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Original Research

Complication Risk in Secondary Thyroid Surgery

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Abstract

Objectives: Secondary thyroid surgery is rare, compared with primary thyroid surgery. However, secondary surgery has a greater risk of complications due to the formation of scar tissue as well as increased fragility of the tissues following the previous surgery. Several surgical techniques and strategies have been recommended to decrease the complication rate associated with secondary surgery. The aim of this study was to evaluate the complication rate in patients who underwent secondary thyroid surgery using a lateral approach and intraoperative nerve monitoring (IONM).

Methods: The data of 44 patients who underwent secondary surgical intervention after thyroid surgery performed for benign or malignant thyroid disease (Group 1), and of 44 patients who underwent primary surgery (Group 2) were compared. Lobectomy patients with a histopathological result of malignant disease, whom were applied completion thyroidectomy were excluded from the study. Secondary surgery was performed using a lateral approach. Access was achieved between the anterior edge of the sternocleidomastoid muscle and the strap muscles. In primary surgery, the thyroid lodge was entered through the midline. Standard IONM was applied in all cases. Hypocalcemia was defined as a serum calcium level of ≤8 mg/dL within the first postoperative 48 hours, regardless of clinical symptoms. Transient and permanent recurrent laryngeal nerve paralysis was evaluated based on the number of nerves at risk. The lobectomy was considered to be high-risk with the presence of recurrence, Graves' disease, substernal goiter, and application of central dissection.

Results: The mean age of Group 1 and 2 was 49.9±14.1 years and 45±12.6 years , respectively (range: 22-90 years; p=0.69). Female patients constituted 90.9% (n=40) of the population in Group 1 and 75% (n=33) of the patient population in Group 2 (p=0.87). In Group 1, 11 (25%) patients, and 7 (15.9%) patients in Group 2 underwent surgical intervention due to the presence of a malignant disease (p=0.29). Bilateral intervention was applied in 26 (59.1%) patients in Group 1 and 28 (63.6%) patients in Group 2. The rate of transient and permanent hypocalcemia in Groups 1 and 2 was 34.1% (n=15) vs 22.5%, and 2.5% (n=1) vs 0%, respectively, without any significant intergroup difference (p=0.237, p=1). In Group 1, 71 lobes were operated on, and there were 72 in Group 2. All of the interventions in Group 1 (100%), and 31.9% (n=23) of those in Group 2 were high-risk, and there was a significant intergroup difference (p<0.0001). The rate of transient and permanent vocal cord paralysis were 4.2% (n=3) vs 2.8% (n=2) and 6.9 % (n=5) vs 0% in Groups 1 and 2, respectively (p=0.719; p=0.245).

Conclusion: When performed with a meticulous and attentive technique, secondary surgical intervention can be applied without increasing the incidence of permanent complications. Though there is substantial risk associated with all of these procedures, the rate of vocal cord paralysis was similar to that seen after primary intervention, and was thought to be related to surgical experience and technique, as well as the use of IONM.

Keywords: Intraoperative neuromonitoring, lateral approach, secondary thyroidectomy, vocal cord paralysis.

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Thyroid surgery is the most frequent endocrinological surgical intervention, and in the majority of cases, it is a primary surgery. However, occasionally, a secondary intervention may be required due to a recurrent goiter or thyroid cancer.[1] A secondary intervention offers an opportunity to both the patient and the surgeon. Yet specific postoperative complications, including recurrent laryngeal nerve (RLN) paralysis and hypoparathyroidism, which directly affect the quality of life of the patient, have a markedly higher incidence rate following a secondary intervention.[1-3]

Many surgical techniques and strategies have been recommended in an effort to decrease the complication rate of secondary surgeries.[2] One of these is a lateral approach thyroidectomy, which allows access to the posterolateral region with a lower rate of adhesive complications compared with surgery via a midline approach, which has been associated with a higher rate of postoperative formation of scar tissue and adhesions.[4] Another technique is the use of intraoperative nerve monitoring (IONM), which can protect the RLN. IONM is now increasingly used in thyroid surgery as a supplement to the gold standard of intraoperative visualization of the RLN.[5] Although a general consensus on its use in thyroid surgery does not exist, routine use has been recommended, especially in secondary surgery, and other high-risk thyroidectomies.[6]

In our clinic it is standard to perform a secondary thyroid surgery using a lateral approach and an anterior approach in primary thyroid surgery. The use of IONM has been standard both in primary and secondary interventions since 2012. In this study, a comparison of complications encountered in patients who underwent primary and secondary thyroidectomies was performed. Since the risk of complications is generally greater in secondary interventions compared with primary interventions,[1] the objective was to determine if the complication rate in patients undergoing a secondary intervention was comparable to that of a primary intervention.

