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Intraoperative Nerve Monitoring in Thyroidectomies for Malignancy: Does it Matter?

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Abstract

Background: Recurrent laryngeal nerve (RLN) injury and postoperative hypocalcemia are potential complications of thyroidectomy, particularly in malignancy. Intraoperative nerve monitoring (IONM) remains controversial. We sought to evaluate the impact of IONM on these complications using a national data set.

Methods: The American College of Surgeons National Surgical Quality Improvement Program thyroidectomy-targeted data set was queried for patients who underwent thyroidectomies from 2016 to 2017. Patients were grouped according to IONM use. Logistic regression models were constructed to evaluate associations of variables with 30-day hypocalcemic events (HCEs) and RLN injury. Associations were expressed as odds ratios (ORs) with 95% confidence intervals (95% CIs). A subgroup analysis was performed of patients with malignancy.

Results: A total of 9527 patients were identified; 5969 (62.7%) underwent thyroidectomy with IONM and 3558 (37.3%) without. By multivariable analysis, IONM had protective associations with HCE (OR = .81, 95% CI = .68-.96; *P* = .013) and RLN injury (OR = .83, 95% CI = .69-.98; *P* = .033). Malignancy increased risk of HCE (OR = 1.21, 95% CI=1.01-1.45; *P* = .038) and RLN injury (OR = 1.22, 95% CI = 1.02-1.46; *P* = .034). A large proportion (5943/9527, 62.4%) of patients had malignancy; 3646 (61.3%) underwent thyroidectomy with IONM and 2297 (38.7%) without. In the subgroup analysis, IONM had stronger protective associations with HCE (OR = .73, 95% CI = .60-.90; *P* = .003) and RLN injury (OR = .76, 95% CI = .62-.94; *P* = .012).

Discussion: Malignancy was associated with increased risk of HCE and RLN injury. Intraoperative nerve monitoring had a protective association with HCE and RLN injury, both overall, and in the malignant subgroup. Intraoperative nerve monitoring was correlated with improved thyroidectomy outcomes, especially if the indication was malignancy. This warrants further study to clarify cause and effect.

Keywords
thyroidectomy, thyroid cancer, intraoperative nerve monitoring, recurrent laryngeal nerve injury, hypocalcemia

Introduction

Patients undergoing thyroidectomy are exposed to the standard risks of any surgery, including bleeding and infection, but also the specific risks of recurrent laryngeal nerve (RLN) injury and symptomatic hypocalcemia.[1,2] These complications are relatively well studied among cohorts that include thyroidectomies performed for all indications.[1-3] Factors identified that influence rates of these complications include lower surgeon volume and the presence of thyroiditis.[3,4]

Factors associated with complications in patients who undergo thyroidectomy for malignancy are not as well studied. There is some evidence that malignancy may be associated with higher rates of postoperative complications, but this has not been conclusively proven.[1,2,5] Theorized reasons for this include the desmoplastic

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reaction induced by the tumor and more extensive and aggressive surgery in the setting of cancerous or indeterminate fine-needle aspiration biopsy results.[5,6] In an effort to reduce the risk of RLN injury, intraoperative nerve monitoring (IONM) was developed. Intraoperative nerve monitoring aids in RLN identification, and as a result, better defines the anatomy of surrounding structures, including the parathyroid glands, thyroid arteries, and thyroid veins.[9] Even so, there has been vigorous debate regarding its value, with numerous conflicting studies reported.[7-10]

Due to our belief that IONM helps define anatomy, we hypothesized that IONM lowers rates of RLN injury and hypocalcemic events (HCEs). We felt IONM would be especially beneficial in those with malignancy, where anatomy is more likely to be altered and dissection more likely to be extensive. To test this hypothesis, we employed the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) thyroidectomy-targeted data set.

Methods

Due to the deidentified and publicly available nature of the data, this study was deemed exempt from review by our institutional review board.

Data Source and Patient Selection

The ACS-NSQIP thyroidectomy-targeted data set is nationally validated, obtained by reviewers trained specifically for ACS-NSQIP data collection at each participating site, and annually audited by the ACS to ensure interrater reliability. The general data set includes over 150 variables, including preoperative patient characteristics, intraoperative factors, and postoperative complications up to 30 days. The thyroidectomy-targeted data set adds thyroidectomy-specific variables unavailable in other national data sets, including intraoperative factors and postoperative complications.

