

Does intraoperative neuromonitoring during thyroidectomy reduce the risk of hypoparathyroidism?

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Abstract

Objective: To evaluate the effect of intraoperative neuromonitoring on postoperative hypoparathyroidism after bilateral total thyroidectomy.

Method: The prospective study was conducted at the General Surgery Clinic of the University of Health Sciences Haseki Training and Research Hospital, Türkiye, from February 2016 to December 2020, and comprised patients who had undergone bilateral total thyroidectomy. They were evaluated for recurrent laryngeal nerve damage, hypocalcaemia and hypoparathyroidism. Further, it was explored whether the use of intraoperative neuromonitoring had an effect on postoperative complications between experienced surgeons with >5 years of experience and less-experienced surgeons with <5 years of experience. Data was analysed using SPSS 15.

Results: Of the 64 patients 59(92.2%) were females and 5(7.8%) were males. The overall mean age was 47.7±10.8 years. Experienced surgeons operated 38(59.4%) patients, while the less experienced operated 26(40.6%). The most common complications were transient hypocalcaemia 38(59.3%) and transient unilateral vocal cord paralysis 9(14%). There was no significant difference between experienced surgeons and less experienced surgeons in terms of postoperative complications ($p>0.05$).

Conclusion: The use of intraoperative neuromonitoring during bilateral total thyroidectomy reduced the risk of hypoparathyroidism regardless of the surgeon's experience.

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Introduction

Bilateral total thyroidectomy (BTT), a very common procedure in surgical practice, has potential complications, such as recurrent laryngeal nerve (RLN) injury, hypoparathyroidism and hypocalcaemia. In order to avoid RLN damage, the RLN must be dissected and followed up to the point where it enters the trachea during BTT. Parathyroid glands should also be seen during the surgery, and it should be ensured that their perfusion is not impaired.¹

Intraoperative neuromonitoring (IONM) is one of the methods that can be used for dissection and identification of RLN during thyroid surgery. Temporary hypoparathyroidism and hypocalcaemia are common complications after thyroid surgery and may occur even if all parathyroid glands are preserved. Using IONM reduces nerve dissection and operative time.²⁻⁴ IONM might be used to assist less experienced surgeons with anatomical

identification.⁵ However, the benefits of IONM are still controversial.⁶

Performing minimal dissection in this area carefully with a shorter operation time may reduce the risk of impaired perfusion of the parathyroid glands, and, thus, the risk of hypoparathyroidism. The current study was planned to determine the effect of IONM on complications related to BTT.

Materials and Methods

The prospective study was conducted at the General Surgery Clinic of the University of Health Sciences Haseki Training and Research Hospital, Türkiye, from February 2016 to December 2020, and comprised patients who had undergone BTT. After approval from the institutional ethics review committee, the sample size was determined using G*Power 3.1.9.2 software,⁷ with alpha level 0.05 and estimated power 95%. The complication rate for experienced surgeons was kept at 1%, and that for less-experienced surgeons 5%.^{8,9} The sample was raised using consecutive sampling technique. Those included were euthyroid patients aged at least 18 years who underwent BTT and furnished informed consent. Patients who had undergone unilateral thyroidectomy, thyroidectomy due to hyperthyroidism, Bethesda score 5-6¹⁰ on fine needle aspiration cytology (FNAC), presence of preoperative vocal cord paralysis, cases in which IONM could not be used in

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surgery due to technical reasons, and those with previous neck surgery were excluded.

The indications, date and duration of surgery, surgical findings, length of hospital stay (LOS), sociodemographic information of the patients, preoperative thyroid stimulating hormone (TSH), free thyroxine (FT4), calcium (Ca), parathyroid hormone (PTH), 25-hydroxy vitamin D (25[OH]D) measurements, neck ultrasonography (USG) findings and FNAC results for thyroid nodules were recorded.

The surgeons who performed the surgeries were divided into two groups as experienced, meaning those who had performed thyroid surgery for >5 years, and less-experienced, meaning those who had performed thyroid surgery for <5 years.

All patients underwent standard BTT. During the surgery, IONM was performed using a commercial kit (NIM Response 3.0 system, Medtronic, Jacksonville, Florida, United States).

