



# The effect of intraoperative nerve monitor use on recurrent laryngeal nerve injury and hypocalcemia in benign thyroid diseases after total thyroidectomy or lobeisthmectomy: Thirteen years single surgeon experience

✉ Mehmet Emrah Ceylan<sup>a,\*</sup>, ✉ Mehmet Ercan Kesici<sup>b</sup>

<sup>a</sup>Private Davraz Yasam Hospital, Department of Otolaryngology, Isparta, Türkiye

<sup>b</sup>Private Davraz Yasam Hospital, Department of General Surgery, Isparta, Türkiye

## ARTICLE INFO

### Keywords:

Recurrent laryngeal nerve injury  
Hypocalcemia  
Thyroidectomy

Received: Nov 18, 2021

Accepted: Sep 21, 2022

Available Online: 27.09.2022

DOI:

[10.5455/annalsmedres.2021.11.625](https://doi.org/10.5455/annalsmedres.2021.11.625)

## Abstract

**Aim:** Hypocalcemia is the most common complication after thyroidectomy, and recurrent laryngeal nerve (RLN) injury is the most serious complication. In this study, we aimed to investigate the effect of intraoperative nerve monitor (IONM) use on postoperative RLN injury and hypocalcemia in a uniform low-variability group.

**Materials and Methods:** Between April 2007 and December 2020, data of patients who underwent surgery due to benign thyroid disease were retrospectively analyzed. Patients under 18 and over 65 years of age, having no euthyroid status during surgery, and having neoplastic pathologies were excluded from the study. A total of 428 patients were included in the study and were divided into two groups. There were 313 patients in Group 1 (non-IONM group) and 115 patients in Group 2 (IONM group). The correlation of the use of IONM with postoperative RLN injury and hypocalcemia was analyzed.

**Results:** There was no permanent vocal cord paralysis. Of the patients, transient vocal cord paresis was seen in 0.61%, transient hypocalcemia in 8.1%, and permanent hypocalcemia in 3.9%. There was no statistically significant difference between the groups regarding RLN injury; however, there was a significant difference in hypocalcemia between the groups ( $p=0,008$ ).

**Conclusion:** Our study results suggest that IONM use does not significantly reduce the risk of RLN injury, but decreases hypocalcemia, which is one of the most common complications of thyroid surgery, in patients with benign disease undergoing thyroid surgery. Further prospective studies in larger patient series are needed to investigate the IONM use considering pathological examination results, surgical techniques, and demographic data of patients.



Copyright © 2022 The author(s) - Available online at [www.annalsmedres.org](http://www.annalsmedres.org). This is an Open Access article distributed under the terms of Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

## Introduction

Hypocalcemia is the most common complication after thyroidectomy, and recurrent laryngeal nerve (RLN) injury is the most serious complication [1]. Hypocalcemia incidence after thyroidectomy is 1.2% to 40% [2]. Iatrogenic excision of the parathyroid glands or decreased blood supply after traumatic dissection during surgery may play a role in the etiology of hypocalcemia. Recurrent laryngeal nerve injury is a well-known cause of morbidity in thyroid surgery. Injury mechanisms may be traction, compression, or direct trauma to the nerve.

The use of an intraoperative nerve monitor (IONM) enables the identification of the RLN prior to visualization

during surgery and the evaluation of the RLN's functional integrity following surgery [3]. In order to prevent vocal cord palsy, use of IONM is advised, particularly in cases of revision surgery, bilateral surgery, and pre-existing RLN paralysis (4). In addition, IONM may provide gentle dissection and easier detection of RLN. This tissue-respectful surgery may provide lower hypocalcemia in patients undergoing thyroid surgery. The benefits of routine IONM use, in patients with benign thyroid disease, are still up for debate today. Despite early enthusiasm for IONM, the majority of studies have been unable to demonstrate a significant difference in the incidence of RLN injury between IONM and visualization alone [4].