The ACS-NSQIP thyroidectomy-targeted data set was queried for adult (age 18 years and above) patients who underwent thyroidectomies (Current Procedural Terminology codes: 60220, 60225, 60240, 60252, 60254, 60270, and 60271), from January 2016 to December 2017. Exclusion criteria included nonelective surgery (n = 145, 1.4%), surgery performed by specialties other than general surgery and otolaryngology (n = 29, .3%), and approaches other than planned open (n = 58, .6%). Those with missing data regarding analyzed variables were also excluded (n = 565, 5.5%) (Figure 1).

Variables analyzed included demographic, clinicopathologic, intraoperative, and postoperative variables. Demographic and clinicopathologic variables included age, body mass index, sex, American Society of Anesthesiologists (ASA) class, and malignant pathology. Intraoperative and postoperative variables included central neck dissection (CND) performance, use of vessel sealant devices (VSDs), use of IONM, 30-day readmission, 30-day HCE, and RLN injury. Hypocalcemic events were defined as events of clinically significant hypocalcemia requiring treatment. Recurrent laryngeal nerve injury was analyzed as a categorical variable, with the presence of injury inclusive of both mild and severe hoarseness.

Statistical Analyses

Patients were stratified based on IONM use and variables compared between groups. A subgroup analysis of those with malignancy was compared in a similar fashion after being stratified by IONM use. Descriptive statistics were reported as means with standard deviations for continuous variables, and totals with percentages for categorical variables. Variables were compared using Student's t-tests or chi-square tests as appropriate.

Our outcomes of interest were 30-day readmission, 30-day HCE, and RLN injury. In order to assess associations of variables with our outcomes of interest, univariate and multivariable logistic regression models were created. The multivariable model included age, body mass index, sex, ASA class, use of IONM, use of VSD, malignant pathology, and performance of CND. A subgroup analysis of patients with malignancy was performed with the same statistical method. Associations of variables with the outcomes of interest were expressed as odds ratios (ORs) with 95% confidence intervals (95% CIs), along with P-values. Significance was established at $P < .05$. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, North Carolina).

Results

Descriptive Statistics

A total of 9527 patients met inclusion criteria. Of these, 5969 (62.7%) underwent surgery with IONM and 3558 (37.3%) without (Table 1). The IONM group had a higher body mass index (31.0 ± 7.8 kg/m^2 vs. 30.3 ± 7.7 kg/m^2; $P < .001$), more benign pathology (38.9% vs. 35.4%; $P < .001$), higher rates of VSD use (73.6% vs. 57.9%; $P < .001$), and higher rates of CND performance (28.1% vs. 18.9%; $P < .001$). The malignancy subgroup consisted of 5943 (62.4% of total) patients, 3646 (61.3%) of which underwent surgery with IONM and 2297 (38.7%) without. In the malignancy subgroup, the IONM group had higher rates of VSD use (69.1% vs. 56.9%; $P < .001$) and higher rates of CND performance (34.3% vs. 23.6%; $P < .001$).

