years 2000–2015. Four electronic databases (CENTRAL, MEDLINE, Cochrane and EMBASE) were used to retrieve relevant reports published from January 1, 2000 to September 1, 2016. The search terms included "endoscopic thyroidectomy", "robotic thyroidectomy", "IONM", "continuous IONM (CIONM)", "neural monitoring", "recurrent laryngeal nerve monitoring", and "superior laryngeal monitoring". The following data were retrieved from eligible studies of patients undergoing endoscopic or robotic thyroidectomy: objective of study, design and setting of study, population, intervention examined, quality of data, follow-up and dropout rate, risk of bias, and outcomes assessed. Of 160 studies retrieved, only 9 (5%) studies used IONM. Eight studies reported 522 nerve at risk (NAR) with IONM. Only three were prospective randomized studies. Reports of IONM endoscopic and robotic procedures included their use for re-surgery and use in both benign and malignant cases. None of the IONM endoscopic procedures involved bilateral palsy. Two studies reported the use of a staged strategy. The rates of recurrent laryngeal palsy were 0–3.6% for transient and 0–0.4% for permanent. Only 30% of the studies performed vagus nerve stimulation, and only 25% performed superior laryngeal nerve monitoring. In addition to the use of IONM as an assistive technology for navigating the anatomy in challenging procedures such as endoscopic and robotic thyroidectomy, IONM has potential use as a routine adjunct to the conventional video-assisted nerve identification in thyroidectomy.

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Introduction

Rapidly, growing volumes of endocrine surgeries have raised concerns about the effectiveness and outcomes of endoscopic thyroid surgery [1–16].

In some centers, endoscopic procedures comprise as many as 70% of all thyroidectomies [2–23].

A direct and logical benefit of technical advances such as minimally invasive and endoscopic approaches is improved cosmetic outcome [3, 7, 9, 24–33]. Cosmetic outcome also improves as surgeons gain experience through routine use of endoscopic procedures [16, 24, 34–40].

In young age groups, the prevalence of thyroid disease is significantly higher in women than in men [1–3]. Because of the emphasis on physical attractiveness in the media and modern society, cosmetic outcomes of thyroid surgery are a particularly important to women [17, 19]. The growing presence of women in the work force is another contributing factor in the demand for improved cosmetic outcomes [2, 5, 8, 9, 41–59].

Therefore, as long as the surgical objectives and patient safety are not compromised, achieving an aesthetically pleasing surgical outcome should always be a primary consideration in pre-surgical planning and discussion with patients [35].

Since intraoperative neural monitoring (IONM) was developed to increase the safety of endoscopic procedures [34, 42, 59], this study performed a systematic literature review to explore and assess the use of IONM in endoscopic thyroidectomy.

Methods

Four electronic databases (CENTRAL, MEDLINE, Cochrane, and EMBASE) were used to retrieve relevant reports published from January 1, 2000 to September 1, 2016. The search terms included “endoscopic thyroidectomy”, “robotic thyroidectomy”, “IONM”, “continuous IONM (CIONM)”, “neural monitoring”, “recurrent laryngeal nerve monitoring”, and “superior laryngeal monitoring”. To identify relevant articles that were not found in the initial search, the researchers manually retrieved additional studies cited in the retrieved articles and meta-analyses. Unpublished studies were also identified by reviewing the proceedings of relevant conferences.

If data published in the article were not sufficiently precise for data extraction, the authors of the article were contacted as needed to obtain additional data. The researchers continued to contact authors of relevant articles and other researchers with experience in endoscopic or robotic procedures until 1 May 2016.

This meta-analysis was only included studies that used a control or comparison population. Retrospective or contemporaneous comparisons from the same region were accepted if the between-population similarities and differences were clearly stated. No restrictions on language, follow-up, or study quality were imposed. The investigators used standardized forms for independent screening of abstracts and extracted data.

Outcome measures

The following data were retrieved from eligible studies of patients undergoing endoscopic or robotic thyroidectomy: objective of study, design and setting of study, population, intervention examined, quality of data, follow-up and dropout rate, risk of bias, and outcomes assessed.