In a recent meta-analysis, the prevalence of RLN injury was reported as 2.8 to 9.8% [4]. On the other hand, the prevalence varies, ranging from 0.3% to 38% in the litera-

\*Corresponding author:

Email address: [mrhcyln@gmail.com](mailto:mrhcyln@gmail.com) (✉ Mehmet Emrah Ceylan)

ture [3]. The reasons for the variation in the RLN injury in previous studies can be attributed to the differences in the definition of injury, the focus of previous studies on risk groups only, the use of data from large-volume centers with a low complication rate, variations in surgical techniques, and statistical analysis procedures applied [3, 5]. With a study that minimizes the number of variables, the relationship between IONM use and RLN damage may be shown more clearly.

In the present study, we aimed to investigate the effect of IONM use on postoperative RLN injury and hypocalcemia, particularly in a uniform group with low variability in benign thyroid diseases, in which total thyroidectomy or loboisthmectomy was performed by a single experienced surgeon.

## Materials and Methods

This study was conducted at the ear, nose and throat and general surgery clinics of Private Davraz Yaşam Hospital between April 2007 and December 2020. In order to determine the sample size, it was decided to screen the surgeries retrospectively, between the time the senior surgeon started working in the clinic and the ethics committee approval date.

### *Ethical considerations*

The study protocol was approved by the Süleyman Demirel University Clinical Research Ethics Committee (27.11.2020-375). A written informed consent was obtained from each patient for all diagnostic and therapeutic procedures. The study was conducted in accordance with the principles of the 1964 Declaration of Helsinki and its later amendments.

### *Study design and population*

The main inclusion criteria were: (1) unilateral loboisthmectomy or total thyroidectomy in a male or female patient; and (2) the presence of benign thyroid disease, including multinodular goitre and thyroiditis. The main exclusion criteria were: (1) pre-operative laryngeal palsy; (2) thyroid cancer (except tumor size <1 cm incidental papillary microcarcinoma); (3) lymph node dissection; (4) goitre with cervicothoracic or toxic goitre and complementary surgery; (5) Graves' disease; (6) having no euthyroid status during surgery; and (7) patients under 18 and over 65 years of age. All patients received the following pre-operative assessments: ultrasound examination of the neck, assays for serum thyroid-stimulating hormone and calcitonin levels, and indirect laryngoscopy. According to the inclusion and exclusion criteria, 428 of 552 patients operated by a single experienced surgeon were included in the study. The senior surgeon started to use IONM after January 2015. Before this date, visualization only technique was used. Patients were retrospectively assigned to one of two groups using an ordinal allocation based on the date IONM was introduced for randomization. The patients were divided into two groups according to the IONM use during surgery. There were 313 patients in Group 1 (non-IONM group) and 115 patients in Group 2 (IONM group). The primary outcome variable of this study was the use

of IONM in a uniform patient group with benign thyroid disease. The primary endpoint variables were hypocalcemia and vocal cord paralysis. The medical records of the patients were reviewed and the relationship between RLN injury, hypocalcemia, and IONM use during thyroid surgery was investigated.

### *Surgery technique*

All patients were operated under semi-fowler position with a low collar skin incision under general anesthesia. Subcutaneous tissue and platysma were incised, and the strap muscles were retracted laterally. Hemostasis was achieved using the LigaSure Precise™ (LigaSure Vascular Sealing System; Covidien LP, MA, USA) and the upper thyroid poles were tied with 2/0 silk sutures. The RLN was visualized in the tracheoesophageal groove in all patients. Loboisthmectomy was completed after resection of the tracheal ligamentous connections. In total thyroidectomy, these steps were applied for both sides. A negative-pressure Hemovac drain was used in all patients. An endotracheal-based system (Dr. Langer Medical GmbH, Germany) was used to visualize bilateral thyroarytenoid muscles. Neural stimulation (1.5 mA and 100 mV threshold) was performed with a disposable probe. The signal from RLN was acquired from the tracheoesophageal groove and retested after complete dissection.

