



# Recurrent Laryngeal Nerve with Loss of Signal During Monitored Thyroidectomy: Percentage Reduction in Sum of the Amplitude of Left and Right Channel

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## Abstract

**Purpose** The prognostication for the injured recurrent laryngeal nerve (RLN) with incomplete loss of signal (LOS) and its function outcome have not been well unified. A warning criterion was proposed to predict RLN injury during monitored thyroidectomy.

**Methods** A retrospective review of prospectively collected data from consecutive 357 patients with 560 nerves at risk was conducted. Vocal cords mobility with laryngoscope was performed preoperatively, on the second day, and once a month postoperatively until complete recovery. Different cutoff values of the percentage reduction in sum of the amplitude of left and right channel at the end of the surgery, for postoperative vocal cord paralysis (VCP) prediction were compared.

**Results** Percentage reduction in sum of the amplitude of left and right channel at the end of operation ranged from 30.2 to 63.6% in 27 nerves with incomplete LOS (absolute amplitude value of final  $R_2 > 100 \mu\text{V}$  with reduction  $> 50\%$  of  $R_1$ ). Seven (1.25%) nerves experienced transient postoperative VCP, in which one nerve with postoperative VCP showed no amplitude reduction. The positive predictive value of VCP for the sum amplitude reduction exceeding 30, 40, 50, and 60% was 22.2, 40, 85.7, and 100%, respectively. Accuracy was 96.1, 98.2, 99.6, 99.4%, respectively.

**Conclusion** Percentage reduction in sum of the amplitude of left and right channel is a meaningful method to improve the accuracy of VCP prediction. When the sum amplitude reduction  $\geq 50\%$ , surgeons should consider the possibility of postoperative VCP and correct some surgical maneuvers.

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## Introduction

Intraoperative neuromonitoring (IONM) is crucial in thyroid surgery because the recurrent laryngeal nerve's (RLN) functional integrity and visual anatomic integrity are not equivalent [1]. The use of intermittent IONM (I-IONM) during monitored thyroidectomy allows for the early detection of the RLN while avoiding overly aggressive manipulation of the nerve and potential extra-laryngeal branch or anatomic abnormalities. Evaluation of the RLN function before, during, and after surgery with confirmation of the RLN's functional integrity is another advantage of IONM. Eventually, reorienting the surgical strategy when loss of signal (LOS) occurs after resection of the first lobe

in bilateral thyroidectomy. The positive predictive value (PPV) of IONM to predict recurrent laryngeal nerve palsy, however, is only 30% to a maximum of 75% [2–6].

The most frequent causes of false positives (FP) (LOS with intact vocal cords mobility) are as follows: endotracheal tube (ETT) displacement, equipment problems, blood covering the stimulated nerve segment; neuromuscular blockage, and early neural recovery [7]. Care must be taken in positioning the ETT accurately, verification of ideal position of ETT before the beginning of the operation is a necessary step to guarantee functional high quality of I-IONM. According to the International Neural Monitoring Study Group (INMSG) for monitoring a patient positioning, correct ETT electrodes position should be assessed by directing laryngoscopy, respiratory variation of the baseline and obtaining appropriate values of electromyography (EMG) amplitude in predissection vagal nerve (VN) stimulation  $V_1$  ( $> 500 \mu\text{V}$ ) [7, 8]. However, tube-rotation accounted for 44% of the initial I-IONM failure [9], and ETT could be displaced after the patient has been fully positioned with head extension or during surgical procedure because of the in-field traction on the trachea, which could reflect a neurophysiologic event or a LOS signal with normal postoperative vocal cords mobility [10].

Considering that ETT position correction is a time-consuming and possibly traumatic procedure. A novel warning criterion, percentage reduction in sum of the amplitude of left and right channel, was proposed in our institution to reduce the false-positive events caused by tube-rotation due to inadvertent in-field traction on the trachea during the surgery. Different cutoff values of the warning criterion for predicting postoperative vocal cord paralysis (VCP) were compared in this study, aiming to find out the most appropriate cutting off percentage point related with sum amplitude reduction to predict post-VCP.

