


ORIGINAL RESEARCH

Thyroid lobe size predicts risk of postoperative temporary recurrent laryngeal nerve paralysis

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Abstract

Objectives: In patients who had undergone thyroidectomy in Japan for benign tumor, we determined whether thyroid lobe size correlates with temporary recurrent laryngeal nerve paralysis (T-RLNP).**Methods:** We retrospectively collected medical record data on usage of intraoperative neuromonitoring, laterality of thyroidectomy, amount of bleeding during surgery, duration of surgery, and whether the surgeon was a board certified otorhinolaryngologist as determined by the Oto-Rhino-Laryngological Society of Japan. Thyroid size was measured in preoperative axial computed tomography (CT) images. Receiver operating characteristic (ROC) curve analysis was used to determine the thyroid size that predicted a high risk of T-RLNP or permanent recurrent laryngeal nerve paralysis (P-RLNP).**Results:** Of the 146 eligible patients identified, 9 (6.2%) developed T-RLNP and 2 (1.4%) developed P-RLNP. The amount of bleeding during thyroidectomy was significantly greater in T-RLNP patients than in P-RLNP patients. Thyroid sizes in CT images were significantly larger in T-RLNP patients compared to patients who did not develop RLNP (referred to hereafter as N-RLNP). ROC analysis revealed that 1.3% of thyroid lobes with an area of less than 1000.0 mm², and 9.9% of thyroid lobes with an area of greater than 1000.0 mm² were at risk for T-RLNP.**Conclusion:** We presented evidence that thyroid sizes, as measured on preoperative axial CT images, were larger in T-RLNP patients than in N-RLNP patients. Our results indicate a connection between benign thyroid tumor stretch injuries and T-RLNP.**Level of Evidence:** IV.

KEYWORDS

benign, recurrent laryngeal nerve, thyroid, thyroidectomy, vocal cord paralysis

This report includes some cases that were also included in a preliminary report in Japanese: Tsuzuki N, Sasaki S, Endo R, Kida A, Abe M. A study of postoperative recurrent laryngeal nerve paralysis in thyroid surgery—consideration of features of temporary and permanent paralysis. *J Jpn Broncho-esophageal Soc.* 2017;68:379-387.

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1 | INTRODUCTION

The recurrent laryngeal nerves (RLNs) are intimately related to the thyroid gland. As they course toward the larynx, the RLNs pass in close apposition to the posterior middle part of the outer lobes of the

thyroid gland, and penetrate into the larynx just posterior to the cricothyroid joint. This anatomical intimacy with the thyroid puts the RLNs at risk of injury during thyroidectomy and during thyroid tumor growth.

The RLNs are important for voice function and swallowing. As RLN paralysis (RLNP) may cause hoarseness and dysphagia, for intractable RLNP, the patient's quality of life (QoL) is much diminished. Therefore, preservation of the RLNs is very important in thyroidectomy. However, even when RLNs appear to be preserved during surgery, RLNP can still occur postoperatively in some cases. Some patients with postoperative RLNPs fail to recover and have permanent paralysis of the RLNs. RLN injuries can result from inadvertent transection, compression, crushing, stretching, electro-thermal injuries, ligature entrapment, and ischemia,¹ and certain RLN injuries often occur even when nerve integrity is visually confirmed during surgery.¹⁻³

Why paralysis of the RLNs is sometimes temporary and why it is sometimes permanent is not well understood. Some studies have analyzed the prognosis and frequency of RLNP resulting from various types of RLN injuries and found that RLNP from stretch injuries have a good prognosis.⁴⁻⁷ RLNP arising from stretch injuries is the most frequent type of paralysis observed following thyroid surgery.⁵ RLNs are often stretched forward during thyroidectomy, especially in patients with a large thyroid lobe.¹

These findings prompted us to analyze thyroidectomies in cases of benign diseases with the aim of elucidating whether thyroid lobe size, stretch injuries, and temporary RLNP are systematically associated. We limited our analysis to benign cases, because the surgical protocol used to resect the thyroid in benign cases is less invasive than that for malignant cases. In malignant cases, for example, risk of RLNP is increased because of the need for paratracheal lymph node dissection or because of neural invasion.

