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CASE REPORT

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The utility of intraoperative nerve monitoring in secondary and tertiary Hyperparathyroid surgery

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Abstract

Objectives: Recurrent laryngeal nerve (RLN) injury is a well-known complication of parathyroid surgery. Despite ample data, there is still uncertainty about the role of intraoperative monitoring (IONM) in mitigating RLN damage.

Study Design: A retrospective review.

Methods: We included all patients presenting for total, subtotal, or completion parathyroidectomy at a tertiary referral hospital from 2013 to 2018. Information about demographics, previous neck surgery, perioperative data, pathology, and possible RLN injury was collected. Two groups were formed for analysis: IONM vs. non-monitored (NM).

Results: 105 patients underwent 107 surgeries with IONM utilized in 71 cases. The groups were similar in demographics, but significantly differed (all $P < 0.05$) in preincision parathyroid hormone level (IONM = 2091.44 vs NM = 1334.87), surgery type (IONM = 62.9% vs NM = 27.8% subtotal), and surgery length in minutes (IONM = 155.21 vs NM = 182.22). We observed six cases (6/71 = 8.45%) of persistent RLN complaints (three or more weeks postoperatively) and four cases (4/71 = 5.63%) of temporary complaints with the use of IONM compared with only one temporary complaint (1/36 = 2.78%) in unmonitored procedures ($P = 0.129$).

Conclusions: These results suggest that the use of IONM does not provide a protective effect on the RLN in patients with secondary or tertiary hyperparathyroidism undergoing total, subtotal, or completion parathyroidectomy. Prospective, randomized studies with pre- and postoperative flexible laryngoscopy are needed to explore the use of IONM in this patient population further.

KEYWORDS

anatomy, monitoring, parathyroid, recurrent laryngeal nerve, surgery

1 | INTRODUCTION

Injury to the recurrent laryngeal nerve (RLN) is one of the feared complications of thyroid and parathyroid surgery. Unilateral RLN injury can affect a patient's breathing, voice, and swallow function. Therefore, protecting the RLN is a key component of thyroid and parathyroid surgeries. Direct visualization of the nerve during surgery is considered the gold standard by many surgeons. Recently, however, intraoperative nerve monitoring (IONM) has gained popularity. Recent studies report similar rates of monitoring between general surgical and otolaryngology-trained surgeons, with approximately 40% to 45% in both groups using IONM in some or all cases.[1]

Several studies have attempted to evaluate the efficacy of IONM in reducing RLN injury. The majority of these studies have examined the effect of IONM on thyroid surgery specifically. A 2019 Cochrane review looked at randomized control trials in thyroidectomy surgeries and demonstrated no conclusive evidence for the superiority or inferiority of IONM over visual nerve identification alone during thyroidectomy surgery on any of the outcomes measured. There were similar operative times and occurrence of transient vs permanent RLN palsies.[2]

Prior studies have examined the use of IONM during parathyroidectomy—mainly focusing on parathyroidectomy for primary hyperparathyroidism. Again, these found no significant difference between the use of IONM vs no monitoring, suggesting that the use of IONM may not yield any additional benefit in preventing nerve injury.[3] Despite these results, the thought persists that the routine use of IONM may reduce pitfalls and provide guidance for surgeons in difficult cases, reoperations, and high-risk patients.[4] One could consider a surgery more difficult and complicated when all four parathyroid glands must be dissected and identified, rather than one gland only; such is the case when performing surgery for patients with secondary or tertiary hyperparathyroidism. Most end-stage renal disease (ESRD) patients who have secondary or tertiary hyperparathyroidism have multigland hyperplasia, for which a subtotal, near-total, or total parathyroidectomy is typically performed as the initial surgery. Theoretically, these surgeries create higher potential for RLN injury.

The purpose of this study was to assess the efficacy of IONM in preventing RLN injury during parathyroid surgery for secondary and tertiary hyperparathyroidism. In this study, we present a series of 107 patients who underwent parathyroid surgery, 36 without IONM and 71 with IONM. This study is the first, to our knowledge, to investigate the effects of IONM in patients with secondary or tertiary hyperparathyroidism undergoing total, subtotal, or completion parathyroidectomy.