Methods

The data of 44 patients who had previously undergone thyroid surgery as a result of either benign or malignant thyroid disease and then underwent a secondary surgical intervention performed by a single surgeon (MU) between May 2012 and January 2015 (Group 1), and the data of 44 patients who underwent primary surgery performed by the same surgeon between August and December 2015 (Group 2) were retrospectively compared. Lobectomy patients with a histopathological examination result of the biopsy material that revealed evidence of malignancy who undergone completion thyroidectomy, and patients who initially had had a lobectomy and underwent a secondary intervention with the indication of benign or malignant disease involving the contralateral lobe were excluded from the study.

Intermittent IONM was used in all cases. The setting and application of IONM and the data collection were conducted in accordance with the International Intraoperative Nerve Monitoring Study Group guidelines[5] The NIM 3.0 Nerve Monitoring System (Medtronic, Inc., Minneapolis, MN, USA) was used. A low dose of a neuromuscular blocking agent (rocuronium, 0.3 mg/kg) was administered to facilitate intubation with an endotracheal tube with a surface electrode (Nerve Integrity Monitor Standard Reinforced Electromyography Endotracheal Tube, size 6.0, 7.0, or 8.0; Medtronic Inc., Minneapolis, MN, USA). Following the induction of anesthesia, no further muscle relaxant was administered, and anesthesia was maintained with inhalers and intravenous agents. Nerve stimulation was achieved using a monopolar probe (Medtronic, Inc., Minneapolis, MN, USA) with an electric current of 1 mA (duration: 100 milliseconds, frequency: 4Hz). If the nerve could not be identified, a current of 2 mA was applied to localize the nerve. Values below 100 V were defined as signal loss.

In compliance with the guidelines, the standardized 4-stage IONM technique was applied (V1, R1, R2, V2). Before accessing the thyroid lodge, the vagus nerve was stimulated (V1), and the RLN was stimulated once it was found in the tracheoesophageal sulcus (R1). The RLN was re-stimulated after complete dissection at the ligament of Berry (R2), and the vagus nerve was tested following the completion of all procedures (V2). All of the results observed were also recorded.[5] Laryngoscopic vocal cord examination was performed by an ear, nose, and throat specialist preoperatively and within the first 48 hours after surgery. A vocal cord examination of patients with vocal cord paralysis (VCP) was performed at the postoperative first, second, fourth, and sixth month. VCP that resolved within 6 months was defined as transient VCP, and if it persisted beyond 6 months, it was considered permanent VCP. Transient and permanent VCP were evaluated based on the number of nerves s at risk. Hypocalcemia was defined as a serum calcium level of ≤8 mg/dL within the first 48 hours, regardless of the presence or absence of clinical symptoms. Lobe intervention was considered high-risk in cases of recurrence, Graves' disease, substernal goiter, or central dissection.[7]

