Original Article

Clinical classification of recurrent laryngeal nerve palsy

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Background: The application of intraoperative neurophysiological monitoring (IONM) has been accepted to avoid injury of a recurrent laryngeal nerve (RLN). Loss of the neuromonitoring signal indicates nerve injury and is subdivided into segmental type and global type nerve paralysis. This study aimed to determine the course of vocal cord function recovery after definitive loss of signal (LOS) types.

Methods: This retrospective study included 1,442 patients (with 2,752 nerves at risk) who had thyroidectomies between January 2018 and December 2021. Preoperative and postoperative vocal cord functions were evaluated by laryngoscopic examination.

Results: LOS occurred in 168 of 1,442 (11.7%) patients and 171 of 2,748 (6.2%) nerves at risk during surgery. Of LOS nerves of benign tumors, 74.2% showed global type. In cancer cases, segmental paralysis was more common, accounting for 51.3% of LOS nerves. Of nerves with segmental LOS in cancer patients, 55.3% needed partial layer resection for RLN invasion. Intraoperative recovery was seen in 9 of 62 nerves (14.5%) with segmental LOS and 32 of 109 (29.4%) nerves with global type LOS. The vocal cord palsy rate on postoperative days (PODs) 2–3 was lower after global type nerve paralysis (63.6%) than after segmental loss (84.9%). At 6 months postoperatively, the rate of vocal cord paralysis in benign tumors was not significantly different between segmental type and global type (P=0.586). However, cancer patients with segmental LOS significantly more often had vocal cord dysfunction than those with global LOS at 6 months postoperatively (rate of nerve palsy: segmental 40.0% *vs*. global 3.4%) (P<0.001).

Conclusions: The intraoperative recovery rate and early nerve recovery rate are significantly higher for patients with global LOS than for patients with segmental LOS. Cancer patients with segmental LOS significantly more often had vocal cord dysfunction than those with global LOS at 6 months postoperatively.

Keywords: Thyroid surgery; recurrent laryngeal nerve (RLN); surgical complication; intraoperative neurophysiological monitoring (IONM)

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Introduction

The application of intraoperative neurophysiological monitoring (IONM) has been widely accepted to avoid injury of a recurrent laryngeal nerve (RLN) or external branches of a superior laryngeal nerve (EBSLN). IONM has many advantages for thyroid surgery. First is that IONM facilitates the identification of the nerve. There are many anatomical variants, including extralaryngeal branching of the RLN, the course of the RLN posterior and/or anterior to the inferior thyroid artery, or the tuberculum of Zuckerkandl. Second is that IONM has the possibility of decreasing paralysis of the RLN. In a meta-analysis of 1,513 thyroidectomy patients, the temporary RLN palsy rate was 4.2% with neural monitoring and 7.7% without it. The permanent RLN palsy rate with and without neural monitoring was 1.0% and 1.6%, respectively (1). The third is that IONM informs surgeons of the functional integrity of the nerve and predicts the time of RLN function recovery. When intraoperative loss of signal (LOS) occurs without mechanical trouble, the first step is to stimulate the RLN from the point of the laryngeal entry point to the vagus nerve to determine the injury point. RLN nerve palsy is clinically divided into two types, segmental injury and global injury. Segmental nerve injury is diagnosed when the signal is completely lost at a specific point of RLN injury. The LOS occurs proximal to the injury point, but it is distally preserved. Global injury is defined as the complete absence of a response to 1–2 mA stimulation to the ipsilateral RLN and the vagus nerve's entire course. There is no specific focal point of damage for global nerve injury. The intraoperative recovery rate and postoperative recovery rate are reported to be significantly lower for patients with segmental LOS than for patients with global LOS (2).

However, few reports have discussed the recovery course of clinical RLN injury types (global type or segmental type) depending on the histological type; thus, the incidence of clinical LOS subtypes and the recovery time based on clinical LOS types by intraoperative nerve monitoring were determined. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-23-149/rc).

Highlight box

Key findings
- The intraoperative recovery rate and early nerve recovery rate are significantly higher for patients with global loss of signal (LOS), than for patients with segmental LOS.
- Intraoperative recovery was seen in 14.5% with segmental LOS and 29.4% nerves with global type LOS.