2 | METHODS

Before beginning the study, institutional review board approval was granted from the University of Tennessee Health Science Center. The purpose of this study was to analyze operative times and surgical outcomes after total, subtotal, or completion parathyroidectomy with and without use of IONM. This was a retrospective study of 107 patients undergoing parathyroid surgery between January 2013 and June 2018. All patients had ESRD with secondary or tertiary hyperparathyroidism and underwent either total, subtotal, or completion parathyroid surgery.

Monitoring was performed using the MedTronic XoMed Tube Nerve Integrity Monitor. The anesthesiologist and the surgical team placed the NIM tube under visual guidance using a glidescope to confirm accurate position between the vocal cords. A probe was provided that was used to stimulate structures to identify the RLN. Throughout the surgery, there was continuous monitoring provided by a nerve monitoring technician. Figure 1 is a pictorial representation of our nerve monitoring setup.

We included all patients presenting for total, subtotal, or completion parathyroidectomy at a tertiary referral hospital from 2013 to 2018. Information about demographics, previous neck surgery, perioperative data, pathology, and possible RLN injury was collected. Two groups were formed for analysis: IONM vs. nonmonitored (NM). The surgeries were performed by two surgeons, each of which performed both monitored and nonmonitored surgeries. All surgeries included identification of all four parathyroid glands. The surgeries were categorized as either total, subtotal, or completion parathyroidectomy. Total parathyroidectomy signifies removal of all four glands. Subtotal signifies all glands are identified, but a portion of one gland was left in place. Completion parathyroidectomy signifies that the remaining gland from a prior parathyroid surgery was removed.

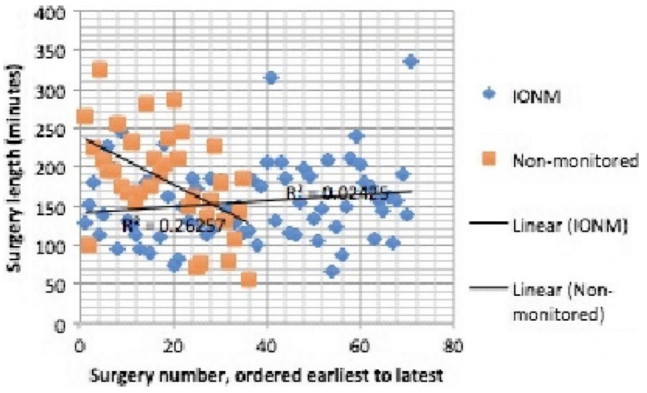

FIGURE 1 The MedTronic XoMed Tube Nerve Integrity monitor (NIM). This represents the setup used in our hospital for IONM. ETT: endotracheal tube

All patients were followed for a minimum of 90 days, during which postoperative vocal fold dysfunction could be documented in the outpatient setting. Flexible laryngoscopy was not performed routinely neither preoperatively nor postoperatively. Inpatient progress notes and clinic notes were searched for any documentation of voice changes or dysphagia, and this was utilized to indicate possible injury to RLN. Any notes from otolaryngology clinic were searched, and findings of flexible laryngoscopies performed pre- or post-op were collected as data.

After all information was collected, the number of patients with documented postoperative dysphonia or dysphagia was compared between both groups using a Fisher test. A threshold of 0.05 was set in order to determine any difference between the two groups.

3 | RESULTS

After review of the patients' medical records, a total of 107 patients were included in the study. These surgeries are subdivided into IONM vs NM. 71 of these surgeries had IONM, whereas 36 were nonmonitored (NM). The groups were similar in demographics, as demonstrated in Table 1. Of the monitored patients, 41 were women and 30 were men (mean age 47.45 years), whereas of the nonmonitored patients, 22 were women and 14 were men (mean age 47.67 years). A majority of patients overall were African American (98) versus Caucasian (9). Average body mass index was comparable between both groups—31.91 vs 30.85. There was no significant difference in preoperative calcium or BUN/Cr ratio between the two groups. However, there was a significantly higher intact serum PTH for patients who underwent IONM (2090.59) vs NM patients (1334.87).