Surgical Technique

Anterior approach: For all patients in Group 2, surgical intervention was performed using an anterior approach. After preparing subplatysmal superficial flaps, the thyroid lodge was entered through the midline between the strap muscles. The sternohyoid and sternothyroid muscles were dissected away from the thyroid, the vena thyroidea media was divided, and the carotid sheath was exposed. The carotid sheath was opened, and the vagus nerve was stimulated (V1). The terminal branches of the thyroid vessels in the vicinity of the thyroid capsule were divided, and thus, capsular dissection was performed.[8] Using a lateral approach, the RLN was explored before or after dissection of the upper pole, at the point of intersection with the inferior thyroid artery. If the RLN was identified, it was stimulated with the IONM probe to confirm that it was indeed the recurrent nerve (R1). If the RLN nerve was not identified, additional exploration in the tracheoesophageal sulcus was performed with the IONM probe using an electric current of 1 to 2 mA. The region that emitted signals was dissected and identified. The RLN was followed with the naked eye beneath the cricopharyngeal muscle to its entry into the laryngeal opening and dissected. After dissection of the region of the ligament of Berry and the affected lobe was completed, the RLN was stimulated and the signals received were recorded (R2). During the dissection of the upper pole, the external branch of the superior laryngeal nerve was monitored with the IONM probe. The anatomical definitions of the central region and the boundaries of the dissection were made in accordance with the recommendations of the consensus statement of the American Thyroid Association (ATA) surgical study group.[9] Unilateral or bilateral central neck dissection was performed according to these recommendations.[10] The parathyroid glands and their vasculature that were observed in the field of dissection were preserved as much as possible. If they could not be spared, they were divided into 1 mm-thick slices, and autotransplanted into the sternocleidomastoid muscle. Upon completion of all procedures in the lodge, the vagus nerve was stimulated, and electromyography (EMG) waves of the vocal cord were recorded (V2). In bilateral interventions, generally suction drains were placed bilaterally. In patients who underwent a unilateral procedure, and in some bilateral cases, drains were not required. The tissue was then closed in layers, according to the anatomy.

Lateral approach: This method is described as the lateral "backdoor" approach. After preparing upper and lower subplatysmal flaps, the strap muscles were dissected away from the anterior border of the sternothyroid muscle and the internal jugular vein was identified.[4] The vagus nerve in the medial part of the surgical field was distinguished, the vocal cord was stimulated, and the EMG waves achieved were recorded (V1). The common carotid artery was found medial to the internal jugular vein, and the thyroid lodge was entered between the carotid artery and the strap muscles. Since the inferior paratracheal region had not been not dissected previously, the RLN was explored in the tracheoesophageal region superior to the clavicle with the IONM probe with an inferior approach, and a current flow of 1mA. The signaling region was dissected to make the RLN visible, and the EMG signal acquired from the vocal cord was recorded (R1). During total dissection of the thyroid lobe, the RLN was mapped using the IONM probe. Once hemostasis was achieved, the RLN was stimulated from the most proximal point of dissection and the vocal cord signal was recorded (R2). If central dissection was to be performed, the strap muscles were dissected away from the midline and the prelaryngeal region was dissected. The lodge was accessed from the lateral side. The RLN was identified and the course was tracked. The central tissue was dissected away posteriorly to the strap muscles and the midline. When necessary, the upper one-third of the strap muscles was dissected. Unilateral or bilateral central dissection was performed based on the recommendations in the ATA guidelines. After completion of the surgical procedure, the vagus nerve was stimulated from the most proximal point of dissection to record an EMG signal of the vocal cord (V2). A suction drain was placed in the lodge, and the layers were closed according to their anatomical position.

Age, gender, diagnosis, type of intervention (unilateral or bilateral), transient or permanent hypoparathyroidism, the rate of interventions considered to be high-risk, and transient and permanent VCP were evaluated.

Statistical Evaluation

Descriptive statistics of the assessment results were expressed as numbers and percentages for categorical variables, and mean, standard deviation, minimum, and maximum for quantitative variables. For comparisons of numerical variables between 2 groups, the nonparametric Mann-Whitney U test was used. Differences in the rates of categorical variables were evaluated using the Pearson chi-square test. $P<0.05$ was accepted as the alpha level of statistical significance.

Results

The diagnoses and procedures performed are summarized in Table 1. No intergroup difference was detected based on age or gender of the patients (Table 2). In Group 1, 11 (25%) patients underwent surgery as a result of a malignant finding, and 7 (15.9%) patients in Group 2 had a malignancy. Benign results were determined in 33 (75%) patients in Group 1, and 37 (84.1%) in Group 2, without any significant intergroup difference (p=0.29). In Group 1, 71 lobes were removed, and in Group 2, 72 lobes were removed. All (100%) of the procedures in Group 1 were classified as high-

Table 1. Diagnoses of the patients and the surgeries performed

	Group 1 n=44	Group 2 n=44
Disease diagnosis		
Benign		
MNG	30	31
Substernal MNG	3	1
Graves' disease	0	5
Malignant		
Papillary Ca	9	7
Medullary Ca	2	0
Surgery performed		
TT	21	24
Lobectomy	15	16
T+SD+LD	8	4

Ca: Cancer; CD: Central neck dissection (unilateral or bilateral); LD: Lateral neck dissection; MNG: Multinodular goiter; T: Completion thyroidectomy; TT: Total thyroidectomy.

