Erciyes Med J 2022; 44(2): 156–60 • DOI: 10.14744/etd.2021.92972
ORIGINAL ARTICLE – OPEN ACCESS

Influence of Recurrent Laryngeal Nerve Variations on Vocal Cord Paralysis

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ABSTRACT

Objective: Vocal cord paralysis (VCP) due to recurrent laryngeal nerve (RLN) injury is a significant potential complication of thyroid and parathyroid surgery. The aim of this study was to investigate the influence on VCP of the anatomical relationship of the RLN to the inferior thyroid artery (ITA) and extralaryngeal branching of the RLN.

Materials and Methods: The data of 123 patients (95 female, 28 male; mean age: 46+13.6 years), a total of 204 neck sides, who underwent a thyroidectomy and/or a parathyroidectomy performed with intraoperative nerve monitoring between March and December 2015 were evaluated retrospectively. Preoperative and postoperative vocal cord examinations were performed in all cases. RLN branching at a distance of >5 mm with both branches entering the larynx was considered extralaryngeal branching of the nerve. Age, gender, nerve side, RLN branching, and the relationship between the RLN and the ITA were evaluated to assess the possible effect on VCP.

Results: Of the 204 neck sides, 11 (5.4%) RLNs developed VCP. Ten cases were temporary (4.9%) and 1 (0.5%) was permanent. There was no significant difference in age, gender, nerve side, or RLN-ITA relationship in the VCP cases. Extralaryngeal branching was detected in 42 (22.7%) of 185 nerves, and the rate of total and transient VCP was significantly higher in branching nerves than in nonbranching nerves (11.9% vs 3.5%, p=0.034; 11.9% vs 2.8%, p=0.030, respectively).

Conclusion: RLN branching is a potential risk factor for total and transient VCP; awareness of this anatomical variation and complete exposure during thyroid surgery are crucial to the prevention of RLN injury.

Keywords: Extralaryngeal branching, inferior thyroid artery, recurrent laryngeal nerve, thyroidectomy, vocal cord paralysis

Cite this article as: Aygün N, Demircioğlu MK, Demircioğlu ZG, Ünlü MT, Akgün İE, İşgör A, et al. Influence of Recurrent Laryngeal Nerve Variations on Vocal Cord Paralysis. Erciyes Med J 2022; 44(2): 156-60.

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Submitted 08.02.2021
Accepted 10.08.2021
Available Online 14.01.2022

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INTRODUCTION

The most commonly performed endocrine surgical procedures are thyroid and parathyroid surgeries. According to extensive studies, hypoparathyroidism, vocal cord paralysis (VCP), recurrent laryngeal nerve (RLN) injury, and cervical hematoma are considered major complications (1).

RLN paralysis is one of the most feared complications of a thyroidectomy. Bilateral injury can lead to respiratory difficulties and be life-threatening, and a unilateral injury can impair quality of life as a result of hoarseness and aspiration of varying severity (2). Therefore, despite advances in surgical techniques and technologies, RLN paralysis remains a serious potential complication. A systemic review of 27 studies that included 25000 cases reported a broad range in the incidence of postthyroidectomy VCP, in part based on different methods of examination: transient RLN paralysis was identified in 9.8% (range: 1.4–38.4%) and the rate of permanent RLN paralysis was 2.3% (range: 0–18.6%) (3).

Increased risk of RLN paralysis is correlated with many conditions, such as thyroid cancer, secondary surgery, substernal goiter, large goiter, Graves' disease, thyroiditis, anatomical variations of the nerve, low-volume hospitals and endocrine surgeons, and surgical technique (4).

RLN has many anatomical variations, including non-recurrent laryngeal nerve, extralaryngeal branching, the specific relationship of the RLN to the inferior thyroid artery (ITA), and changes in the course of the nerve as a result of previous surgery, or a mass effect due to thyroid enlargement (5–11).

Non-recurrent laryngeal nerve is most often observed on the right side, and the prevalence has been reported to be 0% to 4.7% (12). The most common variation is extralaryngeal branching of the nerve, with a prevalence ranging from 18% to 93% (5, 13) (Fig. 1, 2). The relationship between the RLN and the ITA also varies, and this neurovascular relationship should not be assumed to be symmetrical (8). While most of the potential factors that may contribute to injury of the RLN can be determined preoperatively, it is not possible to predict anatomical variations of the nerve preoperatively. Anatomical variations of the RLN may result in inadvertent injury to the nerve (5).

