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Association of Intraoperative Neuromonitoring With Reduced Recurrent Laryngeal Nerve Injury in Patients Undergoing Total Thyroidectomy

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IMPORTANCE Injury of the recurrent laryngeal nerve (RLN) is one of the most serious complications of thyroid surgery. Intraoperative neuromonitoring (IONM) has been introduced to verify RLN function integrity and may be a helpful adjunct in nerve dissection.

OBJECTIVE To determine whether the use of IONM can reduce the incidence of RLN injury in patients undergoing total thyroidectomy.

DESIGN, SETTING, AND PARTICIPANTS This cohort study included 2556 patients who underwent total thyroidectomy between January 2002 and December 2012 in the Department of Otolaryngology–Head and Neck Surgery of Venizeleio General Hospital, Heraklion, Greece. Patients who had IONM during the procedure (n = 1481) were compared with patients who underwent surgery with nerve visualization alone (n = 1075). All patients underwent indirect laryngoscopy–fiberoptic nasopharyngoscopy both preoperatively and on day 2 after surgery to assess vocal cord motility.

MAIN OUTCOMES AND MEASURES Use of IONM and incidence of RLN injury.

RESULTS A total of 2556 patients (2028 women and 528 men [5112 RLNs at risk]; mean [SD] age, 51.35 [14.18] years; age range, 18-89 years) underwent total thyroidectomy. Univariate analysis showed that the use of IONM resulted in a significant reduction in RLN injury incidence (3.3% vs 0.7%) with a relative risk reduction of 2.6% (odds ratio [OR], 5.15; 95% CI, 3.12-8.49; number needed to treat, 19). Multivariate logistic regression showed that no use of IONM was an independent risk factor for RLN injury in patients who underwent total thyroidectomy (adjusted OR [AOR], 5.44; 95% CI, 3.26-9.09). Additional risk factors for RLN injury were operative time (AOR, 12.91; 95% CI, 6.66-25.06), maximum diameter greater than 45 mm of right thyroid lobe (AOR, 4.91; 95% CI, 3.12-8.56) and left thyroid lobe (AOR, 2.24; 95% CI, 1.39-4.32), extrathyroid extension (AOR, 3.26; 95% CI, 1.62-6.59), incidental parathyroidectomy (AOR, 3.30; 95% CI, 2.13-5.09), and tumor size larger than 10 mm (AOR, 3.24; 95% CI, 1.59-6.62).

CONCLUSIONS AND RELEVANCE Our findings showed that the use of IONM decreased significantly both temporary and permanent RLN injuries. The technology of IONM is safe and reliable, and this technique is an important adjunct in nerve dissection and functional neural integrity. The routine use of IONM reduced pitfalls and provided guidance for our surgeons in difficult cases, reoperations, and high-risk patients.

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Injury of the recurrent laryngeal nerve (RLN), resulting in transient or permanent voice changes, is one of the most serious complication of thyroid surgery. It ranks among the leading reasons for medicolegal litigation for surgeons.[1]

Nerves may visually resemble connective tissue and small vessels and can be damaged during dissection. Several studies have shown that routine visual identification of the RLN with or without intraoperative neuromonitoring (IONM) has decreased rates of permanent RLN palsy. A systemic appraisal of the literature showed that RLN palsy rates vary widely after thyroid operation, ranging from 0% to 7.1% for transient RLN palsy to 0% to 11% for permanent RLN palsy.[2]

Many RLN palsies are unexpected and unrecognized, although the visual integrity of RLN is confirmed intraoperatively. The causes of RLN injury could result from transection, clamping, stretching, electrothermal injury, ligature entrapment, or ischemia, but the actual causes of nerve injury are difficult to identify, especially to those nerves in which visual inspection during the operation has confirmed nerve integrity.

Lahey[3] and Riddell[4] have strongly advocated routine nerve dissection and visualization during thyroidectomy to decrease the risk of RLN injury. Several more recent studies have confirmed that RLN integrity was preserved significantly more often with routine visual identification than without it.[5,6] The British Thyroid Association treatment recommendations for thyroid surgery include the routine identification of the RLN, and these recommendations are regarded as the gold standard of care in thyroid surgery.[7,8]

Various medical devices have been developed in the last decades to help surgeons identify the RLN and measure its function immediately before and after thyroid resection. Intraoperative neuromonitoring has been advocated as a means to localize and identify the RLN and predict vocal cord function.[9,10] These devices convert muscle activity into audible and electromyographic (EMG) signals.