Collection of data specifically related to thyroidectomy included (a) design of study; (b) use of IONM; (c) indications for surgery; (d) details of recurrent laryngeal nerve (RLN) palsy (rate, transient vs. permanent, and unilateral vs. bilateral); (e) use of staged procedure strategy in cases with loss of signal; (f) type of approach; (g) mode of IONM (routine use vs. selective; IONM vs CIONM); (h) manufacturer of monitoring equipment; (i) standardized procedure (V1, R1, R2, and V2); (j) superior laryngeal nerve monitoring; and (k) country of authorship.

Results

The literature review obtained 160 studies published during 2000–2015 that met all eligibility criteria, including the required details of endoscopic thyroidectomy outcome (Fig. 1).

Only nine (5%) studies used monitoring. Table 1 summarizes the nine studies. Figures 2, 3, 4 summarize the results of the literature review. Overall, eight studies used IONM and comprehended 522 NAR. Only three studies were prospective randomized studies. The IONM-assisted endoscopic and robotic procedures included both benign and malignant cases as well as re-surgeries [1–59]. The IONM endoscopic procedures revealed no bilateral palsies [1–59]. Two studies reported a staged strategy [2, 12, 45]. Reported rates of RLN palsy were 0–3.6% for transient and 0–0.4% for permanent [1–59]. In general, adherence to International Neural Monitoring Study Group (INMSG) guidelines was low [48]. In fact, vagus nerve stimulation was performed in only 30% of the studies (Figs. 2, 3, 4). In 75% of the studies, IONM was routinely used in all