## Methods

### Patients

A retrospective review of prospectively collected data from patients undergoing thyroid surgery with or without neck dissection was conducted at a single tertiary referral academic medical center, Zhongnan Hospital of Wuhan University, Wuhan, Hubei, P.R. China. From January 2017 to April 2017, 380 consecutive patients undergoing operation for various thyroid diseases by the same surgeon (Gaosong Wu) were enrolled. There were 142 men and 238 women, ages ranging from 17 to 72 years, in which 2 patients were excluded from this study due to preoperative left vocal cord incomplete palsy and 4 patients were excluded because of unilateral complete LOS in the

operations. Seventeen patients underwent reoperations due to locoregional recurrence were excluded from the study. In all, 357 patients with 560 nerves at risk were included in this study.

### I-IONM Procedures

The I-IONM procedure was performed using the NIM-Response 3.0 system from Medtronic, Jacksonville, Florida, which employed an ETT with integrated surface electrodes (Medtronic NIM<sup>TM</sup> 8,229,306 and 8,229,307) in contact with the vocal folds to track EMG activity. After placing the patient for surgery, the electrode placement was checked and confirmed using video-fiberoptic laryngoscopy. A low-dose, quickly acting neuromuscular blocker was used to administer general anesthesia [11].

According to INMSG guidelines, the eight procedures were used to perform thyroidectomies on all of the patients using I-IONM (Table 1). Without cutting open the carotid sheath, VN was activated during the procedure. If a reduction in the EMG amplitude of RLN occurred, RLN was stimulated distally to proximally, serially testing the entire segment of nerve that has been dissected to detect if a neurapraxic segment of LOS could be identified. Negative stimulation was used during the procedure, and any resection near the nerve was carried out when it was confirmed there was no EMG signal response. As a result, the nerve was given the best possible protection, preventing misidentification. The first helper completed this task without lengthening the procedure's overall duration. For consistency, R2 and V2 were stimulated at the same location as R1 and V1, and each recorded EMG signal was calculated as the mean of three signals produced by the same stimulation every 30 s. The troubleshooting strategy outlined in the INMSG guideline was used to manage all procedures [7, 12]. Before the procedure, structured informed consents were signed.

### Definition of LOS and Nerve Injury Mechanism

The lack of the primary, typical biphasic waveform during supramaximal stimulation (2 mA) with an amplitude value of final  $R_2 < 100 \text{ V}$  was considered to be a true total loss in the current investigation. Absolute final  $R_2$  amplitude  $> 100 \text{ V}$  with reduction of  $R_1 > 50\%$  at the end of surgery was considered incomplete LOS. Injury mechanisms were split into two categories [13]. Global type II injury was regarded as the absence of a point of injury and on electrophysiological demonstration of LOS alongside the entire course of the ipsilateral RLN and VN. Segmental type I injury was diagnosed with a LOS proximal to a specific focal point in the operative field on the RLN.

**Table 1** Eight procedures of I-IONM in this study

Steps	Signals	Procedures (Stimulating current)
1	L1	Preoperative laryngeal examination
2	Mean V <sub>1</sub>	Vagal stimulation before thyroid dissection at the level of the inferior pole of thyroid (2 mA)
3	Mean R <sub>1</sub>	RLN stimulation at initial identification at the level of the inferior pole of thyroid. Identify RLN with 2 mA of stimulating current (2 mA). Mapping RLN with 1 mA of stimulating current (1 mA)
4	S <sub>1</sub>	Stimulation of EBSLN at identification (0.2–0.5 mA)
5	S <sub>2</sub>	Stimulation of EBSLN at final dissection (0.2–0.5 mA)
6	Mean R <sub>2</sub>	RLN stimulation at the end of thyroid dissection at the same site with R <sub>1</sub> (1 mA)
7	Mean V <sub>2</sub>	Vagal stimulation at the end of thyroid dissection at the same site with V <sub>1</sub> (1 mA)
8	L2	Postoperative laryngeal examination