Intraoperative neuromonitoring has important uses as an adjunct to the visual identification of the nerve. Endotracheal-based nerve-integrity monitoring (NIM) systems (Medtronic) are used to monitor the bilateral thyroarytenoid muscles for ongoing real-time EMG activity. A sterile nerve stimulator, typically set at 1 mA, is used intermittently to stimulate the RLN for an evoked response. Intraoperative neuromonitoring aids in identification of the nerve in neural dissection and gives prognostic information for postoperative function.

Recent studies have shown that IONM can aid RLN identification.[2,11,12] However, its role in reducing the frequency of RLN injury remains controversial. Dralle et al[13] analyzed the risk factors for postoperative RLN paralysis in 16 448 thyroidectomies performed at 63 different hospitals. They concluded that when the RLN is identified during the surgery, there was no significant difference in postoperative RLN paralysis rates between IONM and non-IONM groups.[13]

In the present study, the potential benefit of an IONM system was evaluated through a retrospective review of a single institution's cases. We examined the rates of paralysis with and without IONM in over 5100 nerves at risk, while a consistent surgical technique and a standardized IONM NIM system was used over the study period. Our study is different from other studies because we examined whether the clinicopathological features of the thyroid gland had an effect on the rate of RLN injury. We analyzed the presence of thyroid carcinoma, lymph node metastasis, extrathyroidal extension, the presence of autoimmune disease, the size of the thyroid lobe (maximum diameter and volume), thyroid gland weight, hypocalcemia, and the duration of the operation.

Key Points

Question Does the use of intraoperative neuromonitoring (IONM) reduce the incidence of recurrent laryngeal nerve (RLN) injury in patients undergoing total thyroidectomy?

Findings In this cohort study that includes 2556 patients who underwent total thyroidectomy, the incidence of RLN injury was significantly lower in the IONM group than in the non-IONM group. The use of IONM significantly decreased both temporary and permanent RLN injuries.

Meaning In our experience, the routine use of IONM reduced pitfalls and provided guidance for our surgeons in difficult cases, reoperations, and high-risk patients.

Methods

A retrospective review of 2556 patients who underwent total thyroidectomy from January 2002 through December 2012 in the Department of Otolaryngology–Head and Neck Surgery, Venizeleio-Pananeio General Hospital, Herakleion, Greece was conducted. This retrospective cohort study was approved by the Venizeleio-Pananeio General Hospital institutional review board of our hospital, waiving patient written informed consent.

All patients included in the study underwent standard total thyroidectomy. Surgical management of the patients was recommended on referral to our hospital for various reasons, including malignant or suspect thyroid nodules found by fine needle aspiration biopsy (FNAB), multinodular goiter, hyperthyroidism, or compression of neighboring structures.

All patients were operated on by the same surgeons, and the pathological evaluation of thyroid specimens was performed by 3 pathologists at the same institution. The entire gland and additional nodal tissue were evaluated from 1-mm-thick anatomical slices. Patients who had metastasis detected preoperatively by FNAB, or intraoperatively by palpation of the central neck compartment, underwent a level VI therapeutic dissection, as described in the American Thyroid Association 2009 guidelines.[14]

Inclusion criteria in our study were adult age (≥18 years) and standard total thyroidectomy. Exclusion criteria were previous neck surgery and thyroid reoperations, preoperative impaired vocal cord function, and laryngectomy concomitant with the total thyroidectomy.

There was no intentional allocation of the patients to IONM vs non-IONM groups. The non-IONM cases were those performed when the nerve monitoring system was not available for use.

A NIM, 2.0, EMG endotracheal tube (Medtronic) was used for patients undergoing IONM. An experienced anesthetist intubated all patients, and the tube was accurately positioned such that the electrodes were situated at the level of the true vocal folds oriented at the 3 and 9 o'clock positions. A sterile stimulation probe (Medtronic, Xomed) was used for nerve stimulation during the thyroidectomy. No muscle relaxants were used after the skin flap elevation. In the non-IONM group, a standard endotracheal tube without EMG electrodes was used.