Table 2 demonstrates the surgical characteristics of our patients. 56 patients underwent subtotal parathyroidectomy, of which 45 were monitored (80.4%). 45 patients underwent total parathyroidectomy (48.9% monitored), and 6 patients underwent completion parathyroidectomy (66.7% monitored). 12 patients had thyroidectomy or thyroid biopsy as part of their procedure (66.7% monitored).The weight of the parathyroid glands removed and the drop of PTH intraoperatively was similar between the IONM and NM groups with no significant difference found using t test and *P*-value of 0.05. There was a significant difference noted between IONM and NM for length of surgery. The average length of surgery in IONM was 155.21 minutes, compared with 182.22 minutes for the NM group. Using the two-sample t test, the p-value is calculated to be 0.019, which achieves significance for our set *P*-value of 0.04. Figure 2 is a plot of surgery length over time, comparing trends for the NM and IONM groups separately. The cases were organized chronologically along the x-axis, and the length of surgery in minutes was used on the y-axis. A line of best fit was created and the R^2 value calculated using Microsoft Excel.

The metrics used to estimate potential injury to RLN were documented dysphagia or dysphonia after surgery, since flexible laryngoscopy was not routinely performed. We separated this into temporary and persistent concern, as seen in Table 3. Temporary concern indicates dysphonia or dysphagia

TABLE 1 Baseline characteristics. Preoperative PTH was significantly higher for monitored vs nonmonitored group

Baseline characteristics			
	Monitored (n = 71)	**Nonmonitored (n = 36)**	***P*-value**
Age (mean ± SD)	47.45 ± 12.24	47.67 ± 12.35	0.932
Gender			
Male	30	14	
Female	41	22	0.738
Race			
African American	68	30	
Caucasian	3	6	0.028
Previous neck surgery			
Yes	4	4	
No	67	32	0.309
BMI (mean ± SD)	31.91 ± 9.35	30.85 ± 7.66	0.558
Preoperative intact PTH (mean ± SD)	2,090.59 ± 1,195.64	1,334.87 ± 798.99	0.0002
Preoperative calcium (mean % ± SD)	9.32 ± 0.92	9.33 ± 1.04	0.976
Preoperative BUN/Cr ratio (mean ± SD)	5.12 ± 2.86	5.23 ± 3.48	0.867

TABLE 2 Surgical characteristics of our cohort. Surgery times were significantly lower in the monitored group

Surgical characteristics			
	Monitored (n = 71)	**Nonmonitored (n = 36)**	***P*-value**
Type of surgery			
Subtotal parathyroidectomy	45	11	
Total parathyroidectomy	22	23	
Completion parathyroidectomy	4	2	
Intentional thyroid removal or biopsy			
Yes	8	4	
No	63	32	
Length of surgery in Mins (mean ± SD)	155.21 ± 50.83	182.22 ± 63.41	0.019
Weight of parathyroid in grams (mean ± SD)	3.72 ± 2.54	3.26 ± 3.75	0.52
Intraoperative intact PTH drop (mean % ± SD)	81.93 ± 28.93	86.84 ± 8.87	0.19

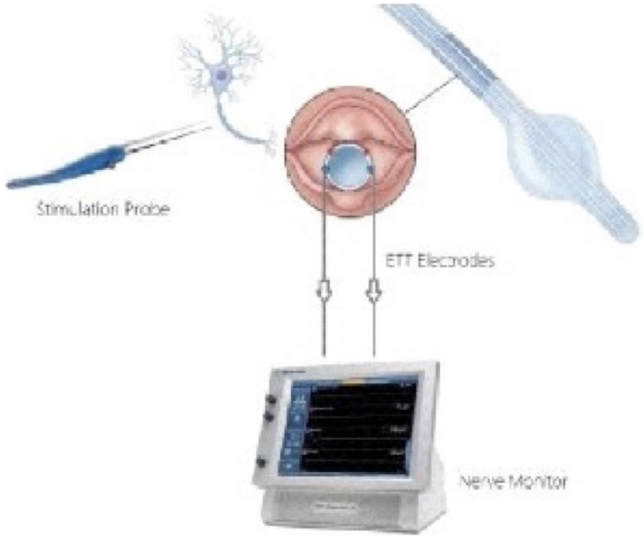

FIGURE 2 Surgery length trended over time. Surgery cases were ordered from earliest to latest and plotted according to surgery length, in minutes. Line of best fit was created and R^2 calculated for IONM vs NM data