What is known and what is new?
- Few reports have discussed the recovery course of clinical recurrent laryngeal nerve injury types depending on the histological type.
- Of the nerves showing LOS, 74.2% were global type in benign tumor cases, and 51.3% were segmental type in thyroid cancer cases.

What is the implication, and what should change now?
- The intraoperative recovery rate and early nerve recovery rate are different depend on clinical nerve LOS type and the histological type. We have to change the management of the LOS nerves according to the clinical nerve LOS type and the histological type.

Methods

This retrospective study included patients who had undergone primary thyroidectomies at Ito Hospital between January 2018 and December 2021. Patients with preoperative vocal cord palsy, those without preoperative examination for vocal cord mobility, and those without IONM were excluded. A total of 1,442 thyroidectomy patients with 2,748 nerves at risk underwent intermittent IONM. All patients underwent laryngoscopic examination for vocal cord mobility on postoperative day (POD) 2. When vocal cord dysfunction occurred, vocal cord function was checked every 1 to 3 months for 1 year. All vocal cord palsies lasting for more than 6 months were considered as permanent.

The standard IONM procedure (IONM equipment, induction, anesthesia maintenance, tube position) according to the 2011 International Neural Monitoring Study Group (INMSG) guideline was performed (3). A Nerve Integrity Monitor [NIM-response 3® and 7–8 mm electromyography (EMG) Endotracheal Trivantage Tube; Medtronic, Minneapolis, MN, USA] was used for monitoring. A monopolar stimulation probe with a current of 1–2 mA was used, and LOS was defined as an amplitude reduction to <100 μV or no response to stimulation with a current of 1–2 mA on the dry field and no laryngeal twitch. The RLN and vagus nerve were repeatedly rechecked during lobe mobilization and removal. Once a possible LOS was detected, the laryngeal twitch and contralateral vagus nerve responses to stimulation were evaluated (3,4). We stimulate the RLN from the point of the laryngeal entry point to the vagus nerve to determine the injury point. The LOS nerves were divided into 2 groups (segmental nerve injury and global nerve injury) according to the previous report (5). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board of Ito Hospital (No. 396) and informed consent was obtained from all individual patients.

Statistical analysis

Data were analyzed with statistical software (JMP software v14.0, SAS Institute, Inc., Cary, NC, USA). The chi-squared test or Wilcoxon test was used to compare categorical variables. Continuous variables were compared

Table 1 Baseline information of 1,442 enrolled patients

Parameters	Without LOS (n=1,274)	With LOS (n=168)
Age (years), median (range)	48.0 (14.0–81.0)	45.5 (21.0–78.0)
Sex (male/female), n/n	285/989	40/128
Clinical diagnosis (malignant/benign), n/n	540/734	78/90
Extent of surgery, n		
Hemithyroidectomy (with/without central node dissection)	130	2
Total thyroidectomy (with/without central node dissection)	1,144	166

LOS, loss of signal; n, number of patients.

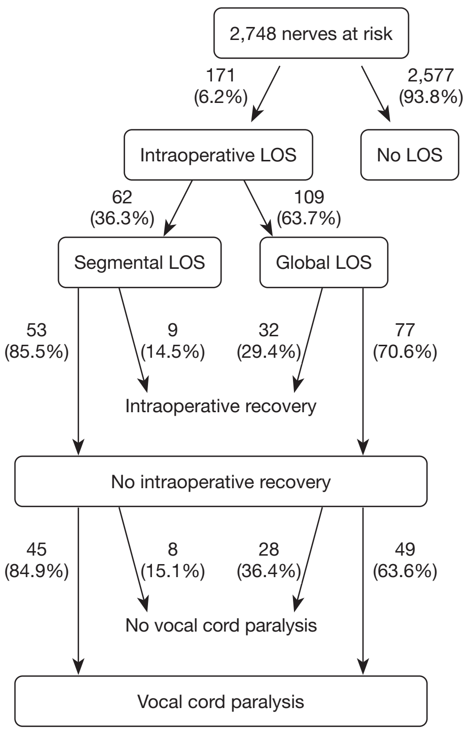

Figure 1 The course of the recurrent laryngeal nerve function after definitive LOS types. LOS, loss of signal.

by the Mann-Whitney *U* test, and categorical variables were compared between two groups by the two-sided Fisher's exact test or the chi-squared test. Multivariate analysis was performed by binary regression of variables showing P<0.05 on univariate analysis.