All patients underwent indirect laryngoscopy–fiberoptic nasopharyngoscopy both preoperatively and on day 2 after surgery. Vocal cord function was diagnosed as normal, paretic (hypomotility without paramedian paralysis), or paralytic (not moving and paramedian position). In patients with RLN paresis, an additional examination was scheduled at 2 weeks and 2, 4, 6, and 12 months after the surgery or until the vocal cord function recovered. Vocal cord paresis that lasted for 12 months postoperatively was considered permanent palsy. In the analysis, paretic and paralytic vocal cords were grouped together as vocal cord dysfunction. The incidence of temporary and permanent vocal cord paralysis was calculated based on the total number of nerves at risk (N = 5112).

The clinical characteristics considered for statistical analysis were age (≤45 years vs ≥45 years), sex (male vs female), weight of thyroid gland (≤30 g vs >30 g), and clinically cervical lymph node metastases at the time of diagnosis (cN0 vs cN+).

The histopathological characteristics considered for statistical analysis were size of the tumor at its greatest diameter (≤10 mm vs >10 mm), histological subtype (pure papillary, follicular, sclerosing, tall cell variant), histopathological evidence of autoimmune thyroid disease, focality of tumor (solitary isthmus nodule vs multifocality), and bilaterality. Multifocal disease was defined as more than 1 tumor focus in thyroid parenchyma. The tumor focus with the largest diameter (dominant nodule) was regarded as the primary carcinoma. Bilateral disease was defined as tumor foci located in both of thyroid lobes.

We also assessed the maximum diameter and the volume of each thyroid lobe, the thyroid capsule invasion, and the incidental parathyroidectomy. The 7th edition of the American Joint Committee on Cancer (AJCC) TNM classification of malignant tumors[15] was used to describe and categorize cancer stages and progression.

Statistical Analysis

Univariate analysis was performed with the Pearson χ^2 test and Fisher exact test, as appropriate. $P < .05$ was considered statistically significant. Statistically significant results obtained from the univariate analysis were subjected to multivariate logistic regression. A backward selection approach was fit to the multiple logistic regression model where all potential predictors were first considered, and in a stepwise fashion, 1 variable at a time was removed, based on its level of significance in the model. To determine cutoff values we used receiver operating characteristics curve analysis. IBM SPSS software, version 17, was used for statistical analysis.

Results

Patient Demographics and Pathology

A total 2556 patients who underwent total thyroidectomy were enrolled, of whom 2028 (79.3%) were women and 528 (20.3%) were men, with a mean (SD) age of 51.35 (14.18) years (range, 18-89 years). Patients' demographic, clinical, and pathological characteristics are detailed in **Table 1**. The median tumor size was 0.9 cm, and 289 patients with thyroid cancer (34.1%) had a tumor larger than 1.0 cm in diameter.

The IONM group consisted of 1481 patients (2962 nerves at risk) in whom the thyroidectomy was performed with IONM, and the identification of the RLN was performed with IONM plus visualization. The non-IONM group consisted of 1075 patients (2150 nerves at risk) for whom IONM was not used, and the identification of RLN was performed with visualization only. In 89 patients, lymph node metastasis to the lateral neck was detected preoperatively by ultrasonography or FNAB, and these patients underwent a lateral modified neck dissection. In 223 patients, metastasis was detected preoperatively by ultrasonography or FNAB, or intraoperatively by palpation of the central compartment, and a level VI therapeutic dissection was undertaken.

The overall incidence of temporary and permanent RLN palsy (considered as a percentage of the nerves at risk) was 1.3% and 0.5%, respectively. The recovery time for temporary RLN palsy ranged from 7 days to 12 months (mean recovery time, 4.3 months). Impairment of postoperative vocal cord mobility (paresis or paralysis) was found in 19 patients from the IONM group (0.7% of nerves at risk) and in 71 patients from the non-IONM group (3.3% of nerves at risk). None of the patients experienced bilateral vocal cord paralysis.

Univariate analysis showed that the non-IONM group was at significantly increased risk of overall RLN injury (relative risk increase of 2.6%) compared with the IONM group (3.3% vs 0.7%; odds ratio [OR], 5.15; 95% CI, 3.12-8.49; number needed to treat, 19). In addition, the non-IONM group was at significantly greater risk of temporary (2.4% vs 0.5%, OR, 4.95; 95% CI, 2.77-8.85) and permanent (0.9% vs 0.2%, OR, 7.28; 95% CI 2.48-21.36) RLN paralysis.