Each detrimental resection was done with negative simulation during the surgery

*I-IONM* intermittent intraoperative neuromonitoring, *RLN* recurrent laryngeal nerve, *EBSLN* external branch of the superior laryngeal nerve

## Follow-up

When compared to normal vocal cord movement on preoperative laryngoscopy, postoperative RLN palsy was considered to be aberrant vocal fold movement. The number of nerves that were at risk was used to calculate the rate of RLN palsy. Vocal cord mobility using a laryngoscope was done before surgery, the day after surgery, and once a month after surgery until complete vocal cord function was restored. An independent laryngologist performed pre- and postoperative follow-up. Every VCP that lasted longer than six months was regarded as permanent.

## Statistical analysis

Using a nonparametric test, continuous variables between the groups were compared. To compare the variations between all patients and patients with incomplete LOS, either the chi-squared test or the Fisher's exact test were used. Statistics were considered significant for P values below 0.05. SPSS statistical software for Windows, version 20.0, was used to conduct all statistical analyses.

## Results

### EMG signal

At the end of operation, 27 out of 560 nerves occurred LOS on the exposed RLNs. The percentage reduction in sum of the amplitude of left and right channel at the end of the operation (final R<sub>2</sub>) ranged from 30.2 to 63.6% in the 27 nerves (Table 2). No significant differences in age, gender,

malignant rate, procedure side, Without removing the carotid sheath, the entire study group was able to visually identify RLN and elicit a V1 signal. A total of 27 nerves were detected with LOS, 19 of which were caused by traction injury. Of these, 15 nerves had an injured point found in the superior segment, near the Berry ligament, and four more suffered type II nerve injuries. All type II nerve injuries were associated with visually integrity. Two nerves damaged by mechanical trauma during complete thyroidectomy, central neck dissection, and lateral neck dissection, which involved separating the RLN from carcinoma adhesion. Six nerves' EMGs dropped as a result of using an energy-based technology (EBD). Table 3 provides descriptions of the demographic traits common to all patients and those with incomplete LOS.

### Outcome of VCP

One RLN (0.2%) out of the 560 nerves had a false negative (FN) result, with no apparent EMG amplitude reduction but developing postoperative transient VCP. After significant dissection from a massive goiter, the case recovered at one month postoperatively, which may be related to delayed neuropraxia. Six of the 27 nerves with LOS had postoperative VCP. About a month after surgery, four of the six nerves affected by the use of EBD that were next to the nerve that had thermal damage were able to move the vocal cords normally. Three months following the surgery, the remaining two nerves that were damaged by the trauma injury mechanism were completely functional. As a result, just seven nerves (1.25%) experienced acute VCP, whereas none of the 560 nerves experienced permanent VCP.

**Table 2** The characteristics of 27 recurrent laryngeal nerves with an EMG amplitude decrease of more than 50% during dissection