### *Data collection and assessment*

Demographic characteristics, peri- and postoperative data of the patients were recorded. Vocal cords were examined by an ear, nose and throat specialist, preoperatively in all patients and if there was a high index of suspicion for postoperative complaints such as hoarseness, with a rigid endoscope. Permanent vocal cord paralysis was defined as an ongoing complaint for more than six months. Transient hypocalcemia was defined as a serum calcium concentration lower than 8.0 mg/dL for shorter than six months. Oral calcium ± vitamin D supplements and intravenous calcium gluconates were used to treat hypocalcemia. Data regarding postoperative RLN injury and hypocalcemia were compared between the groups to investigate a statistically significant correlation.

### *Statistical analysis*

Statistical analysis was performed using the SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed as mean ± standard deviation (SD) or number and frequency, where applicable. Continuous variables were analyzed using the independent samples t-test, while categorical variables were analyzed using the chi-square test. The Fisher exact test was used to examine the association between the variables. A p value of <0.05 was considered statistically significant.

## Results

Of a total of 428 patients included in the study, 313 (608 nerves under risk) were in Group 1 and 115 (224 nerves under risk) were in Group 2. Demographic characteristics of the patients and the type of surgery are shown in Table 1.

**Table 1.** Demographic data of the patients and type of surgery.

	Group 1 (n=313)	Group 2 (n=115)	p
Age (Mean/SD)	43±11.4	45±11.2	0.098
Sex (M/F)	62/251	26/89	0.525
Total thyroidectomy (n,%)	295, (94)	109, (95)	0.832
Loboisthmectomy (n,%)	18, (6)	6, (5)	0.832
NUR (n,%)	608	224	

\* p < 0.05; NUR: Nerve Under Risk, M: Male, F: Female, SD: Standard Deviation.

**Table 2.** Distribution of pathologies.

Pathology	Group 1 (n, %)	Group 2 (n, %)	p
MNG	260 (83)	92 (80)	0.512
MNG + Hashimoto thyroiditis	25 (8)	13 (11)	0.285
Hashimoto thyroiditis	25 (8)	8 (7)	0.723
Hrthle cell adenoma	-	1 (1)	NA
De Quervain thyroiditis	3 (1)	-	NA
Follicular adenoma	-	1 (1)	NA
Total (n)	313	115	

\* p < 0.05; MNG: Multinodular Goiter; NA: Not Available.

**Table 3.** Distribution of complications.

Complication	Group 1 (n, %)	Group 2 (n, %)	p	Total (n, %)
Transient VC paresis	4, (0.6¥)	1, (0.5¶)	0.592	5, (0.6)
Hypocalcemia	46, (15)	6, (5)	0.008*	52, (12)
Transient	32, (10)	3, (2.6)	0.011*	35, (8.1)
Permanent	14, (4.4)	3, (2.6)	0.77	17, (3.9)
Hematoma	-	1	NA	1

\* \* p < 0.05; VC: Vocal cord, NUR: Nerve Under Risk, ¥: NUR=608, ¶: NUR=208, NA: Not Available.

The distribution of pathologies is given in Table 2. In Group 1, Hashimoto thyroiditis was present in 25 patients, a papillary microcarcinoma in 12, palpation thyroiditis in one, and de Quervain thyroiditis accompanied by multinodular goiter (MNG) in one, and papillary micro carcinomas accompanied by Hashimoto thyroiditis in three patients. In Group 2, 13 patients had Hashimoto thyroiditis, seven had papillary microcarcinomas accompanied by MNG, and one had follicular adenoma accompanied by Hashimoto thyroiditis. The overall incidental papillary microcarcinoma incidence was 5%.

In Group 1, one of the 18 patients who underwent loboisthmectomy had transient hypocalcemia. There was no other complication in the patients who underwent loboisthmec-

tomy in Group 2. Permanent vocal cord paralyses were not observed in both groups. Distribution of complications in both groups are summarized in Table 3. However, there was a statistically significant difference in the rate of transient hypocalcemia between the groups (p=0.011).