Table 2. Demographic data and complications

	Group 1 n=44	Group 2 n=44	p
Age mean+SD, years			
(min-max)	49.9+14.1	44.95+12.6	0.069*
Gender, female/male	40/4	33/11	0.087**
Malignant disease n (%)	11 (25)	7 (15.9)	0.290**
Side of the neck intervened	70	72	
Unilateral intervention, n (%)	18 (40.9)	16 (36.4)	0.817**
High-risk intervention, n (%)	71 (100)	23 (31.9)	<0.001
Hypocalcemia			
Transient hypocalcemia, n (%)	15 (34.1)	10 (22.7)	0.345**
Permanent hypocalcemia, n (%)	1 (2.3)	0	1**
Vocal cord paralysis			
Transient	3 (4.2)	5 (6.9)	0.719**
Permanent	2 (2.8)	0	0.245**

*Mann-Whitney U test; **Pearson chi-square test.

risk, while there were 23 (31.9%) in Group 2, which was a statistically significant intergroup difference (p<0.001). A bilateral intervention was performed for 26 (59.1%) patients in Group 1, and 28 (63.6%) patients in Group 2. A unilateral procedure was performed in 18 (40.9%) patients in Group 1 and 16 (36.4%) in Group 2, without any significant intergroup difference. In Group 1, 15 patients underwent a thyroid lobectomy, and a unilateral central neck dissection was performed in 3. In Group 2, all 16 were unilateral lobectomies. Transient hypocalcemia was observed in Group 1 at a rate of 34.1% and 22.5% in Group 2, the incidence of permanent hypocalcemia was 2.5% and 0% in Group 1 and Group 2, respectively, without any significant intergroup difference (p=0.237, p=1). Parathyroid implantation was performed in 6 patients (1 parathyroid gland for 5 patients, and 2 parathyroid glands for 1 patient) in Group 1 and in 2 patients in Group 2. A preoperative laryngoscopic examination detected 4 cases of unilateral VCP in Group 1. Postoperatively, 3 transient and 2 permanent cases of VCP developed in Group 1, and in Group 2, there were 5 cases of permanent VCP. All of the postoperative VCP observed was unilateral. In Group 1, contralateral VCP developed in 1 patient with unilateral VCP, which necessitated a tracheostomy. The postoperative VCP had resolved at the sixth month, so the patient was decannulated and the tracheostomy tract was closed. The rate of transient and permanent VCP seen in Group 1 (4.2% and 2.8%, respectively) and Group 2 (6.9% and 0%) did not yield any significant intergroup difference (p=0.719, and p=0.245, respectively) (Table 2).

Discussion

Hypoparathyroidism is the most frequently seen complication following a thyroidectomy. Transient hypocalcemia has been reported in 0% to 60% of cases, and permanent hypoparathyroidism has been noted after a thyroidectomy in 1% to 10%.[11-13] This large spectrum of complication rates is related to several factors, including differences in the criteria and definitions used for hypocalcemia, scrupulousness in data collection, the experience of the surgeon, the specific characteristics of the patients and the disease.[14, 15] Perioperative biochemical values related to development of postoperative hypoparathyroidism and risk factors associated with the patient, disease, and surgery have been reported in the literature. Secondary surgery is among the risk factors for the development of hypocalcemia.[15] In a multicenter prospective study performed by Thomush et al.[16] on benign goiter surgery in 7266 patients, secondary surgery was determined to be an independent risk factor for both transient and permanent hypoparathyroidism. The relative risk for transient and permanent hypoparathyroidism was found to be 1.8, and 1.9, respectively. In another study, permanent hypoparathyroidism related to secondary thyroid surgery has been reported 3 to 8 times more frequently compared with primary total thyroidectomy.[17] In our study, transient hypocalcemia was more frequently seen in the secondary surgery group relative to the primary surgery group, but without any statistically significant intergroup difference (34.1% vs 22.7%). These rates are within the acceptable limits mentioned in the literature. In this study, we defined biochemical hypocalcemia as a serum calcium level of 8 mg/dL within the first postoperative 48 hours. The rate might have been lower if we had taken symptomatic hypocalcemia into consideration.