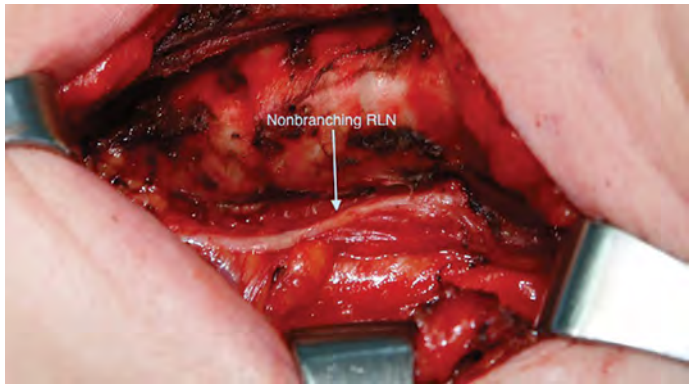

Figure 1. **Nonbranching recurrent laryngeal nerve**

This study was designed to evaluate the effect of the most commonly encountered anatomical variations of RLN, its relationship to the ITA and extralaryngeal branching, and the impact on the rate of VCP.

MATERIALS and METHODS

This study was approved by the ethics committee of the University of Health Sciences, Sisli Hamidiye Etfal Teaching and Research Hospital on September 9, 2020 (no: 2993).

The data of patients who underwent a thyroidectomy and/or a parathyroidectomy with intraoperative nerve monitoring between March and December 2015 were evaluated retrospectively. Patients who underwent a primary thyroidectomy and/or parathyroidectomy with the RLN anatomy exposed to the laryngeal entry and those with recorded data of extralaryngeal branching and/or the relationship of the RLN to the ITA were included in the study. Cases of preoperative VCP, failure to explore the RLN as far as the entry to the larynx (especially during parathyroidectomy), cases of recurrence, and intentional division of the RLN due to tumor invasion were excluded.

Thyroidectomy and RLN exploration techniques have been described in detail in previous studies (6, 14, 15). The RLN was fully explored as far as the entry to the larynx, and extralaryngeal branching and/or its relationship to the ITA was evaluated and recorded. Each neck side was evaluated separately according to the number of nerves at risk. Non-recurrent laryngeal nerve was not observed in this series. The relationship of the RLN to the ITA was identified and recorded in 196 nerves. The remaining 8 nerves were excluded. It was possible to demonstrate the branching characteristics of 185 of 204 RLNs, and those were enrolled in the study; the remaining 19 nerves with an unspecified course were excluded. RLNs branching at a distance of >5 mm from the larynx and with branches entering the larynx were accepted as extralaryngeal branching nerves. Preoperative and postoperative vocal cord examinations were performed in all patients by an independent otolaryngologist using a direct videolaryngoscope. The patients with postoperative VCP underwent vocal cord examination periodically at postoperative 1, 2, 4, and 6 months. Recovery from VCP before the postoperative sixth month was defined as temporary; if there was no evidence of recovery at the 6th month, the VCP was considered permanent. The effect of age, gender, nerve side, extralaryngeal RLN branching, and the relationship between the RLN and the ITA on VCP was evaluated.

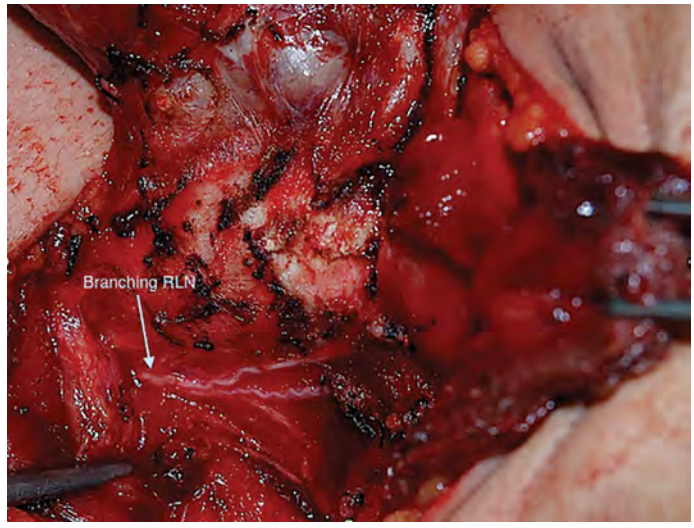

Figure 2. **Branching recurrent laryngeal nerve**

Statistical Analysis

The statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Normal distribution of the continuous data was tested using the Kolmogorov-Smirnov and Shapiro-Wilk tests and analyzed with appropriate methods. Independent categorical data were evaluated with chi-squared testing and the Fisher exact test. A value of $p<0.05$ was considered statistically significant.