2 | MATERIALS AND METHODS

We conducted a retrospective study of the medical records of patients treated in the Departments of Otolaryngology and Head-and-Neck Surgery at two Japanese Red Cross Hospitals (one in Ashikaga and the other in Shizuoka). We included patients who underwent thyroidectomy and whose disease was diagnosed pathologically as benign. Benign thyroid diseases comprise mainly adenomatous goiter, follicular tumors, and includes the hyperthyroidism of Grave's disease. Non-malignant thyroid lobes that were resected in patients undergoing total thyroidectomy were also included. In performing the thyroidectomy, the surgical technique was generally started at the upper pole of the thyroid gland, regardless of the site of benign tumor, and then proceeded to the lower pole.

A total of 154 patients fitting the criteria for benign disease underwent thyroidectomies. Of these, 85 patients underwent surgery at the Japanese Red Cross Ashikaga Hospital between December 2010 and November 2015, and 69 patients underwent surgery at the Japanese Red Cross Shizuoka Hospital between December 2012 and

June 2017. RLNs were affected 90 and 81 times, respectively (ie, 90 nerves of 85 patients, and 81 nerves of 69 patients). The following cases were excluded: preoperative RLNP cases, cases in which the RLN was resected during surgery, cases in which RLNs were not identified during surgery, and cases involving non-RLNs. We also excluded cases lacking sufficient description in their medical records. A total of eight patients (9 RLNs) were excluded. Thus, 146 patients were enrolled and contributed data (162 RLNs).

There were two types of postoperative RLNPs: temporary RLNP (T-RLNP) and permanent RLNP (P-RLNP). T-RLNP was defined as RLNP that recovered within 6 months of thyroidectomy, and P-RLNP was defined as RLNP that persisted for 6 or more months after thyroidectomy. We collected the following types of data from the patients' medical records: whether intraoperative neuromonitoring (IONM) was used, side(s) of operation, amount of bleeding, duration of surgery, whether surgeon was a board certified otorhinolaryngologist, and preoperative computed tomography (CT) images. We quantified the amount of bleeding by weighing any blood collected (in grams) during surgery, if it was measurable. If not measurable, we noted in the patient's records that the amount of bleeding was "A small amount of bleeding." This was operationally defined as 10 g of blood. We also recorded the duration of the surgery (minutes). In Japan, thyroid diseases are frequently treated by otolaryngologists. In our study, certified surgeons were otorhinolaryngologists certified by the Oto-Rhino-Laryngological Society of Japan.

To determine whether preoperative nerve stretching caused by thyroid swelling can lead to T-RLNP and P-RLNP, we analyzed preoperative axial CT images of the neck. We measured 162 resected thyroid lobes. This analysis included measuring tumors that extended beyond the parenchyma of the thyroid gland. The thyroid size was determined using lateral diameter (L-D), antero-posterior diameter (AP-D), and superior-inferior diameter measurements (Figure 1).⁸ As

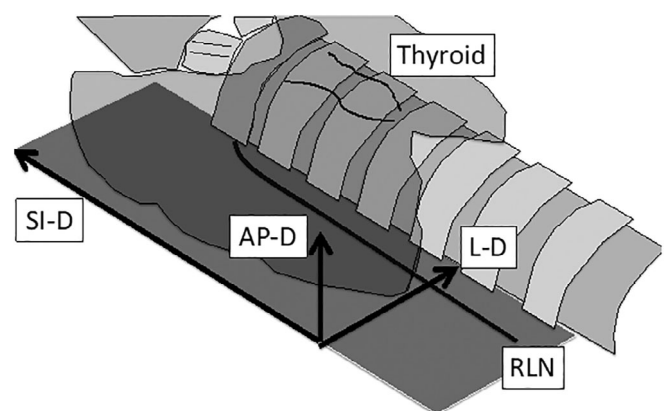


FIGURE 1 Diagram showing the position of the thyroid gland relative to the recurrent laryngeal nerve (RLN) and trachea. The size of the thyroid of each patient was determined by measuring the thyroid's lateral diameter (L-D) and antero-posterior diameter (AP-D) in preoperative axial CT images (see Figure 2), according to the method of Tsuzuki et al.⁸ The superior-inferior diameter (SI-D) of the thyroid was not measured in the present study