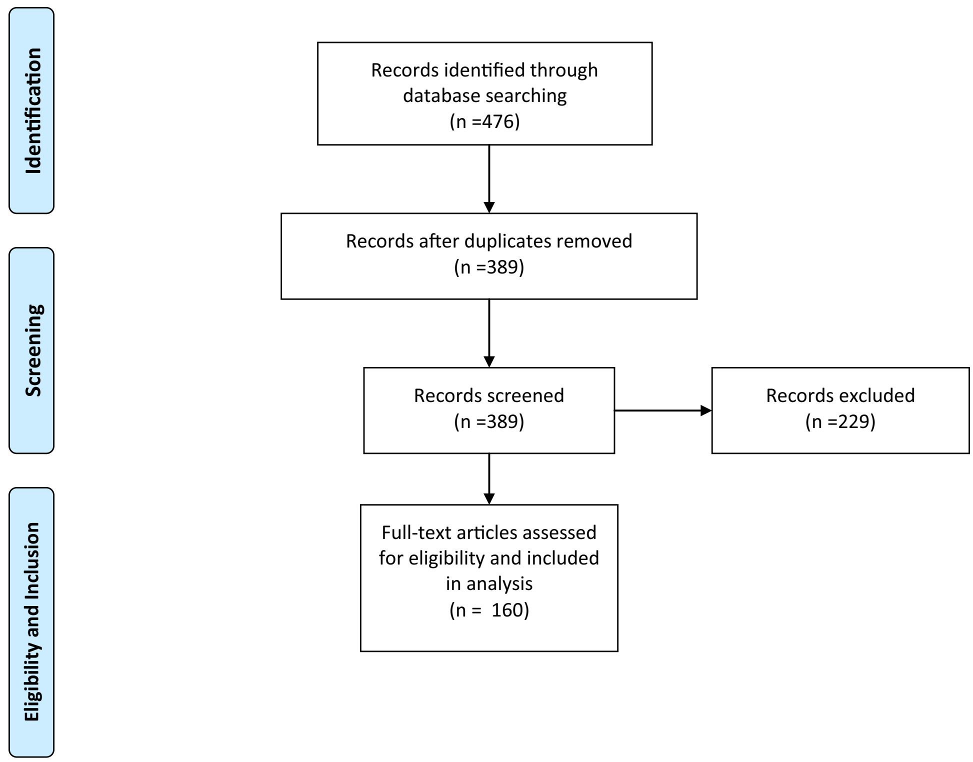


Fig. 1 Flow diagram of the literature search

Table 1 IONM in endoscopic and robotic thyroidectomy

Author	Journal	Year	Procedure	IONM	CIONM	Standardized	Nerves	Total palsy	Partial palsy	Stage thyr	Bilateral Palsy
IONM in endoscopic thyroidectomy											
Wang	J Laparoendosc Adv Surg Tech	2016	TOETVA	Yes	–	Yes	16	–	–	–	–
Xie	J Laparoendosc Adv Surg Tech	2016	TOETVA	Yes	–	Yes	98	1/98	5/98	–	–
Dionigi	Int J Surg	2008	MIVAT	Yes	–	Yes	86	0	1	0	0
Dionigi	Surg Endosc	2009	MIVAT	Yes	–	Yes	72	0	3	0	0
Kandil	Int J otalaryngol	2009	MIVAT	Yes	–	Yes	47	1/47	1/47	–	–
IONM in robotic thyroidectomy											
Lee	J Laparoendosc Adv Surg	2015	RoT	Yes	–	Yes	100	–	–	–	–
Bea	Surg Laparosc Endosc Percut Tech	2015	RoT	Yes	–	Yes	56	–	–	–	–
CIONM in endoscopic thyroidectomy											
Dionigi	Surg Technol Int	2015	MIVAT	Yes	Yes	–	–	–	–	–	–
CIONM in robotic thyroidectomy											
Luginbuhl	Laryngoscope	2012	Robotic Transax	–	Yes	–	–	–	–	–	–

endoscopic or robotic procedures. Superior laryngeal nerve (SLN) monitoring was reported in 25% of the studies.

Several studies should be mentioned in detail. The first report on IONM in minimally invasive surgery, which was published in 2007, evaluated 139 patients [60]. Minimally invasive surgery was defined as endoscopic/non-endoscopic surgery/re-surgery requiring an incision <6 cm. Stimulation of the vagus nerve (VN) at V1 and V2 was not a standard procedure [60]. The study showed that IONM use had a significant reverse correlation with incision

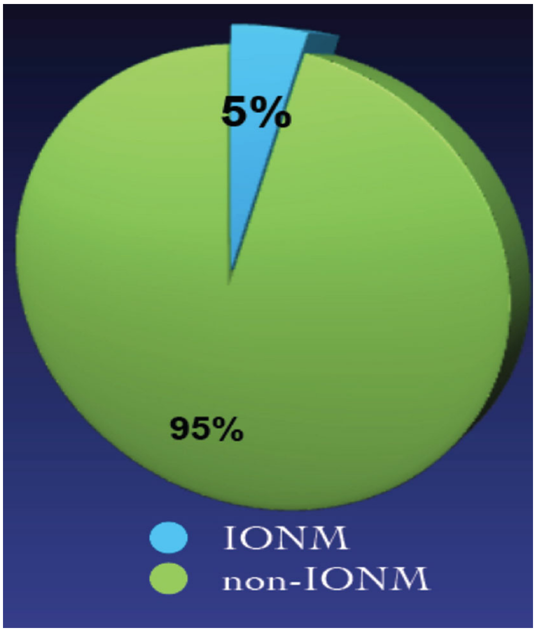


Fig. 2 Use of monitoring in endoscopic and robotic procedures

length (3.7 vs. 3.0 cm) and that the use of IONM increased during the study period (9% in 2004, 23% in 2005, and 90% in 2006) [60].