RESULTS

The data of 204 neck sides of 123 patients (95 female, 28 male) with a mean age of 46+13.6 years were evaluated retrospectively. In all, 11 (5.4%) RLNs developed VCP. There were 10 cases of temporary VCP (4.9%) and the remaining case (0.5%) was permanent. No significant difference was found in VCP (total, transient, permanent) according to age, gender, nerve side, or the relationship between the RLN and the ITA (Table 1). Of 196 nerves with an identified RLN-ITA relationship, 7 (7.6%) of 92 (46.9%) nerves that crossed posterior to the ITA developed VCP, and 4 (4.9%) of 81 (41.3%) nerves that passed anterior to the ITA developed VCP. No VCP was detected in 23 nerves passing through the branches of the ITA. There was no significant difference in the rate of VCP based on the relationship between the ITA and the RLN ($p=0.345$) (Table 1). Transient VCP was detected in 6 nerves (6.5%) and permanent VCP was detected in 1 nerve (1.1%) anterior to the ITA. Extralaryngeal branching of the RLN was observed in 42 (22.7%) of 185 nerves. Transient VCP developed in 5 branching and 4 nonbranching nerves, and permanent VCP occurred in 1 nerve. The rate of total and transient VCP was significantly higher in branching nerves than in nonbranching nerves (11.9% vs 3.5%, respectively; $p=0.034$).

DISCUSSION

Although there are many studies evaluating factors that increase the risk of RLN injury in thyroid and parathyroid surgery, the number of studies evaluating the relationship of the nerve's anatomical variations to the risk of paralysis is limited. Our study examined some of the most common anatomical variations of RLN, extralaryngeal branching and the variable relationship of the RLN to the ITA.

Table 1. Influence of recurrent laryngeal nerve variations on vocal cord paralysis

	Total VCP			Transient VCP			Permanent VCP		
	n	%	p	n	%	p	n	%	p
Age (Mean+SD) /years									
VCP	47.7±12.1		0.735[a](NS)	47.7±12.1		0.735[a](NS)	64		0.192[a]
VCN	45.9±13.8			45.9±13.8			46±13.7		
Gender (NAR=204)									
Female NAR=154 (75.5%)	8	5.2	0.733[b](NS)	7	4.6	0.710[b](NS)	1	0.6	1[b](NS)
Male NAR=50 (24.5%)	3	6		3	6		0	0	
Diagnosis (NAR=204)									
MNG (NAR=117)	7	6	0.668[c](NS)	6	5.2	0.675[c](NS)	1	0.9	0.092[c](NS)
Hyperthyroidism (NAR=24)	0	0		0	0	0	0		
Malignity (NAR=32)	2	6.3		2	6.3	0	0		
Hyperparathyroidism (NAR=31)	2	6.5		2	6.5		0	0	
RLN side (NAR=204)									
Right (NAR=103, 50.5%)	6	5.8	0.782[c](NS)	6	5.8	0.748[b](NS)	0		0.495[b](NS)
Left (NAR=101, 49.5%)	5	5		4	4		1	1	
RLN and ITA relationship (NAR=196)									
Posterior to ITA (NAR=92, 46.9%)	7	7.6	0.345[c](NS)	7	7.6	0.257[c](NS)	0		0.490[c](NS)
Anterior to ITA (NAR=81, 41.3%)	4	4.9		3	3.75		1	1.2	
Between branches of ITA (NAR=23, 11.8%)	0	0			0	0			
RLN branching (NAR=185)									
No branching (NAR=143, 77.3%)	5	3.5	0.034[c](S)	4	2.8	0.030[b](S)	1	0.7	1[b](NS)
Branched (NAR=42, 22.7%)	5	11.9		5	11.9		0	0	

a: Independent samples test; b: Fisher's exact test; c: Pearson chi-square; S: Significant; NS: Not significant; ITA: Inferior thyroid artery; MNG: Multinodular goiter; NAR: Nerve at risk; RLN: Recurrent laryngeal nerve; VCN: Normal vocal cord; VCP: Vocal cord paralysis

No significant difference was detected in RLN paralysis in terms of the relationship between the ITA and the RLN. We recorded a rate of extralaryngeal branching of 22.7%. The rate of total VCP in branching nerves was 11.9% and was 3.5% in non-branching nerves; 2.8% of the cases in nonbranching nerves were transient VCP. The total and transient VCP rate was significantly higher in branching nerves (p=0.034, p=0.030, respectively).

Similarly, the literature indicates that branching may be seen in 18.5% to 37.4% of patients, and that extralaryngeal branching may be associated with greater risk of RLN paralysis (16–19).

Casella et al. (16) reported that the unilateral transient RLN paralysis risk was 7.36 times (95% CI: 1.84–29.4; p=0.0061) and that the unilateral permanent paralysis risk was 13.25 times (95% CI: 1.42–123.73; p=0.0204) greater in branched nerves compared with nonbranched nerves.