No	Gend-er/ Age	Path- ology	Procedure	Mean R1 signal, $\mu$ V			Mean final R2 signal, $\mu$ V			EMG reduction (%)		Injury mechanism	VCP	Re
				Channel 1	Channel 2	Channel 1 + 2	Channel 1	Channel 2	Channel 1 + 2	Channel 1/2	Channel 1 + 2			
1	F/46	PTC	TT	324	905	1229	389	430	819	52.5	33.4	traction	N	
2	F/40	PTC	HT R	964	121	1085	367	385	752	60.1	30.7	traction	N	
3	M/26	PTC	TT	379	906	1285	235	312	547	65.6	57.4	thermal	Y	4
4	M/26	PTC	TT	127	1456	1583	231	658	889	54.8	43.8	traction	N	
5	M/27	PTC	TT	333	658	991	344	243	587	47.7	40.8	traction	N	
6	F/42	PTC	TT	899	148	1047	376	345	721	58.2	31.1	traction	N	
7	F/24	PTC	TT + CND + LND	184	563	747	79	232	311	58.8	58.4	trauma	Y	12
8	F/42	PTC	HT R	404	1902	2306	231	689	920	63.8	60.1	thermal	Y	4
9	M/37	PTMC	HT L	1023	559	1582	453	612	1065	40.2	32.7	traction	N	
10	F/25	BG	TT	597	1865	2462	125	783	908	58	63.1	thermal	Y	4
11	M/37	PTC	HT L	876	762	1638	321	453	774	48.3	52.7	traction	N	
12	M/33	PTC	TT + CND + LND	685	1072	1757	548	495	1043	48.9	40.6	traction	N	
13	F/43	PTC	TT + CND + LND	491	1776	2267	481	785	1266	55.8	44.2	traction	N	
14	F/32	BG	TT	425	2790	3215	532	1230	1763	55.9	45.1	traction	N	
15	F/42	PTC	TT + CND + LND	960	445	1405	434	332	766	54.8	45.5	traction	N	
16	F/24	PTC	TT	236	1954	2181	750	772	1522	60.5	30.2	traction	N	
17	F/42	PTC	TT	1483	656	2139	480	593	1073	60.0	49.8	traction	N	
18	F/41	PTMC	HT L	460	1813	2273	545	893	1438	50.7	36.7	traction	N	
19	M/37	PTC	TT	1146	256	1402	379	553	932	51.7	33.5	traction	N	
20	F/31	PTC	TT + CND + LND	1150	210	1360	372	123	495	67.4	63.6	trauma	Y	12
21	F/42	BG	HT R	470	1076	1546	411	521	932	51.6	39.7	traction	N	
22	M/44	PTC	TT	804	421	1225	352	466	818	42.0	33.2	traction	N	
23	F/29	PTC	TT	896	102	998	124	554	678	38.2	32	traction	N	
24	M/37	FTC	TT + CND + LND	342	678	1020	135	239	374	64.7	63.3	thermal	Y	4
25	F/39	PTC	TT + CND + LND	796	310	1106	143	532	675	33.2	39	traction	N	
26	M/48	PTC	TT	212	962	1174	231	421	652	56.2	44.5	traction	N	
27	F/32	PTC	TT + CND + LND	973	235	1208	346	436	782	55.2	35.3	traction	N	

EMG electromyographic, F female, M male, BG benign goiter, PTMC papillary thyroid microcarcinoma, PTC papillary thyroid carcinoma, FTC follicular thyroid carcinoma, HT hemithyroidectomy, TT total thyroidectomy, CND central neck dissection, LND lateral neck dissection, R right side; L left side; Re recovery time; VCP vocal cord paralysis, Channel 1: left channel electrodes monitor the function of left vocal cord with signal present at channel 1, Channel 2: right channel electrode monitor the function of right vocal cord with signal present at channel 2, Channel 1/2: higher amplitude of channel 1 or channel 2, Channel 1 + 2: sum of the amplitude of left and right channel

**Table 3** Demographics characteristic of patients

Characteristic	Total	Final R <sub>2</sub> signal reduction of vocalis1/2	P value
Case number, <i>n</i>	357	27	
Age (mean)	35.4	35.9	0.866 <sup>a</sup>
Gender, <i>n</i> (%)			0.845 <sup>b</sup>
Male	139(38.9)	10(37.0)	
Female	218(61.1)	17(93.0)	
Thyroid histopathology, no. of patients (%)			0.443 <sup>b</sup>
Benign nodular goiter	68(19.0)	3(11.1)	
Thyroid cancer	289(81.0)	24(88.9)	
Extent of surgery, no. of patients (%)			< 0.001 <sup>b</sup>
Hemithyroidectomy with central neck dissection	154(43.1)	6(22.2)	
Total thyroidectomy with central neck dissection	181(50.7)	13(48.2)	
Total thyroidectomy, central neck dissection, lateral neck dissection	22(6.2)	8(29.6)	
Left side/right side nerve	277/283	12/15	0.610 <sup>b</sup>
Post-op vocal cord paralysis, no	7	6	

Vocalis 1: left vocalis, Vocalis 2: right vocalis

<sup>a</sup>Nonparametric test;