The rate of permanent hypoparathyroidism in the secondary surgery group was 2.3%, which was comparable to that of the primary surgery group. We think that this lower rate of hypoparathyroidism may be related to the lateral dissection technique and the capsular dissection technique applied after identification of the RLN. Especially in cases of secondary intervention, the least adhesive part of the thyroid lodge is the posterolateral region. We think that if the RLN is identified in the inferior aspect of the lodge and capsular dissection is continued superiorly along the anterior aspect of the nerve, an important contribution to preservation of the upper parathyroid gland can be achieved. The upper parathyroid gland is localized on the superficial vascular layer over the RLN.[18] This part of the thyroid gland has been protected, who previously underwent a subtotal thyroidectomy. Capsular dissection over this fascial plane performed well may spare the upper parathyroid glands. Of our secondary intervention cases, 75% were recurrent goiter. When possible, we tried to preserve the lower parathyroid gland with its vasculature. Those that could not be spared with their vessels were autotransplanted into the sternocleidomastoid muscle. Zedenius et al.[19] reported that routine autotransplantation of at least 1 parathyroid gland may minimize the risk of permanent hypoparathyroidism.[19]

Another important complication of thyroid surgery apart from hypoparathyroidism is VCP. Problems concerning unilateral VCP include inappropriate closure of the glottis, which leads to voice problems of varying degree.[20] Though bilateral VCP is rarely seen, this complication can lead to life-threatening respiratory tract obstruction.[21] VCP is the post-thyroidectomy complication that has been the subject of the most malpractice suits.[22] Many risk factors regarding the development of RLN paralysis as a complication of thyroidectomy have been reported. In multicenter studies cited in the literature, secondary intervention, interventions performed to treat a malignancy, extension of surgery, inability to inspect the RLN, substernal goiter, female gender, advanced age, thyrotoxicosis, a low-volume hospital, and an inexperienced surgeon have all been determined to be risk factors that increase the risk of developing VCP.[3, 16, 23-26] The incidence of VCP is higher in secondary interventions relative to primary interventions. In the literature, the approximate rate of transient and permanent VCP has been reported as 12.5% and 3.8%, respectively.[27]

In their study on benign goiter surgery, Thomusch et al.[16] determined that secondary intervention was an independent risk factor for the development of transient and permanent VCP in cases of a recurrent goiter. They detected a relative risk rate for transient and permanent VCP of 3.05, and 3.44, respectively. In a multicenter prospective study of nearly 30,000 cases of RLN determined to be at risk, the investigators determined that secondary intervention was an independent risk factor that increased the risk of permanent VCP with an odds ratio of 4.7 in cases of benign disease, and 6.7 in cases of malignancy when compared with primary thyroid surgery.[3]

Though the use of IONM has gradually increased within the last years, debates concerning its impact still continue.[28, 29] Despite the lack of consensus, an international survey of thyroid surgeons indicated that IONM was widely used.[30] Few studies in the medical literature have comparatively evaluated the rate of VCP related to secondary surgery and IONM. The number of patients has been limited and the study groups were heterogeneous.[27] The impact of IONM use in cases of secondary thyroid surgery has been evaluated in a current meta-analysis encompassing 9 studies, and 2436 RLN judged at risk. Despite a limited number of samples and heterogeneity among studies, the investigators reported that the overall rate of VCP was significantly lower when IONM was used (relative risk: 0.434), as well as and permanent VCP (relative risk: 0.426).[31] Another meta-analysis evaluated the use of IONM in high-risk thyroidectomies, and assessed 6155 RLNs in which IONM was used, and 4460 in which it was not. In the IONM group, the rate of overall VCP and transient VCP was significantly lower when compared with the non-use group (4.5% vs. 2.5%; p=0.003 and 3.9% vs. 2.4%; p=0.016, respectively).[6] Barczynski et al.[12] retrospectively evaluated more than 850 patients who had undergone a secondary thyroid intervention and reported a significant decrease in the rate of transient VCP in IONM cases (2.6% vs 6.3%; p=0.003), though a decrease in permanent VCP was not statistically significantly different (1.4% vs 2.4%; p=0.202). This result was related to a small number of patients; the authors calculated that each group should contain at least 952 patients to determine a significant intergroup difference in the rate of permanent VCP.[32]