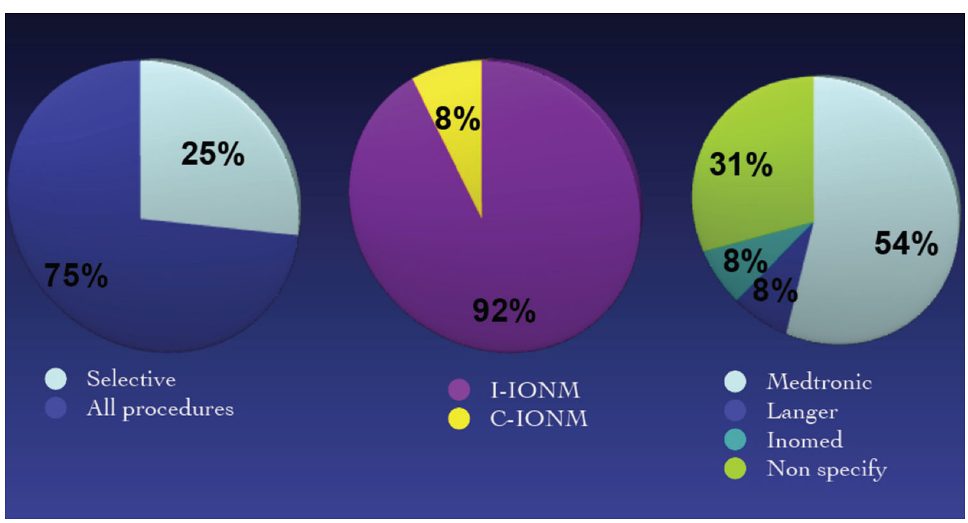
Two studies evaluated the use of IONM in video-assisted thyroidectomy (VAT), particularly its use in identifying the RLN and the external branch of the superior laryngeal nerve (EBSLN) [2, 12]. This prospective randomized series study included 72 standard VAT gasless approaches. In the control group ($N = 36$), the laryngeal nerves were identified with only a 5-mm endoscope (30× magnification). The standard procedure in the IONM group ($N = 36$) was to confirm nerve integrity by localizing the EBSLN, including both the vagus nerve and the RLN, before and after thyroid resection. This study is the first to review the literature on standardized use of IONM in endoscopic thyroid surgery with V1, R1, R2, and V2 stimulation according to INMSG guidelines [48].

All procedures were successful. No instances of equipment malfunction or interference occurred. No permanent complications occurred in either group. The incidences of temporary RLN injury were 2.7% (1 patient) and 8.3% (3 patients) in the IONM and control group, respectively. Identification of the EBSLN was significantly higher in the IONM group compared to the CIONM group (83.6 and 42%, respectively; $P < 0.05$) [2, 12].

A previous study demonstrated that using IONM for total endoscopic thyroidectomy in high-risk thyroid cancer reduces the possibility of RLN injury [44]. The authors also noted that IONM reduces surgery time by significantly decreasing the time spent locating the RLN (9.91 ± 1.68 versus 12.49 ± 1.63 min without IONM; $P < 0.01$) and the duration of thyroid lobectomy (21.10 ± 4.53 versus 27.35 ± 5.38 min without IONM; $P < 0.01$). Notably, the IONM group had a lower prevalence of RLN paresis, but the difference did not reach statistical significance [44].

In another prospective randomized series study of robotic thyroid surgery, the efficacy of IONM was evaluated in terms of voice function recovery after bilateral axillo-breast approach [5]. The authors found that IONM reduced the time needed for recovery of voice function [5]. The IONM and non-IONM groups each included 25 patients. Voice Handicap Index (VHI), voice range profile (VRP), and laryngoscopy were used to assess voice function before surgery and at 2 weeks, 3 months, and 6 months after surgery. Monitoring was performed according to the standard procedure recommended by INMSG (i.e., L1, V1, R1, R2, V2, and L2). The SLN was also monitored. No palsy was diagnosed by laryngoscopy in either group. The two groups did not significantly differ in VHI values or in mean change in VRP maximum

Fig. 3 Mode of IONM application (1)