<sup>b</sup>Chi-square test

### Different cutoff values of the proposed warning criterion

Table 4 lists and compares the study's true positive (TP) results (incomplete LOS with post-VCP), true negative (TN) results (normal EMG signal without post-VCP), true

positive (FN) results (normal EMG signal with post-VCP), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy (TP + TN/total number). When using the percentage reduction in sum of the amplitude of left and right channel as the warning criteria for RLN injury and vocal cord

**Table 4** Comparison of statistics results between different warning criterion threshold values to predict the postoperative vocal cord paralysis

Final R <sub>2</sub> signal ( <i>A<sub>m</sub></i> > 100 $\mu$ V)	Channel 1/2		Channel 1 + 2		
	> 50%	> 30%	> 40%	> 50%	> 60%
No. of events(total)	27(560)	27(560)	15(560)	7(560)	4(560)
True positive	6	6	6	6	4
False positive	14	21	9	1	0
True negative	539	5302	544	552	553
False negative	1	1	1	1	3
Sensitivity	85.7%	85.7%	85.7%	85.7%	57.1%
Specificity	97.5%	96.2%	98.4%	99.85	100%
PPV	30.0%	22.2%	40.0%	85.7%	100%
NPV	99.8%	99.8%	99.8%	99.8%	99.5%
Accuracy <sup>a</sup>	97.3%	96.1%	98.2%	99.6%	99.4%

<sup>a</sup>calculated as TP + TN /total number

*A<sub>m</sub>* amplitude, *PPV* positive predictive value, *NPV* negative predictive value,

Channel 1: left channel electrodes monitor the function of left vocal cord with signal present at channel 1, Channel 2: right channel electrode monitor the function of right vocal cord with signal present at channel 2, Channel 1/2: higher amplitude of channel 1 or channel 2, Channel 1 + 2: sum of the amplitude of left and right channel

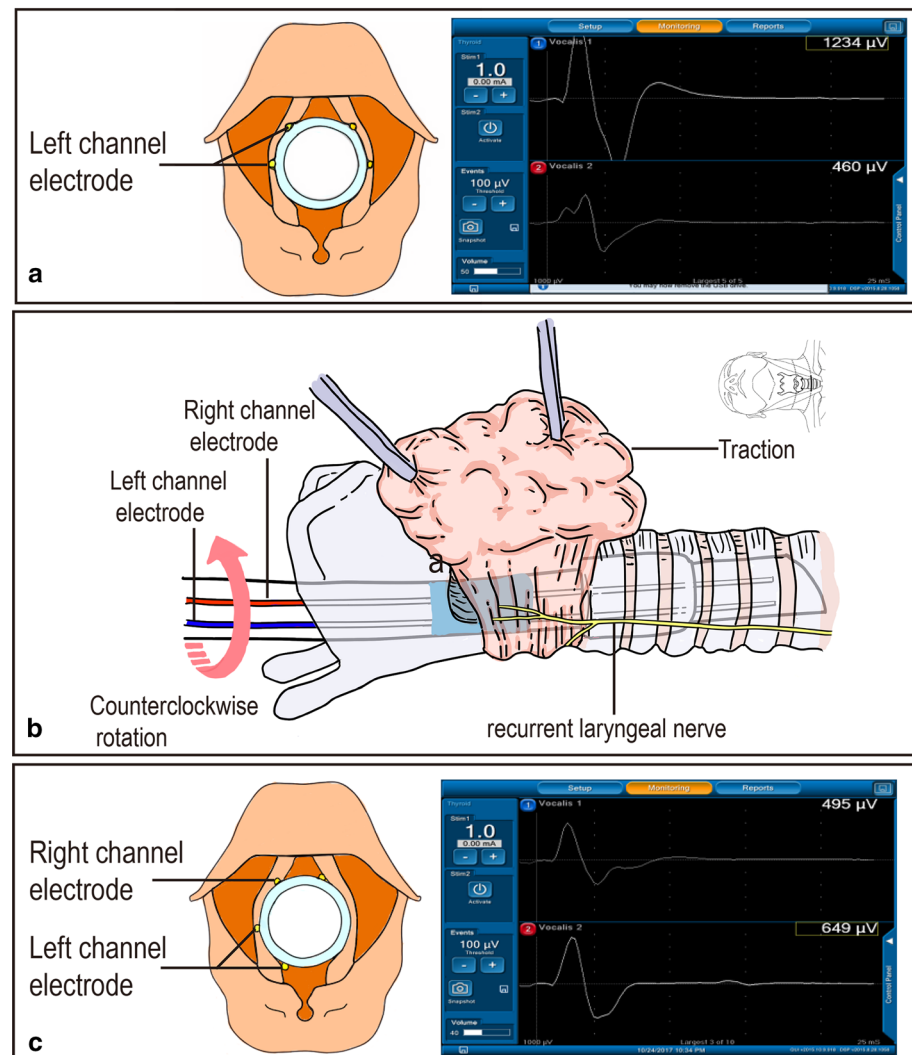
function impairment, we concluded that 50% sum amplitude reduction showed highest accuracy when compared with other percentage values. The PPV of VCP for the percentage reduction in sum of the amplitude of left and right channel exceeding 30, 40, 50, and 60% was 22.2, 40, 85.7, and 100.0%, respectively. Accuracy was 96.1, 98.2, 99.6, 99.4%, respectively. 50% threshold value shows the highest accuracy (99.6%) and better PPV (85.7%) when comparing different warning criterion threshold values.