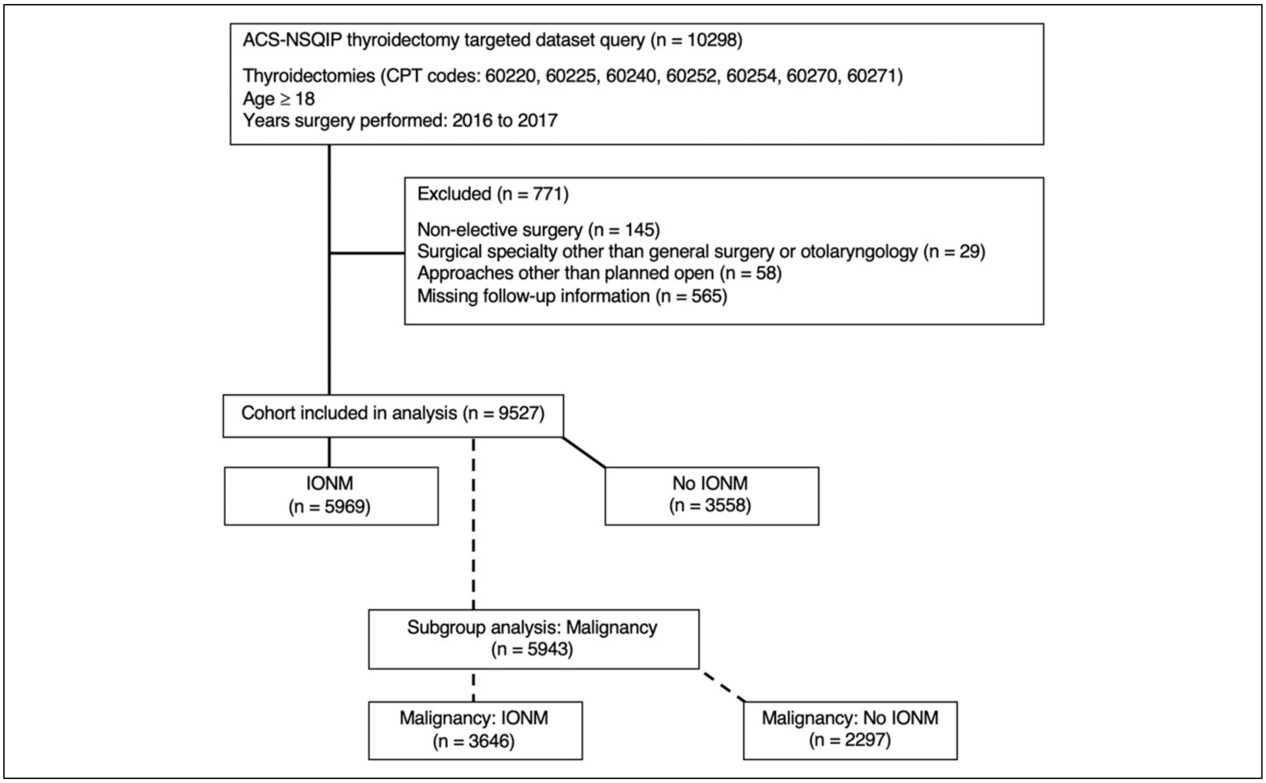

Figure 1. Data sorting process from initial ACS-NSQIP thyroidectomy-targeted data set query to final cohort and subgroup selection. Abbreviations: ACS-NSQIP, American College of Surgeons National Surgical Quality Improvement Program; CPT, Current Procedural Terminology; IONM, intraoperative nerve monitoring.

All Patients: Predictors of 30-Day Readmission, HCE, and RLN Injury

Logistic regression analyses of all patients for associations of variables with 30-day readmission are shown in Table 2. By multivariable analysis, higher ASA class (ASA 3-4 vs. reference 1-2: OR = 1.93, 95% CI 1.47-2.53; $P < .001$) and performance of CND (OR = 1.44, 95% CI 1.10-1.89; $P = .008$) were associated with 30-day readmission.

Logistic regression analyses of all patients for associations of variables with 30-day HCE are shown in Table 3. By multivariable analysis, increasing age (age per 5-year increase: OR = .90, 95% CI .88-.93; $P < .001$), male sex (OR = .71, 95% CI .57-.88; $P = .002$), and IONM use (OR = .81, 95% CI 0.68-.96; $P = .013$) were protected against 30-day HCE. Higher ASA class (3-4 vs. reference 1-2: OR = 1.23, 95% CI 1.01-1.49; $P = .036$), malignant pathology (OR = 1.21, 95% CI 1.01-1.45; $P = .038$), and performance of CND (OR = 2.25, 95% CI 1.89-2.67; $P < .001$) were associated with 30-day HCE.

Logistic regression analyses of all patients for associations of variables with RLN injury are shown in Table 4. By multivariable analysis, increasing age (age per 5-year increase: OR = 1.07, 95% CI 1.03-1.10; $P < .001$), malignant pathology (OR = 1.22, 95% CI 1.02-1.46; $P = .034$), and performance of CND (OR = 1.29, 95% CI 1.06-1.56; $P = .010$) were associated with RLN injury, while IONM use (OR = .83, 95% CI 0.69-.98; $P = .033$) was protected against RLN injury.

Patients With Malignancy: Predictors of 30-Day Readmission, HCE, and RLN Injury

Subgroup analyses of patients with malignant pathology were then performed. Univariate and multivariable logistic regression analyses of patients with malignant pathology for associations of variables with 30-day readmission are shown in Table 2. There were no significant associations by multivariable analysis.

