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Incidence and risk factors for recurrent laryngeal nerve injury after thyroid surgery

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Abstract

Objectives Injury to the recurrent laryngeal nerve (RLNI) is a known possible morbidity after thyroid surgery. The clinical presentation varied in severity, from changes in voice quality and swallowing in unilateral cases to airway compromise in bilateral cases. In minor cases, vocal fold paralysis (VFP) may occur unnoticed. Although many intraoperative measures have been implemented to minimize nerve injury, the risk remains, either transient or permanent. This study evaluated the incidence and potential risk factors of recurrent laryngeal nerve injury after thyroidectomy.

Methods Retrospective data analysis was conducted on 1368 patients who underwent thyroidectomy at the National Guard Hospital, King Abdul-Aziz Medical City, Jeddah, Saudi Arabia, between January 2008 and December 2021. Evaluations were conducted on the pathological features, surgical procedure type, and state of the recurrent laryngeal nerve during surgery as contributing to recurrent laryngeal nerve injury. All patients underwent preoperative and postoperative indirect laryngoscopy examinations with or without videostroboscopy. Physiological testing of the RLN using neurostimulation and laryngeal palpation (NSLP) or intraoperative neuromonitoring (IONM) was performed in all cases. VFP was considered present when vocal fold mobility was absent or significantly reduced.

Results A total of 1368 patients (2177 nerves at risk) who underwent thyroidectomy and fulfilled the inclusive criteria (809 bilateral, 559 unilateral) were evaluated. A total of 62% of patients were more than 45 years old, and the mean age was 48.36 ± 13.03 with a male-to-female ratio of 1:3.6. Eight-hundred one (58.6%) patients underwent total or subtotal thyroidectomies (1602 nerves at risk). Two-hundred seventy-six patients underwent hemithyroidectomy (276 nerves at risk), and 291 patients underwent completion or redo surgeries (299 nerves at risk). Of these 1368 patients, post-surgery laryngoscopy showed reduced or absent vocal fold mobility in 47 (3.4%) patients. Forty-three out of 47 patients had unilateral vocal fold paralysis, and 4 had bilateral VFP. When we analyzed the three risk factors statistically significant for postoperative RLN palsy, age (*OR*, 1.01; 95% *CI*, 0.98–1.05; *p* = 0.365) became non-significant. The other risk factors (extent of surgery and histopathological diagnosis) remained statistically significant (*p* = 0.004 and 0.031). After adjustment, the extent of surgery, including total thyroidectomy and revision surgery, was strongly associated with a higher risk of odds of postoperative RLN palsy. Physiological RLN stimulation was performed in all cases with NSLP or INOM, and no significant association was observed in the incidence of VFP (*p* = 0.365). In most cases, symptoms were spontaneously resolved with recovery of vocal fold movement within a few months.

Conclusion In this study, 3.4% of the recurrent laryngeal nerve showed postoperative dysfunction either transient or permanent VFP. Intraoperative identification of the nerve remains the gold standard of care during thyroidectomy. Neuromonitoring aids in detecting the nerve, particularly in severe cases, but does not reduce the nerve injury compared to NSLP.

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Background

Thyroidectomy is the most common endocrine surgical procedure in the Kingdom of Saudi Arabia [1]. Thyroidectomy has been used to treat malignant lesions and some benign thyroid diseases. One of the most feared morbidities of thyroid surgery is recurrent laryngeal nerve injury, which is also one of the main causes of surgical malpractice. In the literature, the incidence of RLN palsy varies widely. Even in experienced hands, approximately 0.3–10.9% of patients experience transient RLN paralysis, and 0.3–5.8% of patients experience permanent paralysis [2–10]. Possible mechanisms of injury to the RLN during thyroid surgeries include over-traction of the nerve at Berry's ligament, direct trauma during dissection as transection or clamping, thermal electrocautery injury, or perineural devascularization [2, 11]. Although RLNI is rare, it can significantly affect the patient's quality of life [12]. Unilateral injury leads to voice change, while bilateral injury results in life-threatening airway compromise [13]. It is necessary to identify the laryngeal nerve anatomically and evaluate its function physiologically to prevent injury to the recurrent laryngeal nerve during thyroidectomy. The surgical approach has changed to routine identification associated with a lower incidence of RLNI [13–17]. Intraoperative neuromonitoring (IONM) has gained acceptance as a useful complement to functional RLN evaluation in recent years [18]. There is strong evidence to support the necessity of capsular dissection and routine intraoperative identification to preserve the RLN. In patients who have had a previous thyroidectomy, RLN detection can present difficulties. Surgeons should locate the RLN and assess its function because an intact nerve does not necessarily correlate with normal vocal fold function. This cohort study aims to evaluate the incidence of RLN paralysis in our patients and to identify risk factors that raise the possibility of RLN injury during thyroid surgery.