## Discussion

As an additional tool for the early detection and function assessment of RLN after thyroid and other neck surgeries, IONM has accumulated organizational support [14]. Staged thyroidectomy has been advised in cases of bilateral goiter, Graves' disease, or low-risk thyroid cancer where

LOS from intraoperative neuromonitoring occurred [15]. More reliable data on the prevalence of first-side LOS and potential RLN function should be carefully analyzed before staged thyroidectomy is advised. When the RLN is in distress during IONM, the laryngeal EMG amplitude would be lower than the baseline. However, there is ample evidence in the literature that FP (LOS without post-VCP) results are possible [16]. The ETT malposition in surgery, which causes PPV of VCP prediction to vary from 35 to 75%, is the main cause. Displaced ETT can be caused by inadvertent head extension or the in-field traction on the trachea during the surgical procedure. When tube-rotation occurs, vagal stimulation by the surgeon as the anesthesiologist readjusts the ETT is recommended as an effective method for repositioning the tube. However, tube-rotation accounted for 44% of the initial I-IONM failure [9], and this procedure might prolong surgery time, and increase the possibility of tracheal trauma [10]. According to Dionigi

**Fig. 1** Principle of sum amplitude reduction warning criterion. **a:** The  $R_1$  electromyography signal of left vocalis (channel 1) was 1234  $\mu$ V at the beginning of the operation with the proper endotracheal tube position. **b:** Tube rotation was caused by inadvertent head extension or the in-field traction on the trachea contributed to poor left electrodes-left vocal cords contact and partial right electrodes-left vocal cord contact, thus right channel (channel 2) electrodes conducted partial electromyography signal of left vocal cord. **c:** Final  $R_2$  electromyography signal was 495  $\mu$ V present at channel 1 with 649  $\mu$ V present at channel 2



et al., 10% of thyroid surgery patients required intraoperative ETT modification due to insufficient electrodes-vocal cords contact [17]. In Chiang et al.'s study, intraoperative monitor dysfunction caused by a mal-positioned ETT occurred in 6% of thyroidectomy patients, even though the proper electrodes positioning was routinely verified by laryngoscopic examination after neck positioning [4].