We classified the patients into 2 groups, those with RLN injury (n = 90) and those without (n = 2466). Univariate analysis showed that there were significant differences between these 2 groups, respectively, in mean (SD) thyroid weight (78.29 [50.97] vs 34.03 [23.02] g; OR, 1.48; 95% CI, 1.27-1.74), tumor size greater than 10 mm (60.6% vs 33.0%; OR, 3.25; 95% CI, 1.59-6.62), presence of lymph node metastasis (57.6% vs 35.2%; OR, 2.50; 95% CI, 1.23-5.05), presence of thyroid capsular invasion (69.7% vs 49.0%; OR, 2.40; 95% CI, 1.13-5.10), presence of extrathyroidal extension (48.5% vs 24.6%; OR, 2.89; 95% CI, 1.44-5.83), operation time greater than 100 minutes (88.9% vs 38.2%; OR, 12.92; 95% CI, 6.66-25.06), and incidental parathyroidectomy (60.0% vs 16.8%; OR, 7.41; 95% CI, 4.80-11.45) (**Table 2**).

The receiver operating characteristics curve analysis showed that the maximum lobe diameter cutoff point for significantly increased risk of RLN injury was 45 mm for both the

Table 1. Characteristics of the Study Patients Undergoing Total Thyroidectomy With or Without IONM[a]

Characteristic	Total Patients, No. (n = 2556)	No IONM (n = 1075)	IONM (n = 1481)	OR (95% CI)
Nerves at risk, No.	5112	2150	2962	NA
Sex				
Female	2028 (79.3)	857 (79.7)	1171 (79.1)	0.98 (0.79-1.17)
Male	528 (20.7)	218 (20.3)	310 (20.9)	1 [Reference]
Age at diagnosis, y				
Mean (SD) [range]	51.35 (14.18) [18-890]	51.95 (14.02) [18-89]	50.92 (14.29) [18-85]	NA
<45	935 (36.6)	371 (34.5)	564 (38.1)	1 [Reference]
≥45	1621 (63.4)	704 (65.5)	917 (61.9)	0.86 (0.72-1.00)
Thyroid weight, g				
Mean (SD)	35.59 (25.85)	37.72 (26.60)	34.05 (25.19)	NA
≤30	1417 (55.4)	535 (49.8)	882 (59.6)	1 [Reference]
>30	1139 (44.6)	540 (50.2)	599 (40.4)	1.48 (1.27-1.74)
RLN injury				
Yes	90 (1.8)	71 (3.3)	19 (0.7)	5.44 (3.26-9.09)
Temporary	66 (1.3)	51 (2.4)	15 (0.5)	4.95 (2.77-8.85)
Permanent	24 (0.5)	20 (0.9)	4 (0.2)	7.28 (2.48-21.36)
No	2466 (98.2)	1004 (96.7)	1462 (99.3)	1 [Reference]
Side of RLN injury				
Right	72 (80.0)	55 (77.5)	17 (89.5)	2.47 (0.52-11.86)
Left	18 (20.0)	16 (22.5)	2 (10.5)	1 [Reference]
Bilateral	0	0	0	NA
Hypocalcemia				
Yes	505 (19.7)	255 (23.8)	250 (16.9)	0.65 (0.54-0.79)
No	2051 (80.3)	820 (76.2)	1231 (83.1)	1 [Reference]
Tumor				
Yes	848 (33.2)	314 (29.2)	534 (36.1)	1.37 (1.15-1.62)
No	1708 (66.8)	761 (70.8)	947 (65.9)	1 [Reference]
Tumor size, mm				
Mean (SD) [range]	9.26 (8.41) [1-77]	9.19 (8.85) [1-68]	9.30 (8.15) [1-77]	NA
≤10	559 (65.9)	206 (65.6)	353 (66.1)	1 [Reference]
>10	289 (34.1)	108 (34.4)	181 (33.9)	0.98 (0.73-1.31)
Lymph node metastasis				
Yes	306 (36.1)	101 (32.2)	205 (38.4)	1.25 (0.93-1.68)
No	542 (63.9)	213 (67.8)	329 (61.6)	1 [Reference]
Thyroid capsular invasion				
Yes	422 (49.8)	158 (50.3)	264 (49.4)	0.90 (0.68-1.19)
No	426 (50.2)	156 (49.7)	279 (50.6)	1 [Reference]
Extrathyroidal extension				
Yes	216 (25.5)	80 (25.4)	136 (25.6)	0.99 (0.72-1.37)
No	632 (74.5)	234 (74.6)	398 (74.4)	1 [Reference]

Abbreviations: IONM, intraoperative neuromonitoring; NA, not applicable; OR, odds ratio; RLN, recurrent laryngeal nerve.