Results

Patients' details are presented in *Table 1*. Overall, 90.8% of the surgical procedures were total thyroidectomy (n=1,310), and 9.2% were hemithyroidectomy (n=132). LOS occurred in 168 of 1,442 (11.7%) patients and 171 of 2,748 nerves at risk (6.2%) during surgery. *Figure 1* shows the recovery course by LOS type. Of the LOS nerves during surgery, 62 nerves (36.3%) were segmental type, and 109 nerves (63.7%) were global type. Intraoperative recovery occurred in 9 of 62 nerves (14.5%) with segmental LOS type and 32 of 109 nerves (29.4%) with global LOS type. Of the segmental loss and global loss types at the end of surgery, 84.9% and 63.6%, respectively, had vocal cord paralysis on POD 2.

Because different diseases might have different rates of RLN damage, benign thyroid disease (1,541 nerves at risk) and thyroid cancer (1,207 nerves at risk) were evaluated separately (*Table 2*). During surgery, cancer patients more often have segmental LOS than patients with benign tumor (48.7% *vs.* 25.8%, P=0.0019). Of the segmental loss cases in 38 cancer patients, 21 nerves (55.3%) needed nerve partial layer resection to remove cancer. Intraoperative recovery was seen in 27 of 93 LOS nerves (29.0%) of benign tumor cases and 14 of 78 LOS nerves (17.9%) of thyroid cancer cases (P=0.0909). In benign tumor and thyroid cancer patients, 48 (72.7%) of 66 LOS nerves and 56 (87.5%) of 64 LOS nerves at the end of surgery, respectively, showed vocal cord paralysis. In particular, 95.2% of cancer patients with segmental loss caused by nerve layer resection had vocal cord paralysis on POD 2.

Permanent vocal cord paralysis was seen in only one nerve (0.06%) with benign tumor and 15 nerves (1.2%) with thyroid cancer. Of the nerves that needed nerve partial layer resection to remove cancer, 14 (66.9%) showed permanent vocal cord paralysis.

Discussion

Nerve injury is clinically divided into two groups. Nerve

Table 2 Recovery of vocal cord function after intraoperative LOS by histopathological type

Parameters	Histopathological type		P
	Benign (1,541 nerves at risk)	Cancer (1,207 nerves at risk)	
Total number of LOS nerves	93 (6.0)	78 (6.5)	0.1289
LOS, segmental/global	24 (25.8)/69 (74.2)	40 (51.3)/38 (48.7)	0.0019
Side of LOS, right/left	43 (46.2)/50 (53.8)	41 (52.6)/37 (47.4)	0.4097
Intraoperative status			0.0909
Intraoperative no recovery	66 (71.0)	64 (82.1)	
Intraoperative recovery	27 (29.0)	14 (17.9)	
Segmental/global	6/21	3/11	
Early vocal cord paralysis	48	56 [20†]	0.0071
Permanent vocal cord paralysis	1	15 [14†]	<0.001

Data are presented as number of nerves (percentage). †, number of nerve layer resections. LOS, loss of signal.

Table 3 Clinical trials investigating the recovery of vocal cord function after LOS at the end of surgery

Type of LOS	Segmental				Global			
	Schneider *et al.*, 2016, (5)	Present study			Schneider *et al.*, 2016, (5)	Present study		
		All	Benign	Cancer		All	Benign	Cancer
LOS subtype at the end of surgery (%)	48.7	40.8	27.3	54.7	51.3	59.2	72.7	45.3
Postoperative day 2 vocal cord paralysis (%)	94.6	84.9	83.3	85.7	69.5	63.6	52.0	82.7
Postoperative month 6 vocal cord paralysis (%)	10.7	28.3	0	40.0	6.8	2.6	2.1	3.4

LOS, loss of signal.

injury with segmental LOS is caused by a suture, vessel, or fibrotic band entrapping the nerve at this point. The mechanism of global LOS is still not well understood, but overstretching during retraction is thought to be the most possible cause, and the nerve might be injured at a more distal laryngeal focus. Some nerve injuries can recover spontaneously during surgery, and others can recover after surgery. They can also develop permanent damage.

