

Transcutaneous Laryngeal Ultrasonography for Assessing Vocal Cord Twitch Response in Thyroid Operation during Predissection Vagus Nerve Stimulation

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- BACKGROUND:** In this study, we aimed to report our experience with the use of intraoperative transcutaneous laryngeal ultrasonography (TLUSG) to evaluate the vocal cord twitch response during predissection vagus nerve stimulation in thyroid surgeries and examine the reliability of this technique when compared with that of laryngeal twitch palpation (LTP).
- STUDY DESIGN:** The prospective data collection of consecutive patients who underwent open thyroidectomy with intraoperative neuromonitoring (IONM) was reviewed retrospectively. We recorded the electromyographic activity and assessed the vocal cord twitch response on LTP, TLUSG. We compared the accessibility, sensitivity, and specificity of the techniques.
- RESULTS:** A total of 110 patients (38 men and 72 women) with 134 nerves at risk were enrolled. The vocal cord was assessable by TLUSG in 103 (93.6%) patients and by LTP in 64 (59.1%) patients. Two patients showed negative predissection IONM signal but positive on TLUSG and the presence of laryngeal twitch response confirmed by laryngoscopy. Fourteen patients showed positive IONM signals and presence of the vocal cord twitch response on TLUSG but not on LTP. The sensitivity and specificity were 70.21% and 100%, respectively, for LTP, and those both were 100% for TLUSG. For patients who could be assessed using both techniques, TLUSG had better accuracy than LTP (100% vs 80.33%, $p = 0.0005$).
- CONCLUSIONS:** The innovative intraoperative application of TLUSG is better for evaluating the laryngeal twitch response than LTP. This technique provides practical troubleshooting guidance for patients with no IONM signals during predissection vagus nerve stimulation. (*J Am Coll Surg* 2022;234:359–366. © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American College of Surgeons. This is an open-access article distributed under the terms of the [Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 \[CCBY-NC-ND\]](https://creativecommons.org/licenses/by-nc-nd/4.0/), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.)

Recurrent laryngeal nerve (RLN) palsy is the most serious complication after thyroid operation and is a leading cause of medicolegal litigation against surgeons.¹ During the last decade, intraoperative neuromonitoring (IONM) of the RLN has gained increasing acceptance among surgeons as a method to predict and document the nerve function.^{2,3} A reliable modality for intraoperative evaluation would

provide the surgeon with real-time information that could help guide the surgical procedure.

A failure of IONM was noted in 23% of the procedures, especially for patients who had undergone the procedure in the learning phase.⁴⁻⁷ As recommended by the guidelines, a systematic strict review of the IONM system on no electromyography (EMG) signal is mandatory. When

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Drs Kuo and Chen contributed equally to this work.

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Abbreviations and Acronyms

EMG	=	electromyography
IONM	=	intraoperative neuromonitoring
LTP	=	laryngeal twitch response assessed by palpation
RLN	=	recurrent laryngeal nerve
TLUSG	=	transcutaneous laryngeal ultrasonography
US	=	ultrasound
V1	=	vagal 1

the normal RLN function is evidenced by the presence of a laryngeal twitch, but no EMG signal is present, it is called a false no IONM signal. The assessment of the laryngeal twitch response by the surgeon's palpation is recommended as one of the first steps for intraoperative evaluation of no EMG signals in the current guideline statement and has a high correlation with the evoked laryngeal EMG activity.^{8,9} However, the twitch responses vary among patients, and the interpretation varies among surgeons. In the current trend of minimally invasive procedures, small incisions limit the possibility of laryngeal palpation before the thyroid gland has been resected. The real-time movement of the vocal cords during stimulations evaluated by laryngoscopy can be an alternative.^{10,11} Considering that laryngoscopy is invasive, is associated with increased costs, and is not always available, it has been questioned whether a noninvasive modality would aid this clinical practice.¹²

Transcutaneous laryngeal ultrasonography (TLUSG) is a technique that specifically assesses the neck structures and is considered to have an applicability index of greater than 90%.¹³⁻¹⁶ TLUSG can be used as an alternative to fiberoptic flexible laryngoscopy¹⁷ and can provide real-time imaging to assess the laryngeal function.¹⁸ In this regard, TLUSG has become an alternative to investigate the laryngeal sequelae after thyroidectomy.¹⁹ This method could become a real asset in the intraoperative management of patients undergoing thyroid and parathyroid surgeries. Therefore, TLUSG may be a promising and noninvasive tool for assessing the laryngeal twitch response during nerve stimulation.

This study is the first to report on the experience with the use of intraoperative TLUSG in evaluating the laryngeal twitch response during thyroid surgeries and examine the reliability of this technique in providing useful information compared with that of laryngeal twitch palpation (LTP).

METHODS

This prospective data collection and retrospective review study enrolled 110 consecutive patients who underwent

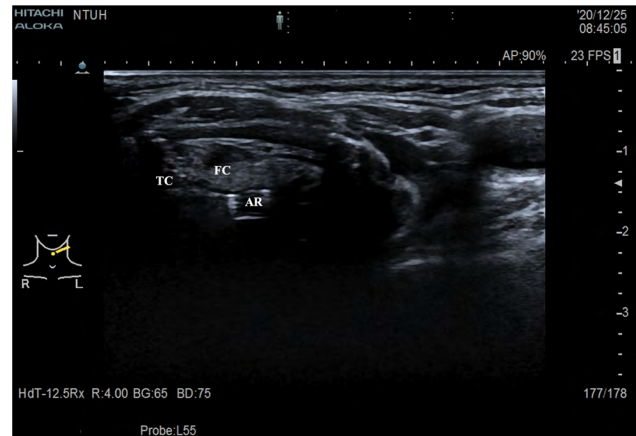


Figure 1. Preoperative transverse ultrasonographic view of vocal cord identification. AR, arytenoid muscle; FC, false cord; TC, true cord.

thyroidectomies with IONM from June 2019 to June 2020 at a tertiary referral hospital and was approved by the research ethics committee (201906051RINA).

TLUSG was performed by endocrine surgeons with a standard protocol, using ALOKA ProSound 2 (Hitachi Medical Systems Europe) with a frequency setting of 12-MHz broadband spectrum and 4-cm linear transducer.

Preoperatively, all patients underwent TLUSG evaluation. After applying the gel over the anterior neck, an ultrasound (US) transducer was placed transversely over the thyroid cartilage and was used to scan craniocaudally until both true and false cords were visualized (Fig. 1). Three laryngeal landmarks, arytenoids, true cords, and false cords, were used for vocal cord recognition. Visualization of the laryngeal landmarks that were adequate for vocal cord movement examination was considered positive visualization. Once the landmarks were localized, the skin was marked for intraoperative TLUSG assessment. Seven patients with preoperative vocal cord localization difficulties on TLUSG were excluded from intraoperative TLUSG assessment (Fig. 2).

Anesthesia and intraoperative nerve monitoring system

The standardized procedures were followed for the equipment setup and anesthesia. All patients were intubated with a nerve integrity monitor standard reinforced EMG endotracheal tube (6.0- and 7.0-mm internal diameter for women and men, respectively; Metronic Xomed) for general anesthesia. All the patients received nondepolarizing muscle relaxant for the induction of general anesthesia using rocuronium in a single dose (0.3 mg/kg) or cisatracurium (Nimbex, GlaxoSmithKline Manufacturing S.P.A., San Polo Torriale, Italy) given depending on the