## Discussion

In the present study, we investigated the effects of IONM use on postoperative RLN injury and hypocalcemia. Our study results showed that hypocalcemia was statistically significantly lower in the IONM group. The same parathyroid gland preservation technique was used in all patients, and there was no parathyroid gland autotransplantation procedure in any of the groups.

In previous studies, the incidence of postoperative hypocalcemia is reported as 1.2 to 40% in thyroidectomy and 11.2% in surgery for benign thyroid diseases [2, 6]. In our study, hypocalcemia was 12%, consistent with the literature. During surgery, iatrogenic damage to the glands or their blood supply or unintentional excision of the parathyroid glands may cause postoperative hypocalcemia. On the other hand, there is a limited number of studies investigating hypocalcemia and IONM use in the literature. Cozzani et al. [7] reported reduced hypocalcemia with IONM use, although not statistically significant, and Demiryas et al. [8] reported a statistically significant lower rate of hypocalcemia with IONM use. In a review, Paduraru et al. [2] found that the gentle manipulation of parathyroid glands and their vessels during thyroidectomy represented a key approach to preventing postoperative hypocalcemia. We believe that the use of IONM may provide gentle dissection and easier detection of RLN. This tissue-respectful surgery may provide lower hypocalcemia in patients undergoing thyroid surgery for benign diseases.

Total thyroidectomy is recommended for the treatment of benign thyroid diseases with a low recurrence and complication rate [9,10]. In our clinic, total thyroidectomy has been widely used as the treatment of choice for the treatment of benign thyroid disease since 2007. Since the first utilization of IONM in 2016, total thyroidectomy has become the preferred surgery option. The effect of IONM use on RLN injury has been the subject of several studies. However, the relationship between them has not been clearly elucidated yet. In recent studies, as many patients as possible have been included to obtain more reliable results [3,11,12]. However, the results of multi-center studies and studies involving large numbers of patients are still contradictory, possibly due to the large number of variables. Therefore, we examined the effect of IONM use on RLN injury in patients operated for benign disease by a single experienced surgeon, as we hypothesized that determining the effect of IONM use on RLN injury in a patient group with low variability could give us a reliable result. In the literature, there are studies indicating a decline in transient vocal cord paresis [13-15] and permanent vocal cord paralysis [16] with the use of IONM, while some authors have shown no statistically significant difference [17-20]. In our study, the rate of RLN injury was 0.6%, and it was not statistically significantly decreased with the use of IONM in Group 2. Our findings are consistent with the

prospective, randomized study of Barczynski et al. [10] Although a recent study reported that the use of IONM in thyroidectomy for benign diseases did not reduce RLN injury, total thyroidectomy was not preferred in this study [21].

In a meta-analysis, Pisanu et al. [18] reviewed 20 studies including 35.513 nerves under risk and compared thyroidectomy with and without IONM. In this meta-analysis, no statistically significant difference was observed in the incidence of RLN injury with the use of IONM versus visualization alone during thyroidectomy. However, the authors reported that these results must be approached with caution and drew attention to the study conducted by Dralle et al. [22] in which a detailed subgroup analysis was performed and a significant reduction was found in the incidence of permanent RLN palsy in low-volume surgeons. Then, Pisanu et al. [18] concluded that further high-quality, multi-center, prospective, randomized studies using strict criteria of standardization and subsequent clustered meta-analysis were required to confirm these findings. Although our study has a retrospective design, we believe that our work may increase awareness on the standardization of the variables and the importance of subgroup analysis while reporting the effects of IONM use during thyroid surgery on RLN injury. In the meta-analysis of Bai et al. [23] in which the results were analyzed in subgroups to obtain more reliable results by reducing the variables, the risk of RLN injury in bilateral thyroid operations significantly decreased with the use of IONM. However, in this meta-analysis, the indications for bilateral operations were not reported.