All of the secondary interventions in our study were high-risk, and 32% of the primary interventions were also considered high-risk. Transient and permanent VCP was seen in 4.2% and 2.8%, respectively, of the secondary interventions, which is consistent with the literature data. A significant difference was not detected in the rate of VCP between patients who underwent a secondary or a primary intervention. We think that the use of a lateral approach together with IONM contributed to the achievement of a comparable rate of VCP. The formation of scar tissue and atypical RLN course after a primary intervention are primary factors leading to injury of the RLN during a secondary intervention.[27] We also think that a lateral approach to the thyroid lodge from an area with minimal scar tissue, and early identification and mapping of the nerve at the inferior aspect with the IONM probe contribute significantly to the preservation of the nerve. Using this method, we were able to identify all of the RLNs, and observe them with the naked eye. However, in their series of recurrent cases, Barczynski et al.[32] reported that only 20% of the nerves could be identified using IONM and seen with the naked eye. Salari et al.[33] indicated that the use of IONM in recurrent thyroid cancer contributed to the identification and preservation of the RLN at the inferior aspect with a potential minimization of the rate of VCP. Wojtczak et al.[34] stated that even in experienced centers, it can be difficult to identify the RLN during a secondary intervention, and reported that the RLN could be seen with naked eye more frequently in the IONM group (91.6%) compared with a group in which it was not used (44.4%). The investigators revealed that the course of the RLN had changed in 80% of the cases, and in 57% the RLN was found in scar tissue.[34] IONM can provide an important contribution to the detection and discrimination of the nerve from any other tubular structure in scar tissue. The use of IONM also significantly increases the ability to detect extralaryngeal branches of the RLN and non-recurrent nerves, which are risk factors for RLN paralysis in a secondary intervention.[32] The use of IONM also affects surgical strategy. IONM decreases risk of bilateral VCP.[35] In our study, 1 patient in the secondary intervention group had preoperative VCP. Severe respiratory distress occurred due to compression from the enlarged thyroid, which led to the need for a primary intervention. A tracheostomy relieved the respiratory distress and greatly improved the patient's quality of life. At the sixth month, the tracheostomy was closed. Bilateral VCP was not observed in the other patients. We generally prefer to terminate the operation in the event of unilateral intraoperative signal loss to prevent the potential development of bilateral VCP.

The limitations of this study include the relatively small number of cases and the retrospective design. The selection of a primary intervention group as a control group rather than a secondary intervention group that did not include the use of IONM may be considered a limitation of the study. IONM has been used routinely in our clinic for all thyroidectomies since 2012; therefore, including a non-use group was not applicable for our case series. Furthermore, the formation of such a control group from high-risk secondary intervention patients at a time when IONM is routinely used could be considered ethically questionable. Therefore, we think that a comparison between a secondary intervention group in which IONM was used with a primary intervention group was an appropriate approach. These patients were selected from among cases that were enrolled in the series at a later date, and given the experience of the team, were less likely to experience complications. We think that the results attained in the secondary intervention group were at least comparable or even better than those obtained in primary interventions, indicating that we have selected an appropriate approach.

Secondary surgical intervention may be performed without increasing the permanent complication rate relative to primary intervention when a meticulous technique is applied. Though all of the secondary interventions were defined as high-risk, the rate of VCP observed was comparable to that of primary intervention, due, we believe, to surgical experience, the technique employed, and the use of IONM.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship contributions: Concept – N.A., M.U.; Design – N.A.; Supervision – M.U.; Materials – N.A., E.B.; Data collection &/or processing – N.A., E.B., G.Y., M.M.; Analysis and/or interpretation – N.A., A.İ., M.U.; Literature search – N.A., E.B.; Writing – N.A.; Critical review – A.İ., M.U.

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