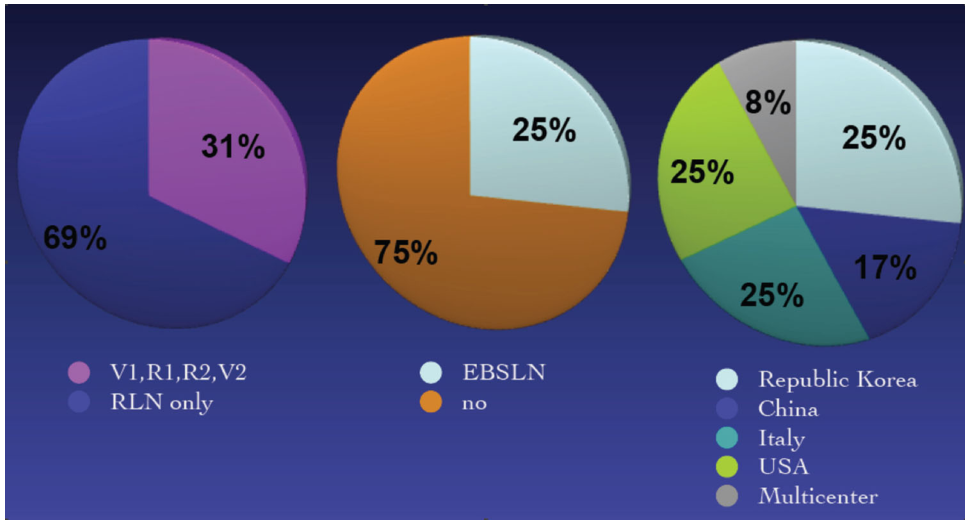


Fig. 4 Mode of IONM application (2)

frequency, maximum intensity, or minimum frequency. However, recovery of VRP minimum intensity was significantly earlier in the IONM group. Notably, [5] is the first technical report to describe a device that integrates dissection, haemostasis, and nerve monitoring in a single device, i.e., the cautery hook used as a stimulator probe in the daVinci Surgical System.

A 2009 study by Inabnet et al. was the first to evaluate the use of neuromonitoring of the external branch of the superior laryngeal nerve during minimally invasive thyroid surgery under local anesthesia. Ten patients were evaluated in this prospective study [60, 61]. After inserting needle electrodes into the cervical tracheal muscle, stimulation was set to 0.5 mA. In 70% of cases, the IONM helped the surgeon to identify the EBSLN. Neuromonitoring showed EBSLN preservation in all cases. A VHI-10 questionnaire survey administered before and 3 weeks after surgery revealed no significant change in self-perceived voice severity [60, 61].

Automatic periodic stimulation (APS) of the vagus nerve is feasible during thyroid robotic surgery. In [62], for example, the authors performed transaxillary robotic thyroidectomy by placing the vagus electrode onto the ipsilateral vagus trunk through a single-incision transaxillary access before docking the da Vinci robot. The APS of the ipsilateral vagus nerve was performed without complications and apparently helped to prevent impending thermal injury to the RLN [62].

Lang et al. [63] described the feasibility of intraoperative vagus nerve stimulation in gasless, transaxillary endoscopic, and robot-assisted thyroidectomy. The use of IONM for predicting postoperative RLN function was also evaluated by comparing direct RLN stimulation (RLN group) versus indirect stimulation via VN (VN group). Vocal cord palsies occurred in 7.3 and 5.7% of the RLN and VN groups, respectively. The RLN group had a significantly lower percentage of true negatives (78.0 vs. 94.3% in VN group, $P = 0.045$) and a significantly higher percentage of false positives (14.6 vs. 0.0% in VN group, $P = 0.018$). Overall, the group comparisons revealed that indirect stimulation via the VN obtains more reliable and accurate IONM test results compared to direct RLN stimulation [63].

Sublingual transoral access for thyroid resection assisted by RLN monitoring has been successfully performed in porcine models and in humans [64, 65]. In ten endoscopic transoral thyroidectomies performed in ten pigs using a neuromonitoring system, the RLN was first identified visually and then bilaterally confirmed with the neuromonitoring system. A complete transoral thyroid resection was successfully achieved in all ten pigs. The neuromonitoring system was used to confirm RLN function on both sides after thyroid gland removal [64, 65]. A subsequent case report and video by Inabnet et al. further demonstrated the feasibility of IONM in transoral thyroidectomy [65].