the distal course of RLNs runs parallel to the superior-inferior plane, we surmised that the superior-inferior diameter of the RLNs is less affected by stretching. The slice thickness of the axial CT images were generally 5 mm in this study. At this slice thickness, superior-inferior diameter measurements would have a large margin of measuring error in coronal or sagittal CT images derived from multiplanar reconstruction of axial images. Therefore, we did not analyze the superior-inferior diameters of the thyroid glands analyzed in this study. Bilaterally, RLNs travel just lateral to, or within, the tracheoesophageal groove. Thus, on axial CT images we took measurement baselines from the lateral end of the trachea to minimize measuring errors for each case. L-D and AP-D of the thyroid were measured as shown in Figure 2.⁸ We also measured the diameters on CT slices in which the thyroid gland was inferior to the cricoid cartilage, and we measured the longest L-D and AP-D for each case. To obtain the area of the largest section through the thyroid, we multiplied the longest L-D by the longest AP-D for each case.

Finally, we used receiver operating characteristic (ROC) curve analysis to determine the thyroid size that was linked to a high risk of T-RLNP or P-RLNP.

Statistical significance was assessed using Fisher's exact test, Kruskal-Wallis test, or the Spearman's rank-correlation coefficient test, as appropriate. SPSS Statistics for Windows version 24 (IBM Corp., Released 2016. Armonk, New York) was used. A *P*-value of <.05 was considered significant.

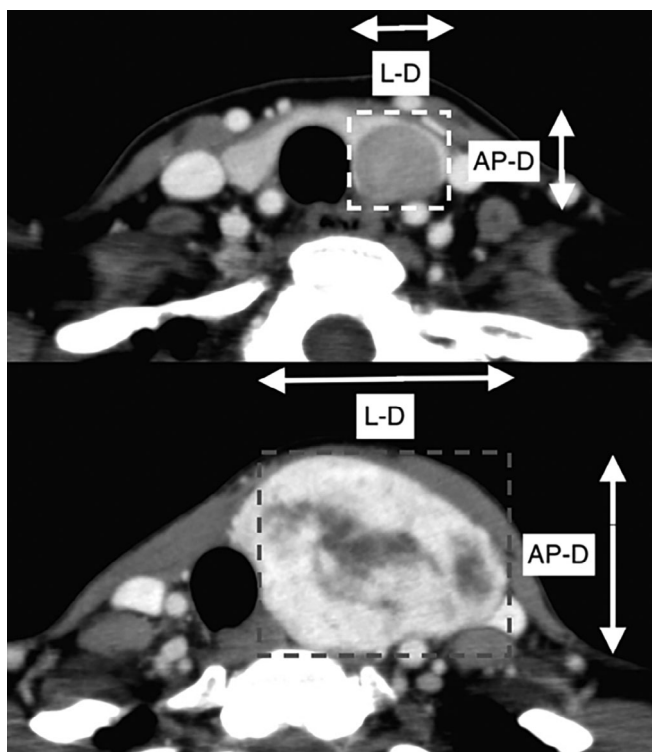


FIGURE 2 CT images of two different cases (one patient had a small thyroid and the other had a big thyroid). The thyroid is shown within the box. To determine thyroid size, the L-D and AP-D were measured in these images. L-D, lateral diameter; AP-D, antero-posterior diameter

All procedures were approved by the Institutional Review Committee of the Japanese Red Cross Ashikaga Hospital and the Japanese Red Cross Shizuoka Hospital. The study conformed to standards stated in the Declaration of Helsinki (World Medical Association 2013).