Methods

Study design and patient inclusion

A retrospective review of patient records was authorized by the Institutional Review Board of the King Abdullah International Medical Research Center (reference number IRBC/0535/19). A retrospective review was conducted of all the medical records of patients who underwent t at King Abdulaziz Medical City (KAMC), Western Region, Department of Otolaryngology, between January 2008 and December 2021. The recruited data was gathered and arranged using a form that was self-developed. Individuals with a past medical history of vocal fold paralysis, those who did not undergo preoperative or postoperative laryngoscopy, those whose data were lost to follow-up, those whose RLN was sacrificed during surgery, and those whose unintentional RLN injury was discovered intraoperatively were all excluded. We divided the collected data into two main groups: First, demographic and operative details included surgical and permanent pathological analysis, and second, details about RLNI (vocal fold injury) and underlying risk factors. In addition, a focused review of RLNI, whether transient or permanent, as well as the management option of conservative, medical, or surgical, were also carried out. The following surgical procedures were carried out: total thyroidectomy, ipsilateral hemithyroidectomy, revision thyroidectomy (removal of residual/recurrent thyroid tissue in a patient with previous ipsilateral thyroidectomy), and completion thyroidectomy (removal of the contralateral lobe in a patient with previous hemithyroidectomy). Cases were divided into bilateral and unilateral operations. Bilateral procedures include operations on both sides of the neck, such as revision or total thyroidectomies. Unilateral procedures include operations on one side of the neck, such as hemithyroidectomy, completion, and revision thyroidectomies. Two experienced head and neck surgeons carried out all the procedures. Before and 3 weeks following thyroid surgery, all patients had a flexible laryngoscopy to record and document vocal fold function. An expert senior speech pathologist performed all documented video-assisted laryngoscopies. When the affected vocal fold moved neither at all nor noticeably less, VFP was considered to be present. Due to the subjective difficulties of distinguishing subtle degrees of vocal fold movement, no attempt has been made to differentiate between paresis and total vocal fold paralysis. For patients with postoperative VFP, repeat laryngoscopy was scheduled, usually within 3–4 weeks. Laryngoscopy and videostroboscopy were performed on patients who still had vocal fold dysfunction every 2 to 3 months until either excellent asymptomatic compensation occurred or normal vocal fold mobility was restored. Every instance of VFP that persisted for more than a year was regarded as permanent.

Surgical technique

Two specialized head and neck surgeons who performed over 120 surgeries annually carried out thyroidectomies. In every case, the same surgical method was applied. The thyroid gland capsule serves as the dissection plane in all procedures. For each case, the same protocol described in the literature was followed for either intraoperative neuromonitoring (IONM) or neurostimulation and laryngeal palpation (NSLP) physiological testing of the RLN [19]. In the case of NSLP, the current intensity of the disposable nerve stimulator (Xomed, Jacksonville, FL, USA) was adjusted between 0.5 and 2.0 mA. The posterior cricoarytenoid muscle was palpated for contraction (laryngeal twitch) once the thyroid cartilage was located. If there was no laryngeal twitch following the thyroidectomy, the NSLP test was deemed positive. In the case of IONM, throughout the procedure, IONM was monitored for RLN function and bursts using the Neurosign 100 (Magstim, Whitland, UK). When postoperative laryngoscopy confirmed the vocal fold palsy, the loss of IONM signals (burst) was classified as true positive; if the paralysis could not be established, it was classified as false positive.

Statistical analyses

Microsoft Office Excel (Microsoft Corporation, Redmond, USA) was used for data entry. Next, data was gathered and analyzed using (SPSS; IBM Inc.'s, Armonk, USA) software version 25.0. Descriptive data were illustrated using means and proportions. For each nerve at risk, the risk factors for RLN paralysis following thyroid surgery were addressed. Based on the risk factors examined, the total group's risk of RLNI was computed for the nerves at risk. For each risk factor under investigation, the relative risk was calculated with 95% confidence intervals. We utilized Fisher's exact test for a comparative analysis to verify statistically significant variations in the incidence of RLNI among the groups. The Mann-Whitney *U*-test was used to compare the continuous variables that were non-normally distributed. The interplay of factors that were statistically associated with postoperative RLN paralysis was examined using logistic regression. The outcomes were shown as odds ratios (OR) and 95% confidence intervals (CI). *p*-values with two sides were computed, and a value of less than 0.050 was deemed statistically significant.