Discussion

Advantages of IONM in endoscopic thyroidectomy

Both intermittent IONM and CIONM are used in endoscopic and robotic thyroid procedures [1–63].

This review outlines the delayed acceptance of IONM in comparison with conventional open thyroidectomy [2, 15, 19, 20, 24–33]. The first report of IONM in endoscopic and robotic surgery was published in 2007 [60]. Possible explanations for the delayed acceptance of IONM since then include technological limitations and interference of monitoring device with endoscope during both endoscopic and robotic thyroidectomy [4, 7, 9, 13, 14, 17, 25, 50]. Both IONM and CIONM clearly need further refinement before they are widely used to facilitate thyroidectomy [46].

Whether neuromonitoring reduces the RLN paralysis rate during endoscopic procedures remains unclear because of the low numbers of endoscopic and robotic procedures performed with IONM and because the number of NAR and complications is too small to draw firm conclusions.

Our review confirms the technical feasibility of endoscopic and robotic thyroidectomy. No IONM malfunctions were reported. The standard IONM technique with V1 and V2 and CIONM with vagus nerve probe is feasible in endoscopic thyroidectomy. In general, however, adherence to INMSG guidelines is generally low [48]. In practice, vagus nerve stimulation is performed in only 30% of endoscopic and robotic procedures (Figs. 2, 3, 4).

In 75% of the studies, IONM was routinely used in all endoscopic and robotic procedures (Figs. 2, 3, 4).

In 25% of the studies, SLN monitoring was performed (Figs. 2, 3, 4).

Established endoscopic and robotic operative technique should not be modified unless they improve patient outcomes and decrease complication rates. The literature agrees that IONM performed complementary to endoscopic thyroidectomy enhances the quality and safety of the procedure [19]. In at least two prospective studies, the efficacy of IONM in endoscopic procedures was demonstrated by more rapid recovery of voice function [44]. That is, the precision that can be achieved by endoscopic procedures is further improved by complementary use of IONM [13].

Larger, prospective randomized studies are clearly warranted for further evaluation of the potential use of IONM and CIONM in endoscopic thyroidectomy. In both conventional and assisted endoscopic thyroidectomy, RLN palsy still occurs when an endoscope is used for RLN identification, with or without the assistance of IONM. Fortunately, the palsy is usually temporary [33, 34]. Further multi-center trials in larger populations are needed to compare the standard endoscopic procedures and IONM-assisted endoscopic procedures [47]. The benefit of IONM is difficult to demonstrate through statistical analysis. Further studies of CIONM of the RLN by vagus nerve stimulation are needed to investigate whether any modifications of CIONM procedures can obtain even better EMG signals for the RLN in endoscopic procedures and further improve safety and optimize the surgical procedure.

This literature review revealed five major advantages of using IONM in endoscopic thyroidectomy. The first advantage is that IONM facilitates RLN and SLN identification (i.e., navigation). Second, it enables testing of RLN and SLN function (i.e., monitoring). Third, it enables corrective action at three stages of surgery: (1) during blunt dissection; (2) during use of energy-based devices; and (3) during thyroid gland retraction. Notably, retraction of thyroid gland by grasp forceps or by forceps without haptic feedback can cause excessive traction and subsequent functional damage of the RLN. Fourth, it enables evaluation of RLN function by vagus nerve stimulation on one side before proceeding to the contralateral lobe. This advantage is particular important for unilateral approaches. Contralateral approaches are much more difficult, especially at the Berry's ligament or in cases involving thyroiditis or a nodule located in the thyroid dorsal area. In these cases, the angle of the RLN limits visualization. The fifth advantage is that, for novice surgeons, IONM increases confidence in performing endoscopic procedures, which have a very steep learning curve. However, skilled surgeons can also use IONM to explore new applications of endoscopic thyroidectomy.