All patients underwent vocal cord examination via indirect laryngoscopy by otolaryngology head and neck surgeons, 1 day before and 1 day after the surgery. Patients who were found to have vocal cord paralysis were given consultation by the same surgeons, and discharged with appropriate doses of methylprednisolone and hydroxycobalamine. Patients with vocal cord paralysis on the first postoperative day were referred for vocal cord re-examination after 6 months of surgery. If the paralysis persisted, it was considered permanent vocal cord paralysis. Vocal cord paralysis that resolved within 6 months was considered temporary vocal cord paralysis.

Postoperative 24th hour Ca levels, PTH levels and terminal pathology findings and complications were recorded. All patients were evaluated for Chvostek and Trousseau signs¹¹ and hoarseness. Patients with postoperative hypocalcaemia were treated according to the degree of hypocalcaemia, and the treatment was continued with daily Ca measurements. These patients were followed up weekly after discharge. All patients were followed up by measuring Ca (Beckman Coulter AU 2700 Chemistry Auto-Analyzer, California, US), PTH, TSH, FT4 and 25(OH)D (Beckman Coulter Unicel DXI 800 Immunoassay Auto-Analyzer, Brea, CA, USA) levels in the 1st and 6th months postoperatively. Ca value 8.4-10.5mg/dL, 25(OH)D value 11.5-84.5 ng/mL, FT4 value 0.61-1.12ng/dL, TSH value 0.34-5.6 mIU/L and PTH value 12-88pg/mL were considered normal.

Data was analysed using SPSS 15. Continuous variables with a normal distribution were expressed as

mean±standard deviation (SD). Categorical variables were expressed as frequencies and percentages. The Kolmogorov-Smirnov test was used to assess data normality. The comparisons between two independent groups were done using student's t test and Mann Whitney U test, as appropriate. Dependent group analyses were performed using paired t test and Wilcoxon test, as appropriate. Chi-square analysis was used to compare the ratios in groups. Logistic regression analysis was applied to identify factors influencing postoperative complications using odds ratio (OR) and significance level. P<0.05 was considered statistically significant.

Results

Of the 64 patients 59(92.2%) were females and 5(7.8%) were males. The overall mean age was 47.7±10.8 years. Experienced surgeons operated 38(59.4%) patients, while the less experienced operated 26(40.6%). The most common indication for surgery was nodule size 30(46.9%), followed by 2 consecutive cytological evaluation of Bethesda score-3 13(20.3%) and patient preference 13(20.3%). Mean operation time was 105.1±22.4 minutes. The most common pathological diagnosis was multinodular goitre 33(51.6%) (Table 1).

There were a significant decrease in PTH (58.5±23.1 vs

Table-1: General characteristics of the patients.

	n (%)
Gender	
Female	59 (92.2)
Male	5 (7.8)
Mean Age (years) (Min-Max)	47.7±10.8 (24-76)
Indication	
Bethesda 4	8 (12.5)
Nodule larger than 3 cm	30 (46.9)
2 consecutive Bethesda 3	13 (20.3)
Patient preference	13 (20.3)
ASA* grade	
1	47 (73.4)
2	17 (26.6)
Preoperative Sonographic Nodule (mm)	29.3±10.9 (7-65)
Preoperative Vocal Cord Examination	
Normal	64 (100)
Surgeon Experience	
Experienced	38 (59.4)
Less experienced	26 (40.6)
Mean Operation Time (Min-Max) (min)	105.1±22.4 (70-210)
Postoperative Pathology	
Multinodular goiter	33 (51.6)
Unilateral micropapillary cancer	9 (14.1)
Bilateral micropapillary cancer	3 (4.7)
Unilateral papillary cancer	6 (9.4)
Bilateral papillary cancer	4 (6.3)
Lymphocytic thyroiditis	9 (14.1)

ASA: American Society of Anaesthesiologists, SD: Standard deviation.

Table-2: Perioperative changes in calcium and PTH levels.