Results

The study included 1368 patients who had thyroidectomies and met the inclusion criteria (809 bilateral, 559 unilateral). The mean age of the patients was 48.36 ± 13.03 with a male-to-female ratio of 1:3.6. Of the patients, 801 (58.6%) had total or subtotal thyroidectomies (1602 at-risk nerves). Sixty-two percent of the patients were over 45 years of age. Two-hundred seventy-six patients underwent hemithyroidectomy (276 at-risk nerves), and 291 underwent completion or redo surgeries (299 at-risk nerves). A total of 64.5% of the surgeries were done on patients with thyroid malignancy (see Table 1 for more details about surgical procedures and permanent pathology). Unilateral or bilateral CCND was performed in 32 patients (56 at-risk nerves). A nonrecurrent right inferior laryngeal nerve was observed in three instances (0.2%). Postoperative laryngoscopy revealed limited or absent vocal fold movement in 47 (3.4%) of these 2177 nerves at risk. In most cases, the surgeon documented technical difficulties during the surgery, such as fibrosis or tumor invasion. Forty-three out of 47 patients had unilateral VFP, and 4 had bilateral VFP. Twenty-nine out of 43 unilateral VFP patients had a transient pattern and recovered in less than 6 months. The remaining 14 cases were permanent, and most of them underwent a total thyroidectomy. A total of 55.2% of all unilateral VFP cases underwent total thyroidectomy. Three out of four cases of bilateral VFP were transient, and only one had a permanent course. All bilateral VFP cases were from the total

Table 1 Demographic data, surgical procedures, and permanent pathology in 1368 patients

Variable	No. (%)
Age (years)	
< 45	520 (38)
≥ 45	848 (62)
Mean ± SD	48.36 ± 13.03
Gender	
Female	1071 (78.3)
Male	297 (21.7)
Surgical procedure	
Total thyroidectomy	783 (57.2)
Hemithyroidectomy	276 (20.2)
Subtotal thyroidectomy (all bilateral)	18 (1.3)
Completion thyroidectomy (all unilateral)	208 (15.2)
Redo	83 (6.1)
Unilateral	75 (5.5)
Bilateral	8 (0.6)
Permanent pathology	
Benign	486 (35.5)
Malignant	882 (64.5)
Papillary thyroid carcinoma (PTC)	787 (57.5)
Follicular thyroid carcinoma (FTC)	68 (5)
Medullary thyroid carcinoma (MTC)	12 (0.9)
Anaplastic thyroid carcinoma (ATC)	9 (0.7)
Poorly differentiated thyroid carcinoma	6 (0.4)

Table 2 Relationship between surgical procedures and postoperative RLN paralysis in 1368 patients with thyroid surgeries

Surgical procedures	No. of patients	Unilateral RLN palsy (%)		Bilateral RLN palsy (%)		No. nerves at risk	Unilateral RLN palsy (%)		Bilateral RLN palsy (%)	
		Transient	Permanent	Transient	Permanent		Transient	Permanent	Transient	Permanent
	1368	**29 (2.1)**	**14 (1.0)**	**3 (0.2)**	**1 (0.1)**	**2177**	**29 (1.3)**	**14 (0.6)**	**3 (0.1)**	**1 (0.04)**
Total thyroidectomy	783	16 (2.0)	9 (1.1)	3 (0.4)	1 (0.1)	1566	16 (1.0)	9 (0.6)	3 (0.2)	1 (0.06)
Hemithyroidectomy	276	4 (1.4)	1 (0.4)	0	0	276	4 (1.4)	1 (0.4)	0	0
Subtotal thyroidectomy	18	1 (5.6)	0	0	0	36	1 (2.8)	0	0	0
Completion thyroidectomy	208	4 (1.9)	2 (1)	0	0	208	4 (1.9)	2 (1)	0	0
Redo	83	4 (4.8)	2 (2.4)	0	0	91	4 (4.4)	2 (2.2)	0	0
Unilateral	75	1	1			75	1	1		
Bilateral	8	3	1			16	3	1		