In their unique meta-analysis, Brandon et al. [5] reported that IONM did not achieve a significant decline in the rate of RLN injury and concluded that most recent developments of IONM technology, including continuous vagal IONM and the concept of staged thyroidectomy in case of loss of signal on the first side to prevent bilateral RLN injury, could provide additional benefits. Consistent with these findings, we also consider that, in studies conducted with the adoption of staged thyroidectomy, the number of loboisthmectomy and total thyroidectomy should be given together, as in our study, to avoid bias. The surgeon may prefer loboisthmectomy rather than the initial surgical plan, if there is a signal loss during total thyroidectomy to prevent bilateral nerve injury.

The main limitations of this study are its single-center, retrospective design with a small sample size. Also, the international guidelines for intraoperative nerve monitoring only accept the results from studies using routine pre- and postoperative laryngoscopy [24]. The presence of hoarseness, or only if the patient has hoarseness, performing laryngoscopy cannot be accepted as a valid evaluation of paralysis. However, it should not be ignored that the rate of paralysis in this study is consistent with the literature. Another limitation is the possibility of a decrease in the frequency of hypocalcemia with the increased experience of the surgeon after 2007. Of note, the surgeon who performed all surgeries was already a senior surgeon with a 15-years of experience in 2007, which reduces this possibility.

## Conclusion

In conclusion, although the use of IONM did not significantly affect the RLN injury rates, it reduced postoperative transient hypocalcemia, which is the common complication of thyroid surgery, in patients with benign disease undergoing thyroid surgery. The use of IONM may provide gentle dissection and easier detection of RLN. This tissue-respectful surgery may yield lower hypocalcemia in patients undergoing thyroid surgery for benign disease. In further studies, while reporting the effects of IONM use in RLN injury during thyroid surgery, standardization of variables and examination of subgroup analyses may provide more reliable results, instead of including as many patients as possible, which causes heterogeneity. Thus, further standardized, well-designed, large-scale, prospective studies using subgroup analysis are needed. Also, we emphasize the importance of giving the number of loboisthmectomy and total thyroidectomy together to avoid bias in such studies.

## Acknowledgements

We thank Hasan Cem Irkilata, MD for his kind help for language editing and valuable technical assistance.

## Ethics approval

Süleyman Demirel University Clinical Research Ethics Committee (27/11/2020 26/375).

## References

1. Christou N, Mathonnet M. Complications after total thyroidectomy. *J Visc Surg* 2013;150:249-56.
2. Păduraru DN, Ion D, Carsote M. et al. Post-thyroidectomy Hypocalcemia - Risk Factors and Management. *Chirurgia (Bucur)* 2019;114:564-570.
3. Gunn A, Oyekunle T, Stang M. et al. Recurrent Laryngeal Nerve Injury After Thyroid Surgery: An Analysis of 11,370 Patients. *J Surg Res* 2020;255:42-49.
4. Cirocchi R, Arezzo A, D'Andrea V. et al. Intraoperative neuromonitoring versus visual nerve identification for prevention of recurrent laryngeal nerve injury in adults undergoing thyroid surgery. *Cochrane Database Syst Rev* 2019;1:CD012483.
5. Henry BM, Graves MJ, Vikse J. et al. The current state of intermittent intraoperative neural monitoring for prevention of recurrent laryngeal nerve injury during thyroidectomy: a PRISMA-compliant systematic review of overlapping meta-analyses. *Langenbecks Arch Surg* 2017;402:663-673.
6. Bellantone R, Lombardi CP, Bossola M. et al. Total thyroidectomy for management of benign thyroid disease: review of 526 cases. *World J Surg* 2002;26:1468-71.
7. Del Rio P, Cozzani F, Puteo N. et al. IONM and thyroidectomy in benign thyroid disease. Analysis of adverse events. *G Chir* 2019;40:174-181.
8. Demiryas S, Donmez T, Cekic E. Effect of nerve monitoring on complications of thyroid surgery. *North Clin Istanbul* 2018;5:14-19.
9. Efreimidou EI, Papageorgiou MS, Liratzopoulos N, Manolas KJ. The efficacy and safety of total thyroidectomy in the management of benign thyroid disease: a review of 932 cases. *Can J Surg* 2009;52:39-44.
10. Barczyński M, Konturek A, Hubalewska-Dydejczyk A. et al. Five-year follow-up of a randomized clinical trial of total thyroidectomy versus Dunhill operation versus bilateral subtotal thyroidectomy for multinodular nontoxic goiter. *World J Surg* 2010;34:1203-13.
11. Kim J, Graves CE, Jin C. et al. Intraoperative nerve monitoring is associated with a lower risk of recurrent laryngeal nerve injury: A national analysis of 17,610 patients. *Am J Surg.* 2021;221:472-477.