Lessons learned from monitoring

As the availability of endoscopic thyroidectomy increases [59–63], improved understanding of the mechanisms of RLN injury during endoscopic procedures is needed for instructional purposes and also for identifying and avoiding potentially reversible causes of RLN injury [62]. For example, a study of minimally invasive video-assisted thyroidectomy (MIVAT) performed with assistive IONM in a standardized fashion revealed no nerve lesions caused by clamping, transection, constriction, or ligature entrapment [2, 12]. These injuries were reduced, because MIVAT minimizes the use of conventional clamps, sutures, and stitches during most of the procedure, which is consistent with the objectives of IONM. In this study [2], most RLN injuries were inadvertent traction and thermal lesions. The Miccoli approach involves preparation of the operative space, ligature of the main thyroid vessels, and visualization and dissection of the RLN. The surgeon then removes the endoscope and retractors and pulls the gland from the cervical wound (incision length, 1.5 cm) [19, 45]. The operation then continues as in open surgery without visual assistance. Injuries occurred during extraction of the lobe from the mini-incision and subsequent retraction and elevation of the gland in a medial direction [20]. Nerve injuries occurred when excessive force was used to pull the gland through the wound incision and down the distal part of the RLN, which caused excess stretching of the laryngeal nerve. At this point in the MIVAT procedure, the surgeon must anticipate that the course of the RLN might be positioned overly vertical to the trachea, fixed to bands of connective tissue in the Berry's ligament, or fixed to branches of the inferior thyroid artery.

Endoscopic and robotic thyroid procedures should be performed without excessive traction on the thyroid to avoid injury over the nerve by Berry's ligament [2, 17, 60]. The Berry's ligament region is reportedly the most common site of RLN injury, because the RLN often swerves anteriorly and becomes fixed to the lateral trachea and cricoid cartilage within the ligament [49]. We suggest that the RLN should be freed as much as possible from the thyroid lobe, the Berry's ligament, small vessels, and the trachea before exteriorization of the gland in MIVAT [2, 12]. While using an endoscope for visualization and IONM for verification of RLN function, the surgeon should gradually, carefully, and gently shift the lobe before and during exteriorization of the gland. To prevent traction injury, the surgeon should also consider slightly increasing the cervical incision length [2, 12].

Finally, "invisible" RLN insults (i.e., thermal and traction injuries) are not detectable by endoscope. Only functional assessment of RLN with IONM can exclude these injuries. The standard use of energy-based devices in many procedures (particularly endoscopic thyroid surgery) can potentially induce invisible RLN insults and heat-related collateral/proximity iatrogenic injury to adjacent structures such as laryngeal nerves [2, 3, 11]. The temperature of the tip of an energy-based device must be carefully checked when legating inferior thyroid vessels. The RLNs and even parathyroid glands and the trachea can be damaged if the tip of the device is held near these structures for too long [35, 65]. The thermal spread of an energy-based device must be studied to determine the minimum average distance between the exposed surface of the instrument and vital structures [7, 65]. Energy-based devices are considered essential for endoscopic surgery, because they facilitate dissection, which significantly decreases operative time. However, the conventional clips are stull useful for avoiding injuries caused using energy-based devices in critical areas near the RLN in endoscopic thyroidectomy [3, 6, 11, 55, 65].

Notwithstanding, the increasing use of neural monitoring in endoscopic thyroid surgery imposes prudence, perfect knowledge of limits, and detail cost calculation. IONM economic assessment includes precise evaluation of its expense in operating room and hospitalization, the opposed actual estimate of an RLN injury, and a conclusive cost-effectiveness analysis. IONM cost-effectiveness has never been investigated.

Author contributions (I) Conception and design of study: GD, HYK, and AA; (II) administrative support for study: GD and RPTAA; (III) collection and assembly of data: GD, HYK, and RPT; (IV) analysis and interpretation of data: GD, HYK, RPT, and AA; (V) preparation of manuscript: all authors; and (VI) final approval of manuscript: all authors.

Compliance with ethical standards

Conflicts of interest The authors have no funding or financial relationships with manufacturers of surgical products and no other conflicts of interest in the publication of this study.

Research involving human participants and/or animals The study was approved by the institutional ethics committee of Hospital.

Informed consent All participants were provided the particular details for their surgeries and informed consent obtained from each patient.

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