Logistic regression analyses of patients with malignant pathology for associations of variables with 30-day HCE are shown in Table 3. By multivariable analysis, increasing age (age per 5-year increase: OR = .91, 95% CI .88-.94; $P < .001$), male sex (OR = .70, 95% CI .54-.90; $P = .005$), and IONM use (OR = .73, 95% CI .60-.90; $P = .003$) protected against 30-day HCE, while performance of CND (OR = 2.59, 95% CI 2.12-3.17; $P < .001$) was associated with 30-day HCE.

Table 1. Comparison of Demographics, Clinicopathologic, Intraoperative, and Postoperative Variables Between No IONM and IONM Groups.

All patients			
Variable	No IONM (n = 3558)	IONM (n = 5969)	*P*-value
Age, years (mean ± SD)	51.8 ± 14.8	51.5 ± 14.9	.300
Body mass index, kg/m^2 (mean ± SD)	30.3 ± 7.4	31.0 ± 7.8	<.001
Sex			
Female	2762 (77.6%)	4707 (78.9%)	.160
Male	796 (22.4%)	1262 (21.1%)	
ASA class			
1	230 (6.5%)	409 (6.9%)	.020
2	2146 (60.3%)	3408 (57.1%)	
3	1116 (31.4%)	2041 (34.2%)	
4	66 (1.9%)	111 (1.9%)	
Use of VSD	2060 (57.9%)	4395 (73.6%)	<.001
Malignancy	2297 (64.6%)	3646 (61.1%)	.001
Central neck dissection	674 (18.9%)	1676 (28.1%)	<.001
30-day readmission	104 (2.9%)	167 (2.8%)	.720
30-day HCE	260 (7.4%)	381 (6.7%)	.150
RLN injury	238 (6.7%)	342 (5.7%)	.058
Patients with malignancy			
Variable	No IONM (n = 2297)	IONM (n = 3646)	*P*-value
Age, years (mean ± SD)	10.3 ± 3.0	10.3 ± 3.0	.780
Body mass index, kg/m^2 (mean ± SD)	6.1 ± 1.5	6.1 ± 1.5	.260
Sex			
Female	1739 (75.7%)	2793 (76.6%)	.430
Male	558 (24.3%)	853 (23.4%)	
ASA class			
1	160 (7.0%)	309 (8.5%)	.063
2	1377 (59.9%)	2125 (58.3%)	
3	716 (31.2%)	1161 (31.8%)	
4	44 (1.9%)	51 (1.4%)	
Use of VSD	1307 (56.9%)	2520 (69.1%)	<.001
Central neck dissection	543 (23.6%)	1250 (34.3%)	<.001
30-day readmission	73 (3.2%)	96 (2.6%)	.720
30-day HCE	192 (8.5%)	256 (7.2%)	.082
RLN injury	167 (7.3%)	221 (6.1%)	.066

Abbreviations: ASAs, American Society of Anesthesiologists; HCE, hypocalcemic events; IONM, intraoperative nerve monitoring; RLN, recurrent laryngeal nerve; SD, standard deviation; VSD, vessel sealant device.

Logistic regression analyses of patients with malignant pathology for associations of variables with RLN injury are shown in Table 4. By multivariable analysis, increasing age (age per 5-year increase: OR = 1.07, 95% CI 1.03-1.11; $P < .001$), use of VSD (OR = 1.26, 95% CI 1.01-1.58; $P = .043$), and performance of CND (OR = 1.56, 95% CI 1.26-1.95; $P < .001$) were associated with RLN injury, while IONM use (OR = .76, 95% CI .62-.94; $P = .012$) was protected against RLN injury.

Discussion

In this study, we used the ACS-NSQIP thyroidectomy-targeted data set to analyze associations between IONM use and rates of 30-day readmission, HCE, and RLN injury in patients who underwent elective open thyroidectomies. We then performed a subgroup analysis of patients with malignancy. Intraoperative nerve monitoring use had a protective association with HCE and RLN injury

Table 2. Univariate and Multivariable Logistic Regression Analyses of Variables and Associations With 30-Day Readmission Among All Patients, and Among Patients With Malignancy.