Sancho et al. (17) observed that the VCP rate was significantly higher in branched nerves than in nonbranched nerves (15.8% vs 8.1%, respectively; p=0.022). They determined that the risk of VCP in branched nerves was 2.2 times higher (95% CI: 1.1–4.5). Barczynski et al. (19) also found that the rate of transient VCP was higher in branched nerves and reported a 2.98-times greater risk of paralysis in branched nerves (95% CI: 1.79–4.95; p=0.001). They did not detect any difference between branched and nonbranched nerves in terms of permanent VCP (1.1% vs 0.2%, respectively) (19). There are also many studies reporting a similar VCP rate in branched and nonbranched nerves (14, 15, 20, 21).

In the literature, the rate of branching reported varies between 18.5% -72% (11, 16, 22). The rate rises to as much as 93% in autopsy series (10, 13).This suggests that some branches may be overlooked intraoperatively, including in our study. The difficulties present in a complete visual identification and preservation of the more vulnerable thinner branches could increase the risk of injury (18).

The varied nature of the relationship of the RLN to the ITA is also an important consideration. In our study, the course of the RLN was posterior to the ITA in 46.9%, anterior to the ITA in 41.3%, and between the branches of the ITA in 11.8%. Henry et al. (8) reported in a meta-analysis of 79 studies (18 intraoperative, 60 cadaveric, 1 intraoperative + cadaveric groups) that included 14,269 RLNs that 27.6% (95% CI: 23.2–30.6) ran anteriorly to the ITA, while 50.7% (95% CI: 45.2–53.5) ran posteriorly, and 21.7% (95% CI: 17.8–24.6) ran between ITA branches. The difference between the neck sides was significant: 62.6% (95% CI: 56.3–65.7) of the RLNs were posterior to the ITA on the left side, whereas only 37% (95% CI: 45.2–53.5) were on the right side. Noussios et al. (23) also demonstrated that the most common type of RLN had a course posterior to the ITA.

To the best of our knowledge, there is only one study evaluating the influence of the relationship of the RLN to the ITA on VCP. Sancho et al. (17) reported a rate of VCP according to the position of the RLN to the ITA (anterior: 14%, posterior: 14.7%, between ITA branches: 9.1%) and concluded that the position of the RLN did not affect the rate of VCP (p=0.529). In our study, the rate of VCP based on the location of the RLN relative to the ITA was posterior: 7.6%, anterior: 4.9%, and between ITA branches: 0%. No significant difference in VCP was found between these groups (p=0.345).

It has been proposed in anatomical studies that the risk of injury is greater if the RLN is anterior to the ITA or runs between the branches of the ITA, and that an RLN positioned anterior to the ITA might cause VCP due to overstretching of the nerve with the traction of the thyroid. It has also been suggested that inadvertent ligation of the ITA could increase the risk of RLN injury in the case of a course between the branches of the ITA (8, 10).The gold standard for preserving the RLN is visual identification. Some researchers recommend that the RLN should be partially explored around the Berry's ligament (24).

Since only partial exposure of the RLN might result in injury due to visual misidentification of the nerve, the RLN should be identified at least to the level of the ITA and completely exposed as far as the laryngeal entry. If the RLN is running parallel to a branch of the ITA, and especially if the nerve is only partially explored, the nerve can be mistaken for the branch of ITA and injured unintentionally (5).

Therefore, complete exploration of the RLN in the surgical area up to the point of laryngeal access can contribute to both further determination of extralaryngeal branching and the course of the branches, as well as minimize the possibility of mistaking the nerve for vascular branches. Additionally, the thinner branches of the extralaryngeal branching nerves may be more vulnerable to traction trauma. No instance of non-recurrent laryngeal nerve, which is a rare anatomical variation typically detected on the right side and associated with greater risk of VCP, was detected in our study. A meta-analysis reported detection on the right side at a rate of 0.7% in clinical series and 1.4% in cadaver studies (12).

The main limitations of our study are the retrospective design and not considering nerve distortions as a risk factor.

In conclusion, the most common anatomical variations of RLN are extralaryngeal branching and positioning in relation to the ITA. Since branching of the RLN presents greater risk of VCP, awareness of this anatomical variation and complete exposure during thyroid surgery are crucial to preventing RLN injury.

Ethics Committee Approval: The Şişli Hamidiye Etfal Teaching and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 22.09.2020, number: 2993).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – NA, İEA, Aİ, MU; Design – NA; Supervision – Aİ, MU; Materials – NA, MKD, ZGD, MTU; Data Collection and/or Processing – NA, MKD, ZGD, MTU; Analysis and/or Interpretation – NA, İEA, Aİ, MU; Literature Search – NA; Writing – NA; Critical Reviews – Aİ, MU.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: There is not any financial disclosure.

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