TABLE 3 Documented dysphagia or dysphonia. Temporary concern was noted during inpatient stay. Persistent concern was noted at first post-op visit (>3 weeks' post-op)

Results			
	Monitored (n = 71)	**Nonmonitored (n = 36)**	***P*-value**
Postoperative dysphonia or dysphagia			
No documented concerns	61	35	
Temporary concern	4	1	
Persistent concern	6	0	0.129

documented in inpatient progress notes during the first few days after surgery, whereas persistent concern is those complaints documented during outpatient follow-up visits. These clinic visits occurred at least 3 weeks after surgery in our cohort. We observed six cases (6/71 = 8.45%) of persistent RLN complaints (three or more weeks postoperatively) and four cases (4/71 = 5.63%) of temporary complaints with the use of IONM compared with only one temporary complaint (1/36 = 2.78%) in the NM group. A Fisher's exact test was used to compare the two groups, yielding a p-value of 0.129. In Table 4, we document in more detail the patients who described postoperative dysphonia or dysphagia. Only two patients were seen in ENT clinic post-op, where flexible laryngoscopy was used to demonstrate left vocal cord weakness in one patient and left arytenoid hypomobility in another patient.

4 | DISCUSSION

Although IONM is widely used among head and neck surgeons, current evidence is lacking that it decreases surgery length or injury to the RLN in thyroid and parathyroid surgery. Randolph has published international standards and guidelines for electrophysiologic recurrent laryngeal nerve monitoring during thyroid and parathyroid surgery that include pre- and postoperative laryngoscopy and multiple episodes of vagus and recurrent laryngeal nerve stimulation.[1] However, no current studies exist

TABLE 4 Monitored and nonmonitored patients with postoperative dysphonia or dysphagia. Only two patients underwent laryngoscopy to evaluate vocal cord function

Monitored patients with postoperative dysphonia or dysphagia									
Patient #	**Age**	**Race**	**Gender**	**BMI**	**Previous neck surgery**	**Length of surgery**	**Thyroid tissue removed**	**Surgery type**	**Injury notes**
Possible temporary injury									
1	46	AA	F	51.6	NO	163	NO	T	Mild hoarseness in progress notes only
2	68	AA	F	25.4	NO	137	NO	ST	Dysphagia that resolved by first post-op clinic visit
3	25	AA	F	19.5	NO	119	NO	ST	Mild dysphagia in progress notes only
4	58	AA	F	34.8	YES	315	YES	C	Mild hoarseness in progress notes only
Mean	49.3			32.8		183.5			
Possible persistent injury									
5	69	AA	F	31.6	NO	110	NO	ST	Saw ENT post-op with left vocal cord weakness
6	69	AA	M	34.4	NO	184	NO	ST	Hoarseness in clinic approx. 1 month post-op
7	75	C	F	36	NO	185	NO	ST	Hoarseness in clinic approx. 3 weeks post-op
8	36	AA	M	46.1	NO	155	NO	ST	Saw ENT post-op with left arytenoid hypomobility
9	40	AA	M	28.7	NO	109	NO	ST	Voice weakness in clinic approx. 3 weeks post-op
10	46	AA	M	24.5	NO	335	NO	T	Voice changes in clinic approx. 3 weeks post-op
Average	53.8			33.5		179.7			

Nonmonitored patients with postoperative dysphonia or dysphagia									
Patient #	**Age**	**Race**	**Gender**	**BMI**	**Previous neck surgery**	**Length of surgery**	**Thyroid tissue removed**	**Surgery type**	**Injury notes**
1	40	AA	M	35.3	NO	286	NO	T	Mild hoarseness only in progress notes

documenting the use of IONM during parathyroid surgery specifically for secondary and tertiary hyperparathyroidism. This study is the first to examine IONM in this specific group.