All patients—30-day readmission analysis					
Variable	Comparison	Univariate OR (95% CI)	*P*-value	Multivariable OR (95% CI)	*P*-value
Age (per 5 year increase)		1.01 (.97, 1.05)	.579	.98 (.94, 1.02)	.361
BMI (per 5 kg/m^2 increase)		1.00 (.92, 1.08)	.941	.93 (.86, 1.02)	.112
Sex	Male vs. female	1.13 (.85, 1.50)	.414	1.04 (.78, 1.39)	.811
ASA class	3/4 vs. 1/2	1.74 (1.37, 2.22)	<.001	1.93 (1.47, 2.53)	<.001
IONM	Yes vs. no	.96 (.75, 1.23)	.722	.89 (.69, 1.15)	.380
Use of VSD	Yes vs. no	1.10 (.85, 1.43)	.478	1.13 (.86, 1.48)	.381
Malignancy	Yes vs. no	1.00 (.78, 1.28)	.995	.96 (.75, 1.25)	.778
Central neck dissection	Yes vs. no	1.41 (1.09, 1.83)	.010	1.44 (1.10, 1.89)	.008
Malignancy patients—30-day readmission analysis					
Variable	Comparison	Univariate OR (95% CI)	*P*-value	Multivariable OR (95% CI)	*P*-value
Age (per 5 year increase)		.99 (.95, 1.05)	.843	.97 (.92, 1.03)	.352
BMI (per 5 kg/m^2 increase)		1.00 (.90, 1.11)	.981	.96 (.86, 1.07)	.491
Sex	Male vs. female	1.10 (.77, 1.56)	.598	1.02 (.71, 1.46)	.915
ASA class	3/4 vs. 1/2	.65 (.15, 2.89)	.603	.77 (.17, 3.56)	.698
IONM	Yes vs. no	.82 (.60, 1.12)	.219	.78 (.57, 1.08)	.132
Use of VSD	Yes vs. no	.93 (.68, 1.27)	.645	.99 (.71, 1.37)	.939
Central neck dissection	Yes vs. no	1.35 (.99, 1.86)	.062	1.35 (.97, 1.88)	.071

Abbreviations: ASAs, American Society of Anesthesiologists; BMI, body mass index; IONM, intraoperative nerve monitoring; OR, odds ratio; VSD vessel sealant device.

Table 3. Univariate and Multivariable Logistic Regression Analyses of Variables and Associations With 30-Day Hypocalcemic Events Among All Patients, and Among Patients With Malignancy.

All patients—30-day HCE analysis					
Variable	Comparison	Univariate OR (95% CI)	*P*-value	Multivariable OR (95% CI)	*P*-value
Age (per 5 year increase)		.90 (.88, .92)	<.001	.90 (.88, .93)	<.001
BMI (per 5 kg/m^2 increase)		.94 (.89, .99)	.028	.95 (.90, 1.01)	.080
Sex	Male vs. female	.74 (.60, .91)	.004	.71 (.57, .88)	.002
ASA class	3/4 vs. 1/2	.91 (.77, 1.08)	.266	1.23 (1.01, 1.49)	.036
IONM	Yes vs. no	.89 (.75, 1.05)	.154	.81 (.68, .96)	.013
Use of VSD	Yes vs. no	.85 (.72, 1.01)	.066	.96 (.80, 1.14)	.604
Malignancy	Yes vs. no	1.40 (1.18, 1.67)	<.001	1.21 (1.01, 1.45)	.038
Central neck dissection	Yes vs. no	2.36 (2.00, 2.78)	<.001	2.25 (1.89, 2.67)	<.001
Malignancy patients—30-day HCE analysis					
Variable	Comparison	UnivariateOR (95% CI)	*P*-value	MultivariableOR (95% CI)	*P*-value
Age (per 5 year increase)		.90 (.87, .93)	<.001	.91 (.88, .94)	<.001
BMI (per 5 kg/m^2 increase)		.92 (.85, .98)	.012	.93 (.87, 1.00)	.063
Sex	Male vs female	.72 (.56, .92)	.009	.70 (.54, .90)	.005
ASA class	3/4 vs 1/2	.85 (.69, 1.05)	.125	1.15 (.91, 1.46)	.244
IONM	Yes vs no	.84 (.69, 1.02)	.082	.73 (.60, .90)	.003
Use of VSD	Yes vs no	.92 (.75, 1.12)	.390	1.06 (.86, 1.30)	.580
Central neck dissection	Yes vs no	2.57 (2.12, 3.13)	<.001	2.59 (2.12, 3.17)	<.001

Abbreviations: ASAs, American Society of Anesthesiologists; BMI, body mass index; HCE, hypocalcemic events; IONM, intraoperative nerve monitoring; OR, odds ratio; VSD, vessel sealant device.