3 | RESULTS

We identified 146 eligible patients, 135 (92%) of which did not develop RLNP (referred to hereafter as N-RLNP). Nine patients (6.2%) developed T-RLNP, and 2 patients (1.4%) developed P-RLNP. Thus, the total incidence rate (T-RLNP plus P-RLNP) for RLNP was 7.5%. None of the patients developed bilateral RLNP. IONM was used in only 14 patients, 2 patients (14.2%) of which developed T-RLNP. None of the patients who underwent IONM developed P-RLNP. Patient characteristics and pathology of resected lobes are summarized in Table 1. No significant differences were found among groups regarding age or operative side. There were also no statistically significant differences regarding the side of operation between the three RLNP groups (*P* = .428). However, the percentage of patients receiving bilateral surgery tended to be higher in the T-RLNP group compared to the other two groups (Table 2).

We sought to determine whether RLNP was associated with the amount of bleeding and surgery duration (Table 2). The amount of bleeding was significantly greater in the T-RLNP group than in the N-RLNP (*P* = .033) and P-RLNP (*P* = .031) groups. Surgery duration did not differ significantly between groups (*P* = .409).

Next, we determined whether the incidence of RLNP was associated with the surgeons' skill (ie, certified or non-certified). The total incidence rate of RLNP (T-RLNP and P-RLNP combined) was 4.4% in the non-certified surgeon group and 12.7% in the certified surgeon group; however, this difference was not significantly different (*P* = .066, Fisher's exact test). For P-RLNP, the total incidence rate was 1.1% in the non-certified surgeon group and 1.8% in the certified surgeon group. Again, this difference was not significantly different (*P* = .613, Fisher's exact test).

Analysis of thyroid size, as measured on preoperative axial CT images, revealed that patients with larger thyroids were more likely to develop T-RLNP (Table 3). We identified 162 eligible nerves for this analysis, and of these, 151 were not associated with subsequent RLNP. However, 9 nerves were related to T-RLNP, and 2 nerves were related to P-RLNP. The L-D and AP-D values and area (L-D × AP-D) were significantly greater in the T-RLNP group than in the N-RLNP group (Table 3).

Given these preoperative tumor measurements, would it be possible to predict T-RLNP or P-RLNP? Using ROC curve analysis, we determined that a tumor area cutoff value of 1064.5 mm² indicated a high risk of T-RLNP (sensitivity: 0.889; specificity: 0.583). P-RLNP nerves were excluded from these analyses. The area under the ROC curve was 0.759 (95% Confidence Interval: 0.593-0.925). We set an area (L-D × AP-D) cutoff value of 1000.0 mm² for convenience. This suggests that 1.3% of thyroid lobes with an area of less than 1000.0 mm², and 9.9% of thyroid lobes with an area of greater than 1000.0 mm² are at risk for T-RLNP.

TABLE 1 Patient characteristics

	N-RLNP (n = 135)	T-RLNP (n = 9)	P-RLNP (n = 2)	Differences between the three groups	Test
Age, median (IQR)	57 (22)	47 (24)	70.5 (–)	<i>P</i> = .184	Kruskal-Wallis
Gender (M/F)	25/110	1/8	1/1	<i>P</i> = .438	Fisher exact
Pathology of resected lobe(s)					
Adenomatous goiter	76	6	1		
Follicular adenoma	36	1	1		
Non-malignant thyroid lobe	5	0	0		
Chronic thyroiditis	4	0	0		
Graves' disease	2	1	0		
Cyst	2	0	0		
Plummer's disease	1	0	0		
Adenoma	1	0	0		
Oxyphilic adenoma	1	0	0		
Oncocytoma	0	1	0		
Comorbid benign disease or tumor	7	0	0		

Abbreviations: IQR, interquartile range; N-RLNP, no recurrent laryngeal nerve paralysis; P-RLNP, permanent recurrent laryngeal nerve paralysis; T-RLNP, temporary recurrent laryngeal nerve paralysis; (–), no IQR available.