[a] Unless otherwise indicated, data are reported as number (percentage) of patients.

right thyroid lobe (area under the curve [AUC], 0.83; 95% CI, 0.78-0.88; *P* = .01) and the left (AUC, 0.77; 95% CI, 0.72-0.82; *P* = .04). Patients with a maximum lobe diameter greater than 45 mm had a significantly increased rate of RLN injury on the right side (OR, 5.07; 95% CI, 1.24-20.74) and on the left side (OR, 5.62; 3.62-8.74) (Table 2 and **Table 3**).

Interestingly, the incidence of malignant thyroid disease was higher in the IONM group, and the difference of 6.9% was significant (OR, 1.37; 95% CI, 1.15-1.62).

A total of 90 patients (3.5%) had postoperative RLN paralysis. Temporary and permanent RLN paralysis occurred in 66 (1.3%) and 24 (0.5%) nerves at risk, respectively. Seventy-two patients presented injury of the right RLN, and 18 patients of the left RLN. Univariate analysis of the 2 groups showed that thyroid weight (OR, 8.85; 95% CI, 1.88-41.64), volume of right thyroid lobe greater than 25 mL (OR, 13.46; 95% CI, 2.35-76.95), and size of right thyroid lobe greater than 50 mm (OR, 16.12; 95% CI, 4.71-55.08) were all significantly associated with right RLN injury.

Of the 90 patients with RLN injury, 66 had temporary palsy (symptoms resolved within 12 months), and 24 had permanent paralysis. Comparing the 2 groups, we found that

Table 2. Characteristics of the Study Patients Undergoing Total Thyroidectomy With or Without RLN Injury[a]

Characteristic	Total Patients (n = 2556)	RLN Injury (n = 90)	No RLN Injury (n = 2466)	OR (95% CI)
Use of IONM				
Yes	1481 (57.9)	19 (22.1)	1462 (59.3)	5.44 (3.26-9.09)[b]
No	1075 (42.1)	71 (77.9)	1004 (41.3)	1 [Reference]
Thyroid weight, g				
Mean (range)	35.59 (25.85)	78.29 (50.97)	34.03 (23.02)	NA
≤30	1417 (55.4)	8 (8.9)	1409 (57.1)	1 [Reference]
>30	1139	82 (91.1)	1057 (42.9)	13.66 (6.58-8.36)
Operation time, min				
Mean (SD)	96.95 (18.40)	118.21 (19.15)	96.18 (17.90)	NA
<100	1533 (60.0)	10 (11.1)	1523 (61.8)	1 [Reference]
≥100	1023 (40.0)	80 (88.9)	943 (38.2)	12.92 (6.66-25.06)
Hypocalcemia				
Yes	549 (21.5)	41 (45.6)	508 (20.6)	3.23 (2.10-4.94)
Temporary	502 (19.7)	34 (37.8)	468 (19.0)	NA
Permanent	47 (1.8)	7 (7.8)	40 (1.6)	NA
No	2007 (88.5)	49 (54.4)	1958 (79.4)	1 [Reference]
Right lobe volume, mL				
Mean (SD)	20.20 (22.82)	63.66 (68.21)	18.62 (17.33)	NA
>20	2393 (93.6)	89 (98.9)	2304 (93.4)	6.25 (0.86-45.21)
>25	1826 (71.4)	83 (92.2))	1743 (70.7)	4.92 (2.26-10.68)
Left lobe volume, mL				
Mean (SD)	19.75 (31.26)	40.72 (37.92)	18.99 (30.73)	NA
>20	2410 (94.3)	90 (100)	2320 (94.1)	9.87 (0.61-159.89)
>25	1782 (69.7)	86 (95.6)	1696 (68.8)	9.76 (3.57-26.70)
Right lobe maximum diameter, mm				
Mean (SD)	44.96 (12.41)	64.32 (18.64)	44.25 (11.53)	NA
>45	2299 (89.9)	88 (97.8)	2211 (89.7)	5.07 (1.24-20.74)
>50	694 (27.2)	67 (74.4)	627 (25.4)	8.54 (5.28-13.84)
Left lobe maximum diameter, mm				
Mean (SD)	44.36 (16.48)	56.59 (14.21)	43.91 (16.39)	NA
>45	2446 (95.7)	90 (100)	2356 (95.5)	8.48 (0.52-137.63)
>50	659 (25.8)	58 (64.4)	601 (24.4)	5.62 (3.62-8.74)