12. Jeannon JP, Orabi AA, Bruch GA. et al. Diagnosis of recurrent laryngeal nerve palsy after thyroidectomy: a systematic review. *Int J Clin Pract* 2009;63:624-9.
13. Yang S, Zhou L, Lu Z. et al. Systematic review with meta-analysis of intraoperative neuromonitoring during thyroidectomy. *Int J Surg* 2017;39:104-113.
14. Zheng S, Xu Z, Wei Y. et al. Effect of intraoperative neuromonitoring on recurrent laryngeal nerve palsy rates after thyroid surgery--a meta-analysis. *J Formos Med Assoc* 2013;112:463-72.
15. Wong KP, Mak KL, Wong CK, Lang BH. Systematic review and meta-analysis on intra-operative neuromonitoring in high-risk thyroidectomy. *Int J Surg* 2017;38:21-30.
16. Sun W, Liu J, Zhang H. et al. A meta-analysis of intraoperative neuromonitoring of recurrent laryngeal nerve palsy during thyroid reoperations. *Clin Endocrinol (Oxf)* 2017;87:572-580.
17. Malik R, Linos D. Intraoperative Neuromonitoring in Thyroid Surgery: A Systematic Review. *World J Surg* 2016;40:2051-8.
18. Pisanu A, Porceddu G, Podda M. et al. Systematic review with meta-analysis of studies comparing intraoperative neuromonitoring of recurrent laryngeal nerves versus visualization alone during thyroidectomy. *J Surg Res* 2014;188:152-61.
19. Lombardi CP, Carnassale G, Damiani G, . et al. "The final countdown": Is intraoperative, intermittent neuromonitoring really useful in preventing permanent nerve palsy? Evidence from a meta-analysis. *Surgery* 2016;160:1693-1706.
20. Sanabria A, Ramirez A, Kowalski LP. et al. Neuromonitoring in thyroidectomy: a meta-analysis of effectiveness from randomized controlled trials. *Eur Arch Otorhinolaryngol* 2013;270:2175-89.
21. Ling Y, Zhao J, Zhao Y. et al. Role of intraoperative neuromonitoring of recurrent laryngeal nerve in thyroid and parathyroid surgery. *J Int Med Res* 2020;48:300060520952646.
22. Dralle H, Sekulla C, Haerting J. et al. Risk factors of paralysis and functional outcome after recurrent laryngeal nerve monitoring in thyroid surgery. *Surgery* 2004;136:1310-22.
23. Bai B, Chen W. Protective Effects of Intraoperative Nerve Monitoring (IONM) for Recurrent Laryngeal Nerve Injury in Thyroidectomy: Meta-analysis. *Sci Rep* 2018;8:7761.
24. Randolph GW, Dralle H, Abdullah H. et al. Electrophysiologic recurrent laryngeal nerve monitoring during thyroid and parathyroid surgery: international standards guideline statement. *Laryngoscope* 2011;121:S1-16.