TABLE 2 Group differences on variables measured

	Between group differences							Test
	N-RLNP (n = 135)	T-RLNP (n = 9)	P-RLNP (n = 2)	N-RLNP, T-RLNP, and P-RLNP	N-RLNP and T-RLNP	N-RLNP and P-RLNP	T-RLNP and P-RLNP	
Operation side				<i>P</i> = .428				Fisher exact
Right	66 (48.9%)	4 (44.4%)	2 (100%)					
Left	54 (40.0%)	3 (33.3%)	0 (0%)					
Bilateral	15 (11.1%)	2 (22.2%)	0 (0%)					
Amount of bleeding (g) median (IQR)	20 (40)	65 (96)	10 (–)	<i>P</i> = .010	<i>P</i> = .033	<i>P</i> = .340	<i>P</i> = .031	Kruskal-Wallis
Surgery duration (min) median (IQR)	124 (71)	161 (107)	114.5 (–)	<i>P</i> = .409	ns	ns	ns	Kruskal-Wallis

Abbreviations: IQR, interquartile range; N-RLNP, no recurrent laryngeal nerve paralysis; ns, not significant; P-RLNP, permanent recurrent laryngeal nerve paralysis; T-RLNP, temporary recurrent laryngeal nerve paralysis; (–), no IQR available.

TABLE 3 Thyroid size as measured on preoperative axial CT images

	Between Group Differences							Test
	N-RLNP (nerve = 151)	T-RLNP (nerve = 9)	P-RLNP (nerve = 2)	N-RLNP, T-RLNP, and P-RLNP	N-RLNP and T-RLNP	N-RLNP and P-RLNP	T-RLNP and P-RLNP	
L-D (mm), median (IQR)	29 (14)	42 (24)	26 (–)	<i>P</i> = .026	<i>P</i> = .028	<i>P</i> = 1.000	<i>P</i> = .248	Kruskal-Wallis
AP-D (mm), median (IQR)	33 (12)	42 (16)	30 (–)	<i>P</i> = 0.039	<i>P</i> = .046	<i>P</i> = 1.000	<i>P</i> = .265	Kruskal-Wallis
L-D and AP-D (mm ²), median (IQR)	986 (895)	1665 (1718)	782 (–)	<i>P</i> = 0.027	<i>P</i> = .027	<i>P</i> = 1.000	<i>P</i> = .282	Kruskal-Wallis

Abbreviations: AP-D, antero-posterior diameter; IQR, interquartile range; L-D, lateral diameter; N-RLNP, no recurrent laryngeal nerve paralysis; P-RLNP, permanent recurrent laryngeal nerve paralysis; T-RLNP, temporary recurrent laryngeal nerve paralysis; (–), no IQR available.

We also examined the correlation between the amount of bleeding and tumor area. Spearman's rank-correlation coefficient test revealed that the amount of bleeding was significantly correlated with tumor area (*r* = 0.362; *P* < .01).

4 | DISCUSSION

The incidence of thyroid cancer has been increasing in many countries over the past three decades,⁹ and thyroid surgery rates have tripled.¹⁰

The most common thyroid surgery-related injury is damage to the RLNs, which are in close apposition to the thyroid gland and are important for voice function and swallowing. Another consideration for the source of injury is whether RLN injury occurs as a result of tumor growth. Regardless, temporary or permanent paralysis of the RLNs severely lowers QoL for sufferers. In our retrospective study of thyroidectomies in patients in Japan, the incidence rate of postoperative RLNP was 7.5% and the incidence rate of P-RLNP was 1.4%. These results are similar to those published in past reports.^{11,12}