Abbreviations: IONM, intraoperative neuromonitoring; NA, not applicable; OR, odds ratio; RLN, recurrent laryngeal nerve.

[a] Unless otherwise indicated, data are reported as number (percentage) of patients.

[b] Number needed to treat, 19.

there was a significant difference between the 2 groups in operation time greater than 100 minutes (OR, 6.29; 95% CI, 1.36-29.08). There was no significant difference when we examined the use of IONM, side of injury, or the presence of tumor.

Multivariate logistic regression showed that no use of IONM was an independent risk factor for RLN injury in patients who underwent total thyroidectomy (adjusted OR [AOR], 5.44; 95% CI, 3.26-9.09). Additional risk factors for RLN injury were the operative time greater than 100 minutes (AOR, 12.91; 95% CI, 6.66-25.06), maximum diameter greater than 45 mm of right thyroid lobe (AOR, 4.91; 95% CI, 3.12-8.56) and left thyroid lobe (AOR, 2.24; 95% CI, 1.39-4.32), extrathyroid extension (AOR, 3.26; 95% CI, 1.62-6.59), and tumor size greater than 10 mm (AOR, 3.24; 95% CI, 1.59-6.62). Also, incidental parathyroidectomy was strongly associated with RLN injury (AOR, 3.30; 95% CI, 2.13-5.09) (**Table 4**).

Discussion

In this study, we investigated whether the use of IONM can reduce the incidence of RLN injury in patients undergoing total thyroidectomy. The results of our analysis revealed that the use of IONM showed a significant relative risk reduction of temporary (1.9%) and permanent (0.7%) RLN injury. The multivariate analysis also showed that the no use of IONM was an independent risk factor for RLN injury.

The use of IONM increased the ability of our surgeons to reliably identify the RLN, and this is presumably one of the reasons for the significant decrease of RLN injuries and the increasing popularity of IONM. Also, IONM helped to verify the functional integrity of the RLN prior to ending the surgical operation and provided guidance for our surgeons in difficult cases with anatomic variants and extensive surgery.

Table 3. Pathological Characteristics of the Study Patients Undergoing Total Thyroidectomy With or Without RLN Injury[a]

Characteristic	Total Patients (n = 2556)	RLN Injury (n = 90)	No RLN Injury (n = 2466)	OR (95% CI)
Tumor				
Yes	848 (33.1)	33 (36.7)	815 (33.1)	1.17 (0.76-1.82)
No	1708 (66.9)	57 (63.3)	1651 (66.9)	1 [Reference]
Tumor size, mm				
Mean (SD)	9.26 (8.41)	14.34 (11.73)	9.06 (8.29)	NA
≤10	559 (65.9)	13 (39.4)	546 (67.0)	1 [Reference]
>10	289 (34.1)	20 (60.6)	259 (33.0)	3.25 (1.59-6.62)
Bilaterality				
Yes	224 (26.4)	10 (30.3)	214 (26.3)	0.82 (0.38-1.75)
No	624 (73.6)	23 (69.7)	601 (73.7)	1 [Reference]
Multifocality				
Yes	280 (33.0)	12 (36.4)	268 (32.9)	0.86 (0.42-1.77)
No	568 (67.0)	21 (63.6)	547 (67.1)	1 [Reference]
Autoimmunity				
Yes	914 (35.8)	35 (38.9)	879 (35.6)	0.87 (0.57-1.34)
No	1642 (64.2)	55 (61.1)	1587 (64.4)	1 [Reference]
Lymph node metastasis				
Yes	306 (36.1)	19 (57.6)	287 (35.2)	2.50 (1.23-5.05)
No	542 (63.9)	14 (42.4)	528 (64.8)	1 [Reference]
Thyroid capsular invasion				
Yes	422 (49.8)	23 (69.7)	399 (49.0)	2.40 (1.13-5.10)
No	426 (50.2)	10 (30.3)	416 (51.0)	1 [Reference]
Extrathyroidal extension				
Yes	216 (25.5)	16 (48.5)	200 (24.6)	2.89 (1.44-5.83)
No	632 (74.5)	17 (51.5)	615 (75.4)	1 [Reference]
Incidental parathyroidectomy				
Yes	469 (18.3)	54 (60.0)	415 (16.8)	7.41 (4.80-11.45)
No	2087 (81.7)	36 (40.0)	2051 (83.2)	1 [Reference]