Table 4. Univariate and Multivariable Logistic Regression Analyses of Variables and Associations With Recurrent Laryngeal Nerve Injury Among All Patients, and Among Patients With Malignancy.

All patients—RLN injury analysis					
Variable	Comparison	Univariate OR (95% CI)	*P*-value	Multivariable OR (95% CI)	*P*-value
Age (per 5 year increase)		1.07 (1.04, 1.10)	<.001	1.07 (1.03, 1.10)	<.001
BMI (per 5 kg/m^2 increase)		1.00 (.95, 1.06)	.982	.99 (.93, 1.05)	.748
Sex	Male vs. female	.99 (.80, 1.21)	.894	.91 (.74, 1.11)	.350
ASA class	3/4 vs. 1/2	1.25 (1.05, 1.48)	.012	1.16 (.95, 1.40)	.140
IONM	Yes vs. no	.85 (.71, 1.01)	.058	.83 (.69, .98)	.033
Use of VSD	Yes vs. no	1.01 (.84, 1.21)	.925	1.07 (.89, 1.29)	.462
Malignancy	Yes vs. no	1.23 (1.03, 1.47)	.021	1.22 (1.02, 1.46)	.034
Central neck dissection	Yes vs. no	1.24 (1.03, 1.50)	.023	1.29 (1.06, 1.56)	.010
Malignancy patients—RLN injury analysis					
Variable	Comparison	UnivariateOR (95% CI)	*P*-value	MultivariableOR (95% CI)	*P*-value
Age (per 5 year increase)		1.07 (1.04, 1.11)	<.001	1.07 (1.03, 1.11)	<.001
BMI (per 5 kg/m^2 increase)		1.01 (.94, 1.08)	.752	.99 (.92, 1.07)	.791
Sex	Male vs. female	.98 (.77, 1.25)	.891	.89 (.70, 1.14)	.375
ASA class	3/4 vs. 1/2	1.38 (1.12, 1.71)	.002	1.25 (.99, 1.58)	.065
IONM	Yes vs. no	.82 (.67, 1.01)	.067	.76 (.62, .94)	.012
Use of VSD	Yes vs. no	1.18 (.94, 1.46)	.150	1.26 (1.01, 1.58)	.043
Central neck dissection	Yes vs. no	1.40 (1.13, 1.73)	.002	1.56 (1.26, 1.95)	<.001

Abbreviations: ASAs, American Society of Anesthesiologists; BMI, body mass index; IONM, intraoperative nerve monitoring; OR, odds ratio; RLN, recurrent laryngeal nerve injury; VSD, vessel sealant device.

among all patients, including those with a cancer diagnosis. Interestingly, the association was more pronounced in the malignancy subgroup.

Knowledge about the incidence of complications following thyroid surgery is crucial for patient counseling and for assessment of quality outcomes. Recognizing patient, surgeon, and disease factors that may increase or decrease the frequency of these complications allows for more individualized and granular risk stratification. One factor that has been reported as potentially influential is malignant vs benign pathology.[1-6] Theorized reasons for increased complication rates among patients with malignancy undergoing thyroidectomy include desmoplastic tissue reactions that obscure anatomy, and need for more extensive dissection, even when formal neck dissection does not take place.[5,6] Intraoperative nerve monitoring was developed as an intraoperative adjunct to help with anatomic definition through identification of nervous structures. We hypothesized that this adjunct would be especially helpful in those with malignancy, due to the critical anatomic relationships of various structures with the RLN.[11,12]

Postoperative hypocalcemia after thyroidectomy is a well-known complication, with a generally accepted etiology of transient "stunning" (usually temporary but occasionally permanent) via devascularization of the parathyroid glands.[13,14] Associations between disruption of arterial supply or venous drainage of the parathyroid glands and postoperative hypocalcemia have been described.[15-17] This is a complication that would seem to be directly related to anatomic definition, something IONM may be useful for. One single-center study from 2017 analyzed 328 patients who underwent total thyroidectomy and identified malignant pathology and CND as risk factors for postoperative hypocalcemia.[3] Our study confirmed these findings by identifying the same risk factors, supporting the hypothesis that anatomic definition may aid in prevention of postoperative hypocalcemia. However, the previous study did not include IONM use as a variable in their study, nor do others that attempt to identify risk factors for postoperative hypocalcemia.[3,13,14] Our study results—that IONM may be protective against development of postoperative hypocalcemia—are novel and essential due to this gap in the literature.