thyroidectomy group. The relationship between surgical procedures and post-surgery RLN paralysis is displayed in Table 2. Patients older than or equal to 45 years old accounted for 33 (2.4%) cases of VFP ($p = 0.034$). Gender and VFP did not significantly correlate ($p = 0.432$). Twenty-six patients got the right VFP in comparison to 21 with the left VFP; however, there was no statistically significant association ($p = 0.324$). Nineteen transient VFP cases and 10 permanent cases were related to total thyroidectomy procedures ($p = 0.004$). In addition, revision thyroidectomy was strongly associated with VFP ($p = 0.001$). The presence of substernal thyroid goiter was seen in 224 (16.4%) cases, and only 6 (2.7%) cases developed VFP ($p = 0.465$). RLN stimulation was done in all cases with NSLP or INOM, and no significant association was reported in the incidence of VFP ($p = 0.365$). Surgery for thyroid cancer was associated with a considerably greater risk of RLN palsy per patient (4.3%) than surgery for benign thyroid disease (1.9%) ($p = 0.031$). There was no discernible difference in the incidence of RLN palsy when we divided instances of benign disease into categories such as multinodular goiter, hyperthyroidism, solitary nodule, cystic lesion, or thyroiditis. Patients over 45, those undergoing total thyroidectomy, and those with malignant pathology all had a considerably higher chance of permanent RLN injury. Specimen weight had no discernible impact on the likelihood of RLN injury. Table 3 displays variables that may affect the likelihood of RLN injury and its correlation with RLN paralysis. When we analyzed the three statistically significant risk variables for postoperative RLN injury, age (*OR*, 1.01; 95% *CI*, 0.98–1.05; $p = 0.365$) became non-significant. The other two risk variables (extent of surgery and malignant pathology) remained statistically significant. Following adjustment, there was a significant correlation between the degree of surgery, including revision and total thyroidectomy, and a greater chance of developing post-surgery RLN palsy. It was not reported that the three nonrecurrent RLN cases were connected to postoperative VFP. The surgeon and a speech pathologist oversaw the long-term VFP follow-up. The clinical presentation of unilateral VFP varied from significant changes in the voice and swallowing quality to mild and subtle vocal changes. Twenty-nine out of 43 patients with unilateral

Table 3 Relationship between potential risk factors and RLN paralysis for 2177 nerves at risk in 1368 patients during thyroid surgery

Risk factor	No. of nerves	Transient RLN palsy		Permanent RLN palsy		Total RLN palsy	
		No. (%)	*p*-value	No. (%)	*p*-value	No. (%)	*p*-value
Age (years)			0.435		0.015		0.034
< 45	810	11 (1.4)		3 (0.4)		14 (1.7)	
≥ 45	1367	21 (1.5)		12 0.9)		33 (2.4)	
Sex			0.137		0.682		0.423
Male	520	13 (2.5)		7 (1.3)		20 (3.8)	
Female	1657	19 (1.1)		8 (0.5)		27 (1.6)	
Side			0.362		0.465		0.324
Right	1136	17 (1.5)		9 (0.8)		26 (2.3)	
Left	1041	15 (1.4)		6 (0.6)		21 (2.0)	
Surgical procedure			0.041	10 (0.6)	0.006	29 (1.9)	0.004
Total	1566	19 (1.2)		0 (0.0)		1 (2.8)	
Subtotal	36	1 (2.8)		1 (0.4)		5 (1.8)	
Hemithyroidectomy	276	4 (1.4)		2 (1.0)		6 (2.9)	
Completion	208	4 (1.9)	0.632	2 (2.2)	0.873	6 (6.6)	0.971
Previous redo	91	4 (4.4)	0.004		0.037		0.001
Substernal goiter			0.332		0.613		0.465
Present	224	4 (1.8)		2 (0.9)		6 (2.7)	
Not present	1953	28 (1.4)		13 (0.7)		41 (2.1)	
RLN stimulation			0.164		0.632		0.365
NSLP	880	21 (2.4)		9 (1.0)		30 (3.4)	
INOM	1297	11 (0.8)		6 (0.5)		17 (1.3)	
Pathology			0.047		0.324		0.031
Benign	512	5 (1.0)		4 (0.8)		9 (1.8)	
Malignant	1665	27 (1.6)		11 (0.7)		38 (2.3)	

VFP were transient and recovered in less than 6 months (median duration of 3 months) either with observation alone, steroid therapy, or speech therapy. Injection medialization laryngoplasty with calcium hydroxylapatite was done in seven cases, five under local anesthesia, and the remaining under general anesthesia, and all demonstrated good voice quality with no adverse events. Three out of four cases of bilateral VFP required tracheotomies. Weaning from tracheotomy was carried out in all cases: one spontaneous during time and the other two cases after lateralization surgery by partial posterior cordectomy.