	Mean±SD	Min-Max	Pre-op vs. Post-op 1st day p-value	Pre-op vs. Post-op 1st month p-value	Pre-op vs. Post-op 6th month p-value	Post-op 1st day vs Post-op 1st month p-value	Post-op 1st month vs Post-op 6th month p-value
Ca			<0.001	0.229	0.117	<0.001	0.294
Pre-op	9.3±0.4	8-10.1					
Post-op 1st Day	8.3±0.5	6.9-9.4					
Post-op 1st month	9±0.5	8.3-10.7					
Post-op 6th month	9.2±0.5	8.3-10.2					
PTH			<0.001	0.001	0.082	0.002	0.141
Pre-op	58.5±23.1	20-135					
Post-op 1st Day	36.6±22	1-100					
Post-op 1st month	43.8±20.9	1-99.4					
Post-op 6th month	47.9±17.7	4-81					

Ca: Calcium, PTH: Parathyroid hormone, SD: Standard deviation.

Table-3: Postoperative complications.

	n (%)
Unilateral temporary paralysis	9 (14.1)
Unilateral permanent paralysis	1 (1.6)
Bilateral temporary paralysis	0 (0)
Bilateral permanent paralysis	0 (0)
Postoperative vocal cords	
Normal	55 (85.9)
Unilaterally paralytic	9 (14.1)
Transient hypocalcaemia	38 (59.4)
Transient Hypoparathyroidism	5 (7.8)
Permanent Hypoparathyroidism	1 (1.6)
Seroma	1 (1.6)

Table-4: Distribution of complications according to the experience level of surgeons

	Experienced group n (%)	Less experienced group n (%)	p-value	OR (Odds Ratio)
Unilateral temporary paralysis of vocal cord	7 (18.4)	2 (7.7)	0.291	0.368
Unilateral permanent paralysis of vocal cord	0 (0)	1 (3.8)	0.406	NA*
Postoperative vocal cords				
Normal	31 (81.6)	24 (92.3)	0.291	0.368
Unilateral paralytic	7 (18.4)	2 (7.7)		
Temporary hypocalcemia	20 (52.6)	18 (69.2)	0.184	2.02
Temporary hypoparathyroidism	2 (5.3)	3 (11.5)	0.389	2.3
Permanent hypoparathyroidism	0 (0)	1 (3.8)	0.406	NA*
Seroma	0 (0)	1 (3.8)	0.406	NA*

NA: Not applicable.

36.6±22, $p<0.001$) and Ca (9.3±0.4 vs 8.3±0.5, $p<0.001$) levels on the first postoperative day compared to preoperative values. Significant increase was noted in PTH (36.6±22 vs 43.8±20.9, $p=0.002$) and Ca (8.3±0.5 vs 9±0.5, $p<0.001$) levels at first operative month compared to the first postoperative day. There was no significant difference between preoperative and 6th postoperative month in PTH and Ca levels (Table 2).

Temporary unilateral RLN paralysis was detected in 9(14.1%) patients and unilateral permanent RLN paralysis was detected in 1(1.6%). Although temporary

hypoparathyroidism was detected in 5(7.8%) patients and permanent hypoparathyroidism was detected in 1(1.6%), temporary hypocalcaemia was observed in 38(59.4%) patients. Postoperative seroma was observed in 1(1.6%) patient. Bilateral RLN paralysis was not detected in the sample (Table 3).

There was no significant difference between experienced surgeons and less experienced surgeons in terms of postoperative complications ($p>0.05$) (Table 4). There was no postoperative mortality, and no parathyroid tissue was detected.

Discussion

The rate of postoperative permanent hypoparathyroidism among patients undergoing thyroid surgery by experienced endocrine surgeons at various centres varies between 0.9% and 1.6%. The incidence of postoperative temporary hypoparathyroidism ranges from 6.9% to 46%.¹²⁻¹⁴ In the study, temporary hypoparathyroidism occurred in 7.8% patients, and permanent hypoparathyroidism in 1.6% patients. Less experienced surgeons performed 40.6% surgeries, and, therefore, the rate of permanent hypoparathyroidism was expected to be higher, but it was similar to that of experienced endocrine surgeons. The rate of temporary hypoparathyroidism has been reported to be up to 46% in the literature, but in the current study it was found close to the lower rate of hypoparathyroidism reported in the literature.^{15,16}