An interesting finding of our study was the significant decrease in surgery length between the NM vs IONM group. There was a significant decrease in the length of surgery for patients who had IONM compared with the NM group, $P=.019$. There are several hypotheses that could explain this finding. It is possible that IONM increased surgeon comfort, allowing for more efficient dissection and confidence with surgical landmarks. The method of IONM was consistent between the two surgeons of our cohort. A greater number of patients were in the IONM (71) vs the NM group (36). Surgeries were completed between 2013 and 2018. Surgeries done later during the study period were more likely to be monitored compared with those done earlier in the period. One might consider that over time, surgeon efficiency would improve and surgery length would decrease, thus showing a decreased surgery length for the IONM group since these cases were more likely done later in the period. Figure 2 does demonstrate a line of best fit with a negative slope, indicating shorter surgery lengths over time for the nonmonitored group. However, this is not shown for the IONM group. Also, the R^2 value for these lines is low (0.26 for NM and 0.02 for IONM), indicating high variance. This does not support a decrease in surgery length over time hypothesis.

Our study does not prove that IONM provides any protective effect on the RLN in patients with secondary or tertiary hyperparathyroidism undergoing total, subtotal, or completion parathyroidectomy. The metrics used to document status of the RLN were limited to documentation of dysphonia or dysphagia. Using these metrics, we found no correlation between use of IONM and decreased dysphonia or dysphagia. Of course, injury to the RLN is only one entity among a list of those that could contribute to dysphonia or dysphagia in a postoperative patient. This is a limitation to our study, as it is well known that possible causes of dysphagia or dysphonia include intraoperative injury to the RLN or the external branch of the superior laryngeal nerve, vascular congestion, laryngeal edema, surgical trauma to the cricothyroid muscle or to the cricoarytenoid joint, endotracheal intubation–related trauma, surgical adhesions, strap muscle injury, lesions of the perithyroid neural plexus, and pain or psychological distress.[1] Only two patients of our patients who suffered dysphonia post-op underwent laryngoscopy to document vocal cord dysfunction, and these patients did not have laryngoscopy performed preoperatively. A clinical practice guideline produced in 2013 by the AAO HNS recommends preoperative laryngoscopy for all patients undergoing thyroidectomy and suggests extending the recommendation to parathyroidectomy as well. They also recommend laryngoscopy postoperatively for patients who report voice changes.[5] In future studies on this topic, pre- and postoperative laryngoscopy to document vocal cord function and RLN status would be essential.

Injury to the RLN is a rare complication of this type of surgery. Because its baseline occurrence is low, a statistical significance comparing two different groups, such as NM vs IONM, would need a large sample size. Over our study period at a tertiary care hospital, our sample size was limited to 107. Singh Ospina et al report a 0.9% occurrence of RLN for bilateral neck exploration parathyroidectomies (2471 patients).[6] With a low occurrence and goals to reach a *P*-value less than 0.05, a large sample size would be necessary. Future studies to look at outcomes for secondary and tertiary hyperparathyroidism could either be multiinstitutional to reach a sample size for which statistical significance could be met. Because IONM has become an unofficial standard of care and is so widespread, it is more difficult to find cases in which it is not used. A randomized control trial would be difficult to design as patients are more likely to wish for the most updated technology in patient care and would be less likely to accept nonmonitoring when nerve monitoring is available.

5 | CONCLUSION

Our results do not prove that the use of IONM provides a protective effect on the RLN in patients with secondary or tertiary hyperparathyroidism undergoing total, subtotal, or completion parathyroidectomy. In our cohort, IONM did decrease length of surgery. Future studies would need formal pre- and postoperative laryngoscopy and a larger sample size to adequately demonstrate a protective effect of the RLN using IONM in this specific population.

6 | ETHICAL CONSIDERATIONS

All issues related to ethics were taken into consideration throughout the study design and proposal and implemented during the research study itself. Informed consent was obtained, beneficence was made a top priority, and respect for confidentiality and privacy were upheld during the study and its various analysis and information assertion components.

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None.

CONFLICTS OF INTEREST

The authors report no relevant financial disclosures related to this current work.

AUTHOR CONTRIBUTIONS

Samuel Dudley, MD: collected data, and wrote and edited the article. Nosratollah Nezakatgoo MD: collected data, and wrote and edited the article. Tyler M Rist MD: collected data, and wrote and edited the article. Courtney Brooke Shires, MD: collected data, and wrote and edited the article. Theodore Klug, MD, MPH: collected data, and wrote and edited the article.

DATA AVAILABILITY STATEMENT

Data are available upon request.

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