Several methods have been reported to avoid tube-rotation and increase the stability of amplitude. In the study by Tsai et al. [17], three marks (two transverse lines and one vertical line) were put on the posterior surface of the ETT in order to ensure proper positioning of electrodes during laryngoscopic examination, with which a higher magnitude of EMG amplitude was elicited [18]. Another study reported by Chiang et al. compared two surface recording methods that were obtained by electrodes on ETT and thyroid cartilage (inserting a pair of single needle electrode obliquely into the thyroid cartilage lamina on each side). The study concluded that the thyroid cartilage electrodes showed significantly higher amplitude and stability [4]. In addition, a method called “Double Channel” was proposed by Chiang et al. to overcome the problem of poor electrodes-cords contact caused by tube rotation or smaller diameter of ETT. Electrode leads were connected to patient interface box with cross insertion, with which EMG signals would be recorded by channel 1 and channel 2 simultaneously and the data from the channel with higher EMG amplitude would be chosen. In addition, The EMG signal reduction from the most distal and proximal ends of the RLN exposed during thyroidectomy (R2p and R2d), respectively, was evaluated and compared by Wu et al. after the procedure. They suggested that a postoperative VCP warning requirement for relative threshold value R2p/R2d reduction reaches over 60%.

As well known, tube rotation caused by unavoidable head extension or the in-field traction on the trachea contributed to poor left electrodes-left vocal cord contact and partial right electrodes-left vocal cord contact. Ordinarily, left channel electrodes monitor the function of left vocal cord with EMG signal present at channel 1 and right channel electrode monitor the function of right vocal cord with EMG signal present at channel 2, respectively (Fig. 1a). Only when the EMG tube is positioned perfectly, can the EMG signal be present at channel 1 with stimulation of the left RLN, showing the amplitude of left vocalis muscle, meanwhile the right EMG signal is extremely low ( $< 100 \mu\text{V}$ ) theoretically. When tube-rotation occurs (Fig. 1b), right channel electrodes (channel 2) conduct partial EMG signal of the left vocal cord, the amplitude of channel 1 decreases and the amplitude of channel 2 increases, leading to the fact that the left amplitude (channel 1) decreased to 50% with normal postoperative vocal cords function (Fig. 1c). The EMG signal present at

the channel 1 and channel 2 were both evoked by the stimulation of the left nerve, and both of the amplitudes should be included and recorded as the EMG signal of the left nerve. Thus, the warning criterion of percentage reduction in sum of the amplitude of channel 1 + 2 is proposed to detect the impaired RLN during the monitored thyroidectomy (Table 2). In this study, six (21.4%) of the 27 nerves detected with incomplete LOS developed postoperative temporary VCP, and FN result was found in one RLN (0.2%). The PPV of the incomplete LOS was 22.2% in the present study. Percentage reduction in sum of the amplitude of channel 1 + 2 tended to be consistent, with a decrease in less than 50%, which reflected an incomplete LOS with normal postoperative vocal cords mobility, additionally augmented surgeons' attention and unnecessary procedures as well. Comparing different cutoff values of the warning criterion, it was concluded that the cutoff value of 50% represented a highest accuracy (99.6%) and better PPV (85.7%).

In the present study, the warning criterion could partially overcome the poor contact between electrodes and vocal cords ipsilaterally caused by tube-rotation, avoiding a troublesome and time-consuming procedure for anesthesiologists. However, several limitations existed in this study, the rotation of the ETT during thyroid surgery with sometimes decreasing amplitude is not related to neuromonitoring globally but specifically to a specific ETT (Medtronic NIM™ 8,229,306 and 8,229,307), which is a major limitation. The current version of the Medtronic ETT (NIM TRIVANTAGE™) has taken this problem under consideration. Second, the metabolism of neuromuscular blockade, laryngeal edema, smaller diameter of EMG tube and other uncontrollable factors could give rise to changes of EMG signal [19]. Exact mechanism and intrinsic characteristics of the presented incomplete loss warning criterion require further investigation and more related data need to be collected and analyzed.

## Conclusions

In conclusion, the percentage reduction in sum of the amplitude of left and right channel is a simple, useful, atraumatic method to evaluate RLN injury after its dissection and predict VCP. When the percentage reduction in sum of the amplitude of left and right channel  $\geq 50\%$ , surgeons should consider the possibility of postoperative VCP and correct some surgical maneuvers, with which surgeons could improve the surgical pitfalls, and avoid the nerve injury in future operations.

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#### Declarations

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