The incidence of temporary and permanent hypocalcaemia ranges 0.3-49% and 0-13% respectively.¹⁷ No permanent hypocalcaemia was detected in the current patients, while temporary hypocalcaemia was seen in

59.3% patients. All patients were asymptomatic except 1 who responded well to medical therapy. The reason for the high rate of hypocalcaemia than earlier studies was because >90% of the patients were female, and the preoperative 25(OH)D level was close to the lower limit of normal. Therefore, the patients may have a higher susceptibility to hypocalcaemia.¹⁸ Some studies indicate that preoperative low level of 25(OH)D is associated with postoperative temporary hypocalcaemia, whereas some studies demonstrated that they were unrelated.¹⁹⁻²¹

IONM was applied to all the current BTT patients. Considering that the RLN can be found more easily with IONM which also reduces dissection, the operation time was recorded to investigate whether less dissection would have a positive effect on parathyroid blood flow, and decrease the rate of hypoparathyroidism. Intermittent RLN monitoring was performed during the operation. Mean operation time for experienced surgeons was 106 minutes, and longer than the mean operation time reported in literature. The mean operation time was 99.4 minutes for less-experienced surgeons and was consistent with the literature.²² Vocal cord paralysis was seen after thyroidectomies lasting >90 minutes.²³

Permanent RLN paralysis rate, which is one of the most serious complications after thyroidectomy, is reported to be 0.1-1.8% and temporary RLN paralysis is 1-5%.²⁴ Surgeons with less experience have been reported to have a higher risk of RLN damage.^{3,4} In the current study, no significant difference was found between the 2 groups of surgeons in terms of postoperative RLN paralysis. This suggests that less experienced surgeons can perform safe surgery as well with the help of assistive devices, such as IONM. Temporary unilateral vocal cord paralysis rate was 14.1% and permanent unilateral paralysis rate was 1.6%. The rate of permanent unilateral paralysis of vocal cord is similar to the literature, but the rate of temporary vocal cord paralysis was higher than the values reported in literature.²⁵ This was probably because of the long operation time and the high rates of chronic lymphocytic thyroiditis and malignancy in terminal pathological diagnoses.

Hypoparathyroidism is the main reason of postoperative temporary and permanent hypocalcaemia. The frequency may vary according to the experience of the surgeon and the facilities available at the healthcare centre.^{19,20} Performing difficult thyroidectomies by experienced surgeons is one of the important factors in preventing hypocalcaemia.^{21,23} There are different opinions in the literature about the effect of the surgeon's experience on complications. It is reported that less complications have developed after thyroid surgery performed by experienced

surgeons.²⁶ In addition, in a prospective study, no difference was found between experienced surgeons and residents in terms of parathyroid injury and related hypocalcaemia.²⁷ A study demonstrated that postoperative hypocalcaemia was not significantly associated with the surgeon's experience.²⁸ In the current study, no significant difference was found in the general characteristics and complication rates of the patients operated by experienced and less-experienced surgeons.

The current study has limitations like a small sample size, and not having a control group. The high rate of female subjects in the sample may have affected the findings since it is a factor that may lead to a high rate of postoperative hypocalcaemia. Finally, the cases operated by experienced and less experienced surgeons were not equal in number.

Conclusion

IONM could help the less experienced thyroid surgeons, especially in reducing complication rates. IONM can be used to reduce dissection around the parathyroid glands to identify RLN, thus it may contribute to the prevention of hypoparathyroidism.

Disclaimer: The prospective study is based on a thesis, and the preliminary results were presented as an oral presentation at the 9th Surgical Research Congress, held on November 10-12, 2017, at Kocaeli, Türkiye. The study then continued till December 2020.

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Author Contribution:

ZZK: Concept, design, data collection, analysis, interpretation, drafting, revision, final approval and agreement to be accountable for all aspects of the work.

ET: Data collection, final approval and agreement to be accountable for all aspects of the work.

MA: Revision, final approval and agreement to be accountable for all aspects of the work.

GC: Concept, drafting, final approval and agreement to be accountable for all aspects of the work.