Abbreviations: NA, not applicable; OR, odds ratio; RLN, recurrent laryngeal nerve.

[a] Unless otherwise indicated, data are reported as number (percentage) of patients.

Recurrent laryngeal nerve injury is a troublesome complication after thyroid surgery. Visual identification of the RLN during thyroid surgery is the gold standard, and it has been shown to be associated with lower rates of RLN paralysis, although postoperative vocal cord paralysis is not guaranteed.[5-8,16,17] Other authors have recommended that the nerve should be identified and dissected out along its course in all cases.[8,18]

Several factors influence the likelihood of injury to the nerve, including the underlying disease (eg, thyroid cancer, toxic goiter, large goiter, retrosternal goiter) and the experience of surgeon.[12,19] In addition, studies have reported that only 10% of nerve injuries are detected visually intraoperatively by surgeons.[10,20] Compression, thermal injury, ischemia, ligature, crushing, stretching, or traction can cause neurapraxia without anatomical interruption of the RLN.

For these reasons, IONM has been proposed and applied as an adjunct to standard visual identification of the RLN, aiming at unequivocal identification and functional control of the RLN. Intraoperative neuromonitoring devices convert muscle activity into acoustic and EMG signals. Several studies have demonstrated the benefits of IONM in thyroid surgery.[5,12,21] Barczynski et al[21] reported that temporary RLN paresis in patients with IONM is reduced by 2.9% in high-risk patients and 0.9% in low-risk patients. A meta-analysis of 8 articles with a total of 5257 nerves at risk revealed a significant effect of IONM in preventing transient RLN injuries (P = .04), but no definitive conclusion was reached regarding the association between IONM and permanent RLN injury.[22] Thomusch et al[12] confirmed that IONM significantly decreases the rate of postoperative temporary and permanent RLN paralyses.

In contrast, there are other studies that failed to confirm such benefits.[13,23] Beldi et al[23] reported that the incidence of RLN injury during thyroid surgery was not decreased by the use of IONM. A multicenter study that included 29 998 nerves at risk showed no statistical difference in the frequency of RLN palsy with the use of IONM compared with the use of visual identification only.[13] A detailed subgroup analysis revealed a significant difference in the incidence of permanent RLN palsy between high- and low-volume surgeons. For low-volume surgeons, the use of IONM reduced the incidence of permanent RLN palsy. However, in many challenging thyroid operations, even experienced surgeons may expect benefit from IONM.[13]

Calò et al[24] examined 2034 consecutive patients who underwent thyroidectomy by a single surgical team. They found that although IONM helps to identify the nerve, in particular

Table 4. Independent Risk Factors for RLN Injury by Multivariate Logistic Regression Analysis

Risk Factor	Adjusted Odds Ratio (95% CI)
No use of IONM	5.44 (3.26-9.09)
Operation time >100 min	12.91 (6.66-25.06)
Extrathyroid extension	3.26 (1.62-6.59)
Maximum diameter, mm	
Right lobe >45	4.91 (3.12-8.56)
Left lobe >45	2.24 (1.39-4.32)
Incidental parathyroidectomy	3.30 (2.13-5.09)
Tumor size >10 mm	3.24 (1.59-6.62)

Abbreviations: IONM, intraoperative neuromonitoring; RLN, recurrent laryngeal nerve.

in difficult cases, it did not decrease nerve injuries compared with visualization alone.[24]