The prognosis of RLN injuries depends on the type of insult to the nerve. Paniello et al showed that stretch injuries cause less severe RLN injuries than other types of injuries (eg, crush, transection, cauterization, etc.), as evidenced by a much quicker recovery in a canine RLN injury model.⁴ This is in line with findings of stretch injuries having a better prognosis than other types of injuries.⁵⁻⁷ One possible explanation is that stretch or traction injuries to the RLN cause less anatomical disruption than other types of injuries. In an experimental porcine RLN injury model, Dionigi et al observed that traction injuries have not only a lower P-RLNP rate and a shorter recovery time, but also are associated with less anatomical damage than that caused by mechanical and thermal injuries.⁵

Ultrasonography is typically used to measure tumor diameters directly. However, this method is not suitable for measuring tumors with indistinct borders, such as those with poorly defined margins or diffuse goiters. Ultrasonographic measurements are subjective, as they depend on individual technicians' subjective assessment of the tumor. Thus, it is susceptible to measurement errors. In the present study, we determined the baseline size of the thyroid lobes by measuring from the lateral end of the trachea in axial CT images. Unlike measurement methods that use ultrasonography, the method we used to measure thyroid lobes has the advantage of error mitigation. This is because the general CT protocols we used produce reproducible images. Also, measuring the outer edge of the thyroid in axial CT images would enable us to assess RLN stretching caused by thyroid swelling, as shown in Figure 2.⁸

We observed that the thyroid dimensions (L-D, AP-D, and L-D × AP-D) of patients with T-RLNP were significantly larger than those of patients with N-RLNP, as measured on preoperative axial CT images. In general, various disorders can lead to an increase in the size of thyroid lobes, such as a large goiter, Graves' disease, and thyroiditis. In these kinds of cases, we often encounter thinning and stretched RLNs during the course of standard thyroidectomy surgery. The results from our study may suggest that a large thyroid can preoperatively stretch RLNs, thus causing stretch injuries during surgery and increasing the risk of T-RLNP.

We also observed that the amount of bleeding was significantly higher in patients with T-RLNP than in the other two groups of patients. The amount of bleeding was also correlated with L-D × AP-D values and hence larger thyroids. Since a large thyroid may increase the amount of bleeding during surgery, intraoperative interventions aimed at reducing or stopping bleeding near the RLNs (eg, applying pressure and using electrocoagulation) may inadvertently damage RLNs and increase the possibility of RLNP.

Although surgery duration was not statistically different among the three groups of patients in our study, surgery duration of patients with T-RLNP tended to be longer than that of patients in the other two groups. This may be because the frequency of bilateral surgery in the T-RLNP group was somewhat greater than that in the other two groups.

IONM is used in surgery to decrease the risk of nerve injuries and has become increasingly common.^{13,14} To date, reports on whether IONM decreases RLNP incidence are limited.¹⁵⁻¹⁸ In our study, we could not determine whether IONM decreased RLNP because IONM was used in only a small number of patients. Recently, continuous IONM has gained increasing popularity not only as a means to reduce surgery-related nerve injuries, but also as a tool to guide and inform surgeons and anesthesiologists during various surgical procedures. Continuous IONM has the potential of effectively preventing stretch injuries, since it can anticipate unexpected nerve injuries before they actually occur. Although various types of injuries could occur during thyroidectomy surgery, we surmise that the most frequent cause of T-RLNP is stretch injuries to the RLNs. This notion is consistent with our present findings as well as those from previous studies.^{19,20} Additional studies are needed to assess whether continuous IONM is capable of determining when and where RLN injuries might occur.

Our study design has some limitations. Because we used a retrospective design in which data from patient medical records were extracted and analyzed, the number of cases was relatively small. We believe, however, that our sample size was sufficiently large to provide reliable results, since the incident rate of T-RLNP and P-RLNP in the present study was comparable to that of past reports.^{11,12} Nonetheless, a larger study population and a variety of cases are necessary for future studies.

5 | CONCLUSION

In conclusion, we presented evidence that thyroid sizes, as measured on preoperative axial CT images, were larger in T-RLNP patients than in N-RLNP patients. Our results also may indicate that stretch injuries and T-RLNP could be causally linked.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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