Recurrent laryngeal nerve injury can result from transection, excessive dissection, tension, or heat exposure. In theory, the risk of this complication is greater with malignancy as these cases often require more extensive dissection and are in the setting of desmoplastic tissue reaction.[5] Intraoperative nerve monitoring was developed and promoted as a possible tool to reduce the risk of RLN injury. At its inception, it was a promising technology whose proponents argued that it could potentially minimize nerve injury and help define anatomy. Evidence, however, has been mixed regarding its utility.[7-10] Several single-center, long-term retrospective studies have reported that IONM use reduced RLN injury. However, other studies have failed to corroborate this protective effect. Due to this, consensus guidelines from the American Association of Endocrine Surgeons discuss IONM use merely as an adjunct that may be helpful in the dissection without necessarily preventing RLN injury.[2] For particular thyroidectomy cases, including for a malignant diagnosis, IONM has shown its benefits more clearly. For example, one single-center study analyzed outcomes of IONM use during total thyroidectomy for well-differentiated thyroid cancer.[6] They concluded that IONM use resulted in lower early RLN injury rates (3% vs. 6.7%), and aided in more thorough resection as measured by levels of postoperative radioactive iodine uptake (uptake lower than 1% in 70.2% vs. 25.2%). This again supports the hypothesis that IONM assists with anatomic definition, which results in improved outcomes. Our study confirmed that malignancy is an independent risk factor for RLN injury and that IONM was particularly helpful at reducing RLN injuries in this group.

Several studies have suggested that IONM can be protective, particularly when used by experienced surgeons.[8,10] The idea of a learning curve raises the possibility that the association between employment of IONM and reduced complications does not directly relate to its intraoperative utility.[10] Although we formed our hypothesis based on the assumption that complications could be avoided with better anatomic definition, it is possible that IONM use may be an indicator of treatment by higher volume surgeons or centers. Multiple studies have shown that higher volume surgeons and centers have improved postoperative outcomes.[18,19] Research has also demonstrated that high volume surgeons are more likely to utilize IONM.[20] It may be that IONM use serves as a proxy for surgical volume, which is in turn associated with improved outcomes. Unfortunately, the database used in this study does not provide information that would allow for further analysis by surgeon or institutional volume. However, it is important to note that regardless of the precise explanation for the association with lower complication rates, IONM use does correlate with improved outcomes. Based on the data from this study, patients may want to include IONM as a factor when selecting their surgeon, especially if being treated for malignancy.

Limitations of this study include those of any study that relies on large, multi-institutional databases, including selection and misclassification bias. As noted above, results may show correlations and associations but cannot prove causality. The nature of the ACS-NSQIP database is such that all outcomes are within a 30-day postoperative period; thus, long-term effects cannot be evaluated, including persistence or recovery of RLN function or of calcium homeostasis. The thyroidectomy-specific data set also contains only patient-associated data and does not provide data regarding surgeon-specific or center-specific variables, including training background or volume of practice. Hypocalcemic events are defined only as "clinically relevant" events and thus exclude asymptomatic hypocalcemia. Data regarding perioperative laryngoscopy, extent of surgery, parathyroid reimplantation, and postoperative use of calcium supplementation were unavailable in the data set. Definitions of RLN injury were vague with respect to the role of laryngoscopy, and using hoarseness as a proxy for RLN injury could result in potential bias with regard to under or overdiagnosis of RLN injury. Despite these limitations, the ACS-NSQIP-targeted thyroidectomy database has many strengths, including a large amount of data, continuous auditing to ensure accuracy, and collection of specific variables to more accurately assess thyroidectomy as a procedure.

In this study, IONM was associated with decreased odds of HCE and RLN injury among patients undergoing thyroidectomy. These associations were even stronger for thyroidectomy done for malignancy. Further studies are needed to better characterize these associations.

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