Nerve damage is evaluated by three factors. The first factor is damage type, such as ligature, transaction, compression, thermal injury, pinching, traction, or stretch. The second is the strength of damage, and the third is the duration of damage. For example, for the nerve damage caused by traction or stretch, a few minutes are needed to injure the nerve. Liu *et al.* reported that 70% of traction injury nerves recovered function intraoperatively after release of the traction, and the longest duration of recovery was 20 min (2). On the other hand, thermal injury by an energy-based device is more severe than mechanical injury and might show segmental loss (6). Dionigi *et al.* suggested not using the device closer than 2–3 mm to the RLN with lag time of at least 2 seconds, because protein denaturation and RLN injuries occur at a temperature of 60 ℃ (7). We avoided using energy-based devices when dissecting the tissue near the RLN. In our procedure, thermal injuries were rare and traction could be more common cause for global LOS damage. Thyroid cancer patients more commonly had segmental paralysis. After partial layer resection of the RLN, 75–83% of patients had functioning vocal cords, and the rest had vocal cord paralysis 1 year after surgery (8,9). These reports did not describe the LOS subtypes, but in the present study, 85% of patients after layer resection showed segmental LOS during surgery, and 66.6% of LOS cases at the end of surgery showed permanent vocal cord paralysis.

Table 3 shows the comparison between previous data and the data of the present study according to clinical nerve damage type. Global type was more common and showed less damage, and the rate of recovery was high. The rate of postoperative vocal paralysis with segmental type was higher than in Schneider's report. That is because the present cases needed partial layer resection of the RLN in patients with invasive papillary thyroid cancer.

When the LOS occurred, we have to exclude the possibility of false LOS. In the case of global LOS especially, we check the monitor dysfunction, change in EMG endotracheal tube position, neuromuscular agents from the anaesthetist, etc. At first, we check the result of neuromuscular monitoring. The train-of-four (TOF) monitoring is available for every patient who undergoes neuromuscular blockade during surgery in our hospital. The TOF ratio >0.7 signifies a satisfactory recovery of the neuromuscular function and when the TOF ratio is low, some waiting time may be needed to wear off the effect, or selective reversal binding agents (sugammadex) should be given.

Next, we perform the contralateral vagus nerve stimulation. Negative contralateral vagus nerve stimulation means the possibility of the monitor equipment dysfunction. The recording electrodes, grounding electrode and associated connections at the interface-connector box and monitor might be dislodged or displaced and should be recheck. We also confirm the accurate surface electrode positions of an EMG tube by fiber-optic laryngoscope.

When the planned surgery was a total thyroidectomy, if the true LOS occurred on the first side, we have to decide whether to continue the surgery or stop it. The INMSG recommends that neural monitoring information should be used in planned bilateral procedures by staging the surgery in the case of ipsilateral LOS (10,11). With our results, we would complete the contralateral side if the LOS was global and benign rather than segmental and malignant.

This study has limitations. First, it was retrospective and when hemithyroidectomy is planned, IONM was not routinely done. So, in this study, the number of hemithyroidectomy was small. When the imaging test [computed tomography (CT) scan or ultrasonography] suggested the tumor has invasion to the RLN palsy, but laryngeal fiber scope test showed normal vocal function, we performed IONM in case of hemithyroidectomy. Second, the exact damage time and recovery time of nerve function during surgery were not obtained, because continuous nerve monitoring was not used for every patient. During surgery, a 4-step procedure (V1, R1, R2, and V2) according to the International Neural Monitoring Guidelines was done and recorded. The EMG wave was saved at each point, but the exact time of LOS and recovery time was not recorded. However, we could predict the nerve recovery at POD 2 and 6 months postoperatively according to the clinical LOS nerve types and the histological type.

Conclusions

The intraoperative recovery rate and early nerve recovery rate are different depend on clinical nerve LOS type and the histological type.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-23-149/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-23-149/dss

Peer Review File: Available at https://gs.amegroups.com/article/view/10.21037/gs-23-149/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-23-149/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board of Ito Hospital (No. 396) and informed consent was obtained from all individual participants.

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