Intraoperative neuromonitoring is not intended as a substitute for adequate surgical technique. The identification of nerves during neck surgery can be difficult even with extensive anatomical knowledge and surgical experience. Monitoring the RLN during thyroidectomy facilitates neural identification and dissection to avoid iatrogenic injury and helps in training of inexperienced surgeons.[10] Although these 2 functions are sufficient to consider IONM as a technology that allows a refinement in surgical technique and its outcome, IONM's main role is based on the ability of predicting intraoperatively postoperative glottis function. Therefore, the use of IONM may also facilitate intraoperative decision making for bilateral thyroid surgery.[25-27]

An additional benefit of IONM is its ability to guide the surgeon in the event of variations in the expected anatomic course of the inferior laryngeal nerve or in case of a nonrecurrent inferior laryngeal nerve where the risk of RLN increases significantly. Such variations include nonrecurrence mainly on the right side nerve displacement by thyroid nodularity or paratracheal lymphadenopathy, extralaryngeal branching of the RLN observed in 30% of patients, and variations in the nerve course in relation to the inferior thyroid artery and the Berry ligament.

Our results also showed that a thyroid carcinoma diagnosed on histopathological examination was not related to an increased rate of RLN injury. Interestingly, we found that there was a significantly increased rate of RLN injury in patients with thyroid carcinomas larger than 10 mm compared with microcarcinomas (<10 mm). In addition, patients with RLN injury had more frequent lymph node metastasis, thyroid capsular invasion, and extrathyroidal extension.

Moreover, it was interesting to find that the size of the thyroid was associated with the rate of RLN injury. Mean thyroid weight in patients with RLN injury was significantly increased compared with that in patients who did not have RLN injury. Maximum thyroid lobe diameter was significantly higher in patients with RLN injury than in the no-injury group. Maximum right thyroid lobe diameter greater than 45 mm and maximum left thyroid lobe diameter greater than 45 mm were each significantly associated with increased risk of RLN injury during surgery.

Our results showed that there was a group of patients with a higher risk of RLN injury. Patients with a large thyroid gland of maximum lobe diameter greater than 45 mm, tumor size greater than 10 mm, and extrathyroid extension experienced an increased incidence of RLN injury. In addition, some parameters related to surgery, such as no use of IONM, operation time greater than 100 minutes, incidental parathyroidectomy, and related postoperative hypocalcemia, were associated with increased risk of RLN.

Several factors favor the routine use of IONM: (1) the reliability of the system that is based on its regular use after an essential learning curve is indispensable; (2) it can aid in difficult cases of nerve identification and anatomic variants that are often unpredictable; and (3) it facilitates RLN identification and assesses RLN functional integrity. On the other hand, the cost of the device and its related endotracheal tube and the possibility of false-positive or false-negative responses can represent obstacles to routine use of this system.

Intraoperative neuromonitoring is a promising tool for nerve identification and protection in extended thyroid surgeries, reoperations, retrosternal goiters, advanced thyroid cancer cases, and cases of anatomical variations.[28-30] Several authors have reported that the use of IONM may improve the outcomes of surgery among patients with well-differentiated thyroid carcinoma by both increasing the completeness of total thyroidectomy and significantly reducing the prevalence of temporary RLN injury.[12,21]

The possible mechanism of this improvement is the aid in dissection at the level of the Berry ligament offered by IONM, which enhances the surgeon's ability to identify a branched RLN and allows for reduction in traction injury and neuroapraxia.[31] In addition to helping the surgeon navigate through challenging anatomies, IONM may lend itself as a routine adjunct to the gold standard of visual nerve identification.

A limitation of our study is its retrospective nature. Because this was a nonrandomized study, complete elimination of patient selection bias was not possible. However, we did not intentionally allocate patients to IONM or to control groups. Nerve monitoring was used based on instrument availability. Unfortunately, a prospective, randomized, 2-arm, multicentric study is difficult to perform because many patients and surgeons expect IONM to provide additional benefits, thus limiting randomization to a non-IONM control group.

Conclusions

This study showed that the use of IONM was associated with a significant decrease of temporary and permanent RLN injury. In our experience, the routine use of IONM allowed adequate familiarity with the device, reduced surgical pitfalls, and provided guidance for our surgeons in difficult cases with anatomic variations and patients at high risk for RLN injury. Other authors also reported that neuromonitoring helps to verify the functional integrity of the RLN prior to ending the surgical operation.[9,17,30] Finally, based on our current data, IONM is an adjunct that may be helpful during thyroidectomy, but it should never replace the meticulous technique of the surgeon.

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