Discussion

The literature reports varying incidences of recurrent laryngeal nerve palsy, ranging from 1 to 20% [20, 21]. In the current study, we discovered that 3.4% of RLNs that had been functioning properly before surgery did not function post-surgery, which resulted in VCP. The underlying condition, the depth of surgical resection, substernal goiters, re-operative thyroid surgeries, and the surgeon's expertise are among the factors that raise the risk of nerve injury [22–24]. Skilled surgeons have been known to inadvertently injure nerves and cause permanent palsy in 1–2% of patients [25, 26]. Recurrent laryngeal nerve injury has a variety of documented underlying mechanisms, such as thermal effect, excessive nerve skeletonization, traction, edema, hemorrhage, challenging tracheal intubation, and neuritis [27]. Within this current investigation, we discovered that the following variables were significantly linked to postoperative VCP: surgically discovered cancer adherent to the RLN, discovered RLN draped widely over the thyroid's surface, or discovered RLN closely linked to the thyroid parenchyma at Berry's ligament. Those surgical technical difficulties were documented by others in the literature [2]. RLN identification and careful dissection are the accepted approaches by most head and neck surgeons. In some circumstances, such as reoperations, surgery for cancer, inflammation such as thyroiditis, anatomic variations, and a history of radiation, this approach can be contested [2, 21]. Particularly in complex instances and high-risk procedures, nerve monitoring makes it easier to identify anatomically and physiologically the recurrent laryngeal nerve that instructs the surgeon [28]. Although this technique is becoming more and more popular, its ability to lower the frequency of postoperative nerve palsy is still up for question and discussion [7]. A comparison of intraoperative neuromonitoring and identification alone in the Higgins [29] meta-analysis failed to show a statistically significant difference in the frequencies of temporary and permanent vocal fold palsy with varying indications of thyroid operations.

In our study, the strategy of nerve identification and physiological stimulation with either NSLP or INOM was used in all cases. According to our research and previous studies, the absence of a signal does not always indicate nerve malfunction following surgery, and physically intact nerve is not always correlated with normal vocal fold function [25]. The literature has also provided documentation of these observations [25]. Intraoperative neuromonitoring is necessary for bilateral thyroid surgery to assist the surgeon in deciding whether to proceed with the surgery or not to minimize the risk of bilateral RLN injury, depending on the status of the first nerve signal [28, 30, 31]. Our investigation showed that while the INOM group had a lower rate of transient VFP, the rates of persistent VFP were the same for both groups. The evidence varies when it comes to the risk of RLNI related to thyroid surgery and distinct histopathologies. According to our research, the likelihood of VFP was considerably greater following thyroid cancer surgery than following surgery for benign thyroid disease. In terms of benign pathologies, such as MNG, solitary nodular disease, thyroiditis, cystic lesions, and hyperthyroidism, there were no significant differences between the groups. The majority of VFP cases were resolved normally within 6 months. The primary limitation of this study is the lack of statistical power to detect a difference; patients were not randomized, which could introduce bias; however, the number of patients is sufficient (1368 and 2177 nerves at risk), and the groups are well matched.

Conclusion

According to our research, 3.4% of RLNs had either temporary or permanent VFP. This is particularly common in surgical exposures when the RLN was in close contact with the thyroid parenchyma at Berry's ligament, in revision procedures, and in situations where malignancy adherent to the RLN required aggressive dissection to preserve it. In thyroid surgery, nerve identification continues to be the gold standard for managing the recurrent laryngeal nerve.

Nerve identification remains the gold standard of recurrent laryngeal nerve management in thyroid surgery. When compared to NSLP, neuromonitoring did not lessen recurrent laryngeal nerve injury, but it did aid in identifying the recurrent laryngeal nerve, especially in challenging instances.

Declarations

Ethics approval and consent to participate
The Institutional Review Board of King Abdullah International Medical Research Center approved this study (Reference No. IRBC/0535/19). Patient consent was waived.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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