



Original Research

Intraoperative neuromonitoring in thyroid surgery: Is the two-staged thyroidectomy justified?



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H I G H L I G H T S

- Intraoperative neuromonitoring is safe, effective, and highly predictive.
- Two-staged thyroidectomy remains a topic of discussion in the surgical field.
- According to the neuromonitoring results, the surgical strategy should be reconsidered in patients with loss of signal.
- It is essential to inform the patient preoperatively about potential changes that could be applied to the surgical strategy.

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A B S T R A C T

Background: The aim of this study was to evaluate the diagnostic accuracy of intraoperative neuro-monitoring (IONM) in predicting postoperative nerve function during thyroid surgery and its consequent ability to assist the surgeon in intraoperative decision making.

Materials and methods: A total of 2365 consecutive patients were submitted to thyroidectomy by the same surgical team. Group A included 1356 patients (2712 nerves at risk) in whom IONM was utilized, and Group B included 1009 patients (2018 nerves at risk) in whom IONM was not utilized.

Results: In Group A, loss of signal (LOS) was observed in 37 patients; there were 29 true positive, 1317 true negative, 8 false positive, and 2 false negative cases. Accuracy was 99.3%, positive predictive value was 78.4%, negative predictive value was 99.8%, sensitivity was 93.6%, and specificity was 99.4%. A total of 29 (2.1%) cases of unilateral paralysis were observed, 23 (1.7%) of which were transient and 6 (0.4%) of which were permanent. Bilateral palsy was observed in two (0.1%) cases requiring a tracheostomy. In Group A, 31 (2.3%) injuries were observed, 25 (1.8%) of which were transient and 6 (0.4%) of which were permanent. In Group B, 26 (2.6%) unilateral paralysis cases were observed, 20 (2%) of which were transient and 6 (0.6%) of which were permanent; bilateral palsy was observed in 2 (0.2%) cases. In Group B, 28 (2.8%) injuries were observed, 21 (2.1%) of which were transient and 7 (0.7%) of which were permanent. Differences between the two groups were not statistically significant.

Conclusions: Our results show that IONM has a very high sensitivity and negative predictive value, but also good specificity and positive predictive value. For these reasons, in selected patients with LOS, the surgical strategy should be reconsidered. However, patients need to be informed preoperatively about potential strategy changes during the planned bilateral surgery. Future larger and multicenter studies are needed to confirm the benefits of this therapeutic strategy.

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1. Introduction

Recurrent laryngeal nerve (RLN) palsy is a serious complication of thyroid surgery that can significantly deteriorate a patient's

quality of life. Unilateral RLN palsy can cause dysphagia, hoarseness of voice, or respiratory complications due to aspiration; bilateral RLN palsy is a rare and severe complication that may necessitate tracheostomy [1,2]. Although visual identification of RLN during thyroid surgeries decreases the rate of permanent RLN injury, RLN injury remains the most common cause of medicolegal litigation after thyroid surgery [2–4]. The incidence of transient RLN palsy ranges from 0.4% to 12%, and that of permanent RLN palsy is reported up to 5–6% [3,5]. Its frequency is 0.2–0.8% in academic and educational hospitals with a large workflow [6], but an even higher rate is seen in patients receiving surgery at low-volume institutions or when performed by low-volume surgeons [2]. Intraoperative RLN injuries are due to transection of the nerve, suture entrapment, traction, suction by aspiration near to the nerve, compression, contusion, pressure, ischemia by excessive skeletonization, and electrical and thermal injuries [7,8]. Revision neck surgery and surgery after radiotherapy have a higher risk of nerve injury due to tissue scarring; the risk of RLN injury increases three-fold for repeat thyroid surgery compared with the initial operation [2,9–11]. In large goiters, Graves' disease, and thyroiditis, enlarged glands put nerves under tension, making them more vulnerable to injury [2,12].

Intraoperative neuromonitoring (IONM) during thyroid surgery has gained widespread acceptance as an adjunct to the gold standard of visually identifying the RLN, detecting anatomic variations in the RLN, and elucidating the mechanisms underlying RLN injury. In addition, this method can help clinicians predict vocal cord (VC) function outcome and plan intraoperative and postoperative treatments [13].

There is a wide variety of techniques for nerve monitoring but the most common method in current use is a special endotracheal tube with electrodes embedded on it that register effects of stimulation in the vocal cords [7].

RLN identification is often hindered by alterations in neck anatomy by a large goiter, advanced-stage thyroid cancer, or scarring from previous procedures. In such situations, IONM may provide great benefit during thyroid surgery by allowing nerve localization through repeated tissue stimulation [14]. IONM has been used to assist in careful RLN dissection in cases of intertwining between RLN branches and the inferior thyroid artery, to map a distorted RLN, to identify a branched RLN, and to detect nerve injury and non-RLN intraoperatively. In addition, IONM has been used to elucidate the mechanisms underlying RLN injury and to improve surgical techniques and outcomes [14–17]. Furthermore, IONM can detect non-functioning nerves that are visibly intact [6]; however, an anatomically intact nerve identified by gross visualization does not confirm a functional nerve [2].

Since IONM has been introduced, it has gained popularity, especially in the last decade [4,18], and has become standard practice in thyroid surgery for many surgeons [19]. In fact, in recent years, it has been reported that about 65% of otolaryngologists and 53% of general surgeons have used IONM in some or all of their cases [4]. IONM is a safe and feasible adjunct to the routine visual identification of the laryngeal nerves [4,20]. Some studies have shown that this method decreases the prevalence of transient RLN injury [4], possibly due to its ability to aid in dissection of the RLN near the Berry's ligament, as it enhances the detection of branched nerves and reduces traction injury of the anterior branches of these nerves [4,21]. Another study reported that IONM is effective in video-assisted thyroidectomy, as it makes surgeons more comfortable with this approach [4,22]. However, RLN injuries still occur with IONM application [13]; therefore, the use of IONM is questionable as evidence is still lacking regarding its efficacy in reducing the rate of postoperative nerve injuries [6]. Multiple studies have failed to demonstrate any statistically significant

reduction in the incidence of RLN palsy when IONM has been used for primary cases [3,4]. This may simply be due to the very low incidence of RLN palsy in high-volume centers and lack of standardization in equipment use; it has been reported that at least 39,907 nerves at risk for both groups, either IONM or visual identification, are needed to show a significant difference in the nerve injury rate [4,23]. There is more evidence supporting the routine use of IONM in re-operative surgery, total thyroidectomy with neck dissection, and malignant cases, where a trend towards reduced RLN palsy rates has been observed [24,25]. In addition, it has been shown to lead to a decreased incidence of permanent RLN palsy in the hands of low-volume surgeons [4,23]. Moreover, Sari et al. [26] showed that IONM decreases the operative time compared to visualization alone by shortening the time needed to identify the RLN [4].

The International Neural Monitoring Study Group has classified nerve injury into two categories: segmental injury, which involves a clear-cut RLN segment that is lesioned; and global injury, where the entire RLN and vagus nerve are nonconductive, indicating an intralaryngeal focus of injury [2,14]. Segmental injury may be correctable in cases of nerve entrapment by a suture or clip, which can be removed to prevent permanent nerve injury [2]. IONM has led to two-stage operations to prevent life-threatening bilateral RLN palsy. Although the specificity of detecting nerve injuries is as high as 94–99%, the fact that it is not 100% means that some patients still suffer from VC dysfunction despite regular neuromonitoring (false-negative IONM) [19]. The possibility of using IONM to assess preservation of functional nerve integrity represents significant progress in the surgical field compared with assessing anatomical nerve integrity alone [14]. This has been particularly important for preventing bilateral RLN injuries, which are associated with the problem of staged thyroidectomy, i.e. the, postponement of resection of the contralateral side due to loss of signal (LOS) during resection of the first thyroid lobe [19,27,28]. Complete LOS at the end of an operation often indicates postoperative RLN palsy [14,19], leading to a positive predictive value that can be as low as 33–37.8% [4]. In cases that do not proceed to second-side surgery, because the recurrent nerve dissected on the first side loses its signal, bilateral nerve palsy can be avoided; in this setting, two-stage thyroidectomy has been proposed as the best approach. However, staged thyroidectomy, defined as resection performed at two different times, is associated with increased nerve and parathyroid morbidity if performed within 3 months and increases the cost of the procedure. In addition, it is unclear whether a LOS predicts postoperative RLN palsy, and anecdotal reports have suggested that signal can be regained quite quickly [28].

One study reports that 95% of surgeons who have had training in IONM admitted that before undergoing an introductory course about this technique, their understanding and experience of IONM were inadequate [29]. The incidence of IONM errors ranges from 3.8% to 23% [24,30]. The fear of making IONM errors can exert considerable psychological pressure on the operator, delay the surgical process, and even cause the operator to make wrong decisions [30]. The outcome of thyroid surgery monitoring is affected by both the experience of the operator and by how much the technique has been mastered [31].

Continuous IONM was introduced as a superior modality that can avoid periodic short timed stimulation and more accurately detect proximal injuries. A clip is placed over the vagus nerve and stimulates it periodically at short intervals. By providing vital intraoperative information about impending RLN injury caused by suture compressing the nerve or traction, continuous IONM allows surgeons to take measures to reverse the adverse condition and save the nerve [4].

The aim of this study was to evaluate the diagnostic accuracy of IONM in predicting post-operative nerve function during thyroid surgery and its consequent ability to assist the surgeon in intra-operative decision making.

2. Materials and methods

Between June 2007 and December 2014, 2365 consecutive patients were submitted to thyroidectomy by the same surgical team: 2038 patients underwent total thyroidectomy (TT), 265 underwent TT with VI level lymphectomy, and 62 underwent completion thyroidectomy (CT). Of the patients, 1873 were female and 492 were male with a mean age of 52.2 years (range, 15–87 years). The final diagnoses were 891 (37.7%) patients with multinodular goiter, 706 (29.8%) with differentiated carcinoma, 480 (20.3%) with Hashimoto's thyroiditis, 256 (10.8%) with Graves' disease, and 32 (1.3%) with medullary carcinoma. The histological diagnoses and surgical procedures are summarized in Table 1. In differentiated carcinoma, lymph node metastasis was found in 61 (9.6%) patients and micrometastasis was found in 14 (1.9%). Overall, lymph node metastasis was observed in 75 (10.2%) patients. The study was approved by the Local Bioethics Committee of the University of Cagliari. All of the patients provided written informed consent to undergo the operation and for the storage and use of their data. All operations were performed by the same surgical team, who used a Kocher incision. All patients were submitted to preoperative and postoperative laryngoscopy.

The RLNs were routinely identified by visualization and completely exposed. Intermittent IONM was performed in 1356 patients (2712 nerves at risk), based on equipment availability. All of these patients underwent general anesthesia and were intubated with a Nerve Integrity Monitor (NIM) Standard Reinforced Electromyography (EMG) Endotracheal Tube (Medtronic Xomed, Jacksonville, FL, USA). The tube (Fig. 1) was placed with the middle of the blue-marked region (3 cm of the exposed electrodes) in good contact with the true VCs under direct laryngoscopy. When the monitor was set up, the impedance of the electrodes was routinely checked. A Prass monopolar stimulation probe (Medtronic Xomed) was used for nerve stimulation during thyroidectomy. EMG activity was recorded on a NIM-response 2.0 or 3.0 monitor (Medtronic Xomed). No muscle relaxants were used after the skin flaps were elevated. The neuromonitoring device was used in various phases of the operation. Specifically, at the beginning of surgery, stimulation was applied at a level corresponding to the vagus nerve (Fig. 2) to ensure that the monitoring system was working; later, stimulation was then applied to the structure believed to be the RLN (Fig. 3). After thyroid removal and complete hemostasis within the surgical field, stimulation was reapplied to the level corresponding with the vagus (indirect stimulation) and with the RLN (direct stimulation) and was used for predicting the postoperative

outcome (Fig. 4).

LOS after RLN injury is defined as an EMG signal <100 μ V following a 1–2 mA stimulation in a dry field, and the absence of any laryngeal or glottic twitching. Patients in whom IONM did not function properly (20) were excluded from the study. Causes of malfunction were rotation of the electrodes on the endotracheal tube in relation to the vocal cords and positioning of an endotracheal tube of inadequate size. Being technical problems, patients were excluded from our study.

Here, we compare patients who had received IONM with those who had undergone surgery with nerve visualization alone. Group A comprises 1356 patients (2712 nerves at risk, 322 males and 1034 females) in whom IONM was utilized. A total of 1171 (86.3%) patients were submitted to TT, 40 (2.9%) to CT, and 145 (10.7%) to TT associated with a VI level lymphectomy. In this group, benign multinodular goiter was diagnosed in 514 (37.9%) patients, differentiated carcinoma in 413 (30.5%), Hashimoto's thyroiditis in 262 (19.3%), Graves' disease in 150 (11.1%), and medullary carcinoma in 17 (1.2%). Group B comprised 1009 patients (2018 nerves at risk, 170 males and 839 females) in whom IONM was not utilized. A total of 867 (85.9%) patients were submitted to TT, 40 (4%) to CT, and 102 (10.1%) to TT associated with a VI level lymphectomy. In this group, benign multinodular goiter was diagnosed in 377 (37.4%) patients, differentiated carcinoma in 293 (29%), Hashimoto's thyroiditis in 218 (21.6%), Graves' disease in 106 (10.5%), and medullary carcinoma in 15 (1.5%). The groups were homogeneous for patient characteristics, diagnosis, and type of surgery. Postoperative laryngoscopy was performed routinely in all the patients with suspected nerve injury (i.e. patients with dysphonia or hoarseness) to assess vocal fold motility. We defined “transient” as an injury in which VC motility was recovered within 12 months of surgery.

The results of IONM were retrospectively assessed. Patients outcome were categorized based on the results of IONM and postoperative findings as follows:

- True positive (TP) result: a LOS found during IONM and a postoperative nerve paralysis;
- True negative (TN) result: normal nerve signal during IONM with no postoperative nerve paralysis;
- False positive (FP) result: a LOS found during IONM with no postoperative nerve paralysis;
- False negative (FN) result: normal nerve signal during IONM and a postoperative nerve paralysis.

We defined:

- Sensitivity: TP Result/(TP Result + FN Result);
- Specificity: TN Result/(FP Result + TN Result);
- Positive Predictive Value: TP Result/(TP Result + FP Result);
- Negative Predictive Value: TN Result/(FN Result + TN Result).

Table 1

Histological diagnosis and surgical procedures. Group A: patients in which IONM was utilized; group B: patients in which IONM was not utilized. TT: Total thyroidectomy; DTC: Differentiated thyroid carcinoma.

	Group A (n = 1356)	Group B (n = 1009)	p
Surgical procedure			
TT	1171 (86.3%)	867 (85.9%)	0.37
TT + VI level Lymphadenectomy	145 (10.7%)	102 (10.1%)	
Completion thyroidectomy	40 (3%)	40 (4%)	
Histopathological diagnosis			
Multinodular goiter	514 (37.9%)	377 (37.4%)	0.10
DTC	413 (30.5%)	293 (29%)	
Hashimoto's thyroiditis	262 (19.3%)	218 (21.6%)	
Graves' disease	150 (11.1%)	106 (10.5%)	
Medullary carcinoma	17 (1.2%)	15 (1.5%)	

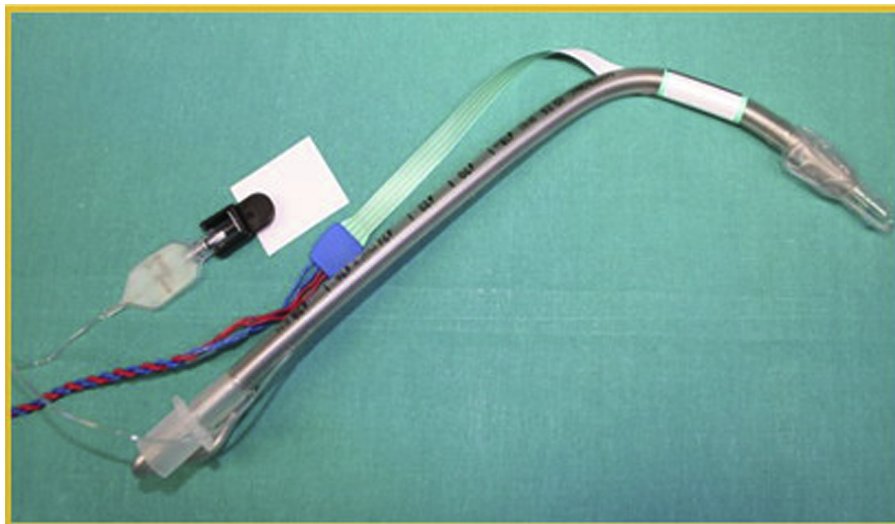


Fig. 1. Nerve Integrity Monitor (NIM) Standard Reinforced Electromyography (EMG) Endotracheal Tube (Medtronic Xomed, Jacksonville, FL, USA). The tube has to be placed with the middle of the blue-marked region (3 cm of the exposed electrodes) in good contact with the true VCs under direct laryngoscopy.

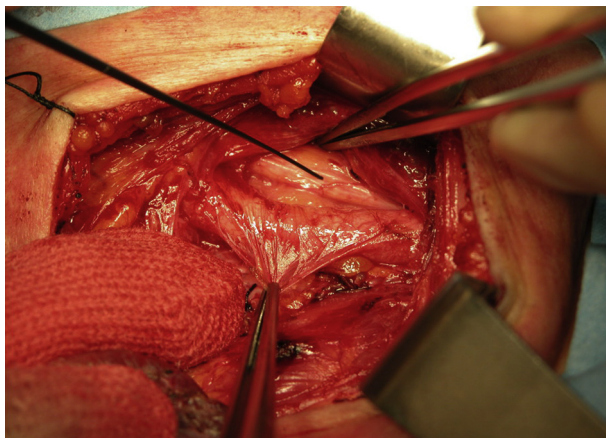


Fig. 2. Stimulation of the vagus nerve.

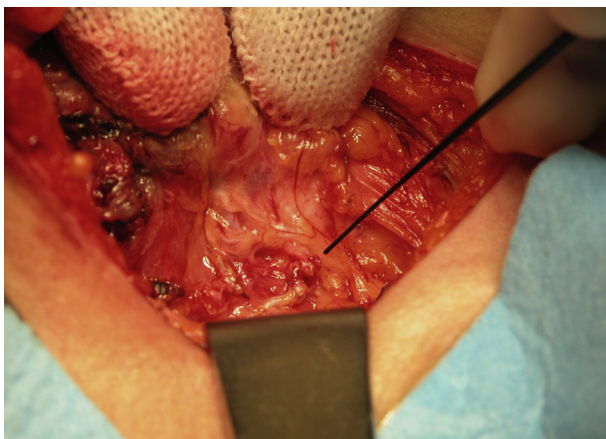


Fig. 3. Stimulation of the RLN.

Parameters were tested using the chi-squared test. A logistic regression analysis was fitted using transient and permanent palsy as measurements of outcome. A P value less than 0.05 was

considered statistically significant. Statistical analysis was done using SPSS software (SPSS, Chicago, IL, USA).

3. Results

In Group A, LOS was observed in 37 cases; there were 29 true positive, 1317 true negative, 8 false positive, and 2 false negative cases. IONM accuracy was 99.3%, positive predictive value was 78.4%, negative predictive value was 99.8%, sensitivity was 93.6%, and specificity was 99.4% (Table 2). A total of 29 (2.1%) cases of unilateral RLN palsy were observed, 23 (1.7%) of which were transient and 6 (0.4%) of which were permanent. In this group of patients, bilateral RLN palsy was observed in two (0.1%) cases, requiring a tracheostomy. Overall, in Group A, 31 (2.3%) RLN injuries were observed, 25 (1.8%) of which were transient and 6 (0.4%) of which were permanent. Transient hypoparathyroidism was observed in 381 patients (28.1%) and definitive hypoparathyroidism in 53 cases (2.9%). In Group B, unilateral RLN palsy was observed in 26 (2.6%) cases, 20 (2%) of which were transient and 6 of which were permanent (0.6%). Bilateral palsy was observed in two (0.2%) cases; in one patient who underwent CT and had unilateral palsy from a previous surgery, the VC completely recovered 3 months after surgery. In the other case, the patient required a tracheostomy and the lesion was permanent. Overall, in Group B, 28 (2.8%) RLN injuries were observed, 21 (2.1%) of which were transient and 7 (0.7%) of which were permanent. Transient hypoparathyroidism was observed in 303 patients (30%) and definitive hypoparathyroidism in 42 cases (4.2%). Differences between the two groups were not statistically significant (Table 3). The mean postoperative hospital stay was 2 days for both groups. RLN palsies in both groups with regard to type of surgery and histology are reported in Table 3. These differences were also not statistically significant. No complications were attributable to IONM use.

4. Discussion

Causes of RLN injury can be transaction, clamping, traction, electrothermal injury, mechanical trauma, ligature entrapment, or ischemia. RLN traction injury is the most common mechanism [13,15,22]. With the exception of transaction injury, it can be difficult to definitively recognize the nerve injury or evaluate its

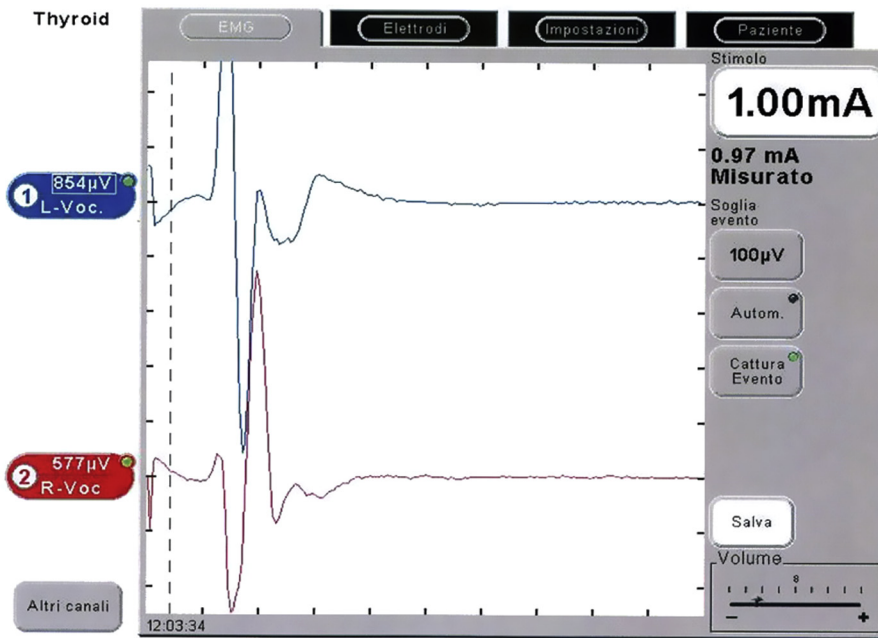


Fig. 4. EMG after stimulation of the vagus.

Table 2

Correlation of neuromonitoring results with postoperative outcomes. True positive (TP): a LOS found during IONM and a postoperative nerve paralysis; True negative (TN): normal nerve signal during IONM and no postoperative nerve paralysis; False positive (FP): a LOS found during IONM with no postoperative nerve paralysis; False negative (FN): normal nerve signal during IONM and a postoperative nerve paralysis. Sensitivity: TP Result/(TP Result + FN Result); Specificity: TN Result/(FP Result + TN Result); Positive Predictive Value: TP Result/(TP Result + FP Result); Negative Predictive Value: TN Result/(FN Result + TN Result).

True positives	29
True negatives	1317
False positives	8
False negatives	2
Accuracy	99.3%
Positive predictive value	78.4%
Negative predictive value	99.8%
Sensitivity	93.5%
Specificity	99.4%

severity solely by visualization [15]. Thus, IONM is now increasingly being used by thyroid surgeons to assist in RLN identification, and to potentially reduce the risk of injury [32,33]. In the United States and Germany, approximately 40% and 90% of thyroid surgery procedures, respectively, are estimated to utilize IONM [12,21]. However, to date, no study has demonstrated a statistically significant reduction in the incidence of permanent RLN palsy using this technique, although this lack of data may be related to the rarity of this condition [23]. It has been estimated that in prospective, randomized trials, the calculated sample size needed to prove that rates of palsy are lower with IONM use is about 9000 nerves at risk [3,34]. Other authors have reported that at least 39,907 nerves at risk per arm are necessary to achieve statistical power that can show a significant difference in RLN palsy rate [3,23]. The incidence of IONM error ranges from 3.8% to 23.0% [24,30]. These errors can cause great psychological pressure to the operator, delay the surgical process, and even cause the operator to make wrong decisions [30].

When loss of EMG signal is detected after initially resecting the thyroid lobe, it has been suggested that surgery should be stopped and the opposite side excised in a second operation, to avoid bilateral RLN palsy [28]. It is the opinion of most surgeons that staged thyroidectomy is fully justified in patients with bilateral non neoplastic thyroid disease, although some believe it is also acceptable in procedures performed for thyroid cancer [6,19,27]; nevertheless, this opinion is not shared by all experts [28]. Second operation can be successfully undertaken after confirming the recovery of the RLN with a laryngoscopy. In case of definitive palsy, carbon dioxide laser surgery and other endoscopic surgeries (arytenoidectomy and cordectomy) or laterofixation of the VC can be taken into account [35]. An enquiry among German endocrine and thyroid surgeons revealed that more than 90% of the surgical departments surveyed would be willing to change their surgical strategy by either discontinuing surgery (85%) or by undertaking a less extensive contralateral procedure (9%) [27,28]. However, there is a lack of high-quality evidence to support this view. The positive predictive value of a LOS for VC palsy is in the range of 30–80% in experienced hands [28]. Most patients actually retain normal VC function despite a LOS, and would undergo an unnecessary delayed CT. The reasons for the relatively low positive predictive value of a lost IONM signal are not completely understood [16,28]. The timing of postoperative laryngoscopy appears to be crucial because the earlier the investigation, the higher the rate of RLN palsy [28,35]. This means that a substantial proportion of patients with neuropraxias may recover quickly [28]. Chiang et al. [15] reported that 42% of patients with pathologic IONM results regained normal nerve activity during surgery [6,28]. Sitges-Serra et al. [28] reported that an initial LOS has a 90% chance of recovery before the end of the operation, making it safe to complete the thyroidectomy.

Goretzki and colleagues [6] retrospectively investigated the impact of IONM on the prevalence of bilateral RLN palsy in a series of thyroidectomies performed by 12 surgeons of different skill levels. These authors noted abnormal IONM signals on first side in 2.7 per cent of the patients, but with a high positive predictive value. Sensitivity of IONM in detecting temporary nerve injuries of macroscopically normal-appearing nerves was 93%; specificity was

Table 3
Recurrent laryngeal nerve palsy and hypoparathyroidism in the two groups in relation to the type of surgery and histology. Group A: patients in which IONM was utilized; group B: patients in which IONM was not utilized.* One patient had bilateral nerve palsy** One patient with prior unilateral nerve palsy had contralateral nerve palsy.

	Group A (1356 patients) n (%)	Group B (1009 patients) n (%)	p value	
Recurrent Nerve Palsy	31 (2.3%)	28 (2.8%)	0.5348	p > 0.05
• Unilateral	29 (2.1%)	26 (2.6%)	0.5745	p > 0.05
• Bilateral	2 (0.1%)	2 (0.2%)	0.8344	p > 0.05
Transient Nerve Palsy	25 (1.8%)	21 (2.1%)	0.7923	p > 0.05
• Total Thyroidectomy	16 (1.2%)	15 (1.5%)	0.6413	p > 0.05
• Completion thyroidectomy	4 (0.3%)	2** (0.2%)	0.9605	p > 0.05
• Total thyroidectomy + lymphectomy	5 (0.4%)	4 (0.4%)	0.8185	p > 0.05
• Multinodular goiter	10 (0.7%)	8 (0.8%)	0.9031	p > 0.05
• Differentiated carcinoma	8 (0.6%)	8** (0.8%)	0.7325	p > 0.05
• Hashimoto's thyroiditis	5 (0.4%)	3 (0.3%)	0.7096	p > 0.05
• Graves' disease	2 (0.1%)	2 (0.2%)	0.8344	p > 0.05
• Medullary carcinoma	0	0	—	—
Permanent Nerve Palsy	6 (0.4%)	7 (0.7%)	0.5917	p > 0.05
• Total Thyroidectomy	5* (0.4%)	5* (0.5%)	0.881	p > 0.05
• Completion thyroidectomy	0	1 (0.1%)	0.882	p > 0.05
• Total thyroidectomy + lymphectomy	1 (0.1%)	1 (0.1%)	0.6133	p > 0.05
• Multinodular goiter	3 (0.2%)	2* (0.2%)	0.7398	p > 0.05
• Differentiated carcinoma	2* (0.1%)	3 (0.3%)	0.7398	p > 0.05
• Hashimoto's thyroiditis	1 (0.1%)	1 (0.1%)	0.6133	p > 0.05
• Graves' disease	0	1 (0.1%)	0.882	p > 0.05
• Medullary carcinoma	0	0	—	—
Hypoparathyroidism				
• Transient	381 (28.1%)	303 (30%)	0.3274	p > 0.05
• Permanent	53 (3.9%)	42 (4.2%)	0.8373	p > 0.05

75–83% at first side of dissection and 55–67% at the second side, with an overall specificity of 77%. Although the positive predictive value in this study was high, it was difficult to draw conclusions on the true impact of IONM in preventing bilateral VC palsy [28]. However, it is clear that patients must be informed preoperatively about the limitations of IONM and any potential strategy changes that may occur during the planned bilateral surgery.

We applied strict standardization of IONM, obtaining very high accuracy (99.3%), negative predictive value (99.8%), and specificity (99.4%), which is in accordance with other reports in the literature. In addition, the sensitivity was high (93.6%), whereas the positive predictive value, although lower (78.4%), was significantly higher than that reported in the literature. It is likely that the large number of procedures completed by the same team, and the fact that the technique has been routinely applied led to our excellent results. Similar to the majority of studies reported in the literature, our study failed to demonstrate a statistically significant decrease in RLN palsy rates with IONM use.

The main weakness of our study was the inadequate power to identify statistical differences; this remains a significant limitation for these types of studies. In addition, the patients were not randomized, which could lead to bias, but the number of patients was very large and the groups were very well matched. Given the fact that a LOS does not always correspond to a nerve injury and considering the risk of delaying the treatment of potentially aggressive tumors, we do not believe that staged thyroidectomy should always be taken into consideration. However, given the high accuracy and significant positive predictive value, we believe that in select LOS cases, the surgical strategy should be reconsidered. The reconsideration of surgical strategy after a LOS in one site must be evaluated mainly for revision surgeries in patients who are at major risk of bilateral RLN palsy [3,6]. Following this recommendation, however, two-thirds of patients might require unnecessary staged thyroidectomy [3,36].

We suggest modifying the surgical approach in such a way that intervention begins on the side with the tumor or suspicious

nodule, or in the case of benign disease, on the more voluminous side, so that the option to stop the intervention can be considered. However, it is essential that the patient is informed of any change in surgical strategy before it is implemented.

Continuous intraoperative vagal neuromonitoring is an interesting evolution of the technique that can detect an impending recurrent laryngeal nerve injury allowing a timely modification of the intra-operative strategy, thus avoiding nerve damage [3,32]. We have started to use this technique, but our results are preliminary; however, the first results reported in the international literature are promising [13,32]. For this reason, we believe that the continuous monitoring represents a very interesting improvement in this field and that it can also lead to improved outcomes.

5. Conclusions

IONM is a safe and effective technique, and is highly predictive of postoperative nerve function. Our results show that it has a very high sensitivity and negative predictive value, as well as good specificity and a positive predictive value. For these reasons, in selected patients with LOS, the surgical strategy should be reconsidered. However, patients must be informed preoperatively about potential strategy changes that may occur during the planned bilateral surgery. Future larger and multicenter studies are needed to confirm the benefits of this therapeutic strategy.

Ethical approval

Ethical approval was requested and obtained from the University of Cagliari ethical committee.

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Author contribution

Pietro Giorgio Calò: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in writing, drafting, and editing of the manuscript.

Fabio Medas: Participated substantially in conception, design, and execution of the study and in the collection, analysis and interpretation of data.

Giovanni Conzo: Participated substantially in execution of the study and in the analysis and interpretation of data.

Francesco Podda: Participated substantially in conception and execution of the study and in the collection, analysis and interpretation of data.

Gian Luigi Canu: Participated substantially in conception and execution of the study and in the collection and interpretation of data.

Claudio Gambardella: Participated substantially in conception and design of the study and in the interpretation of data.

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Conflicts of interest

All Authors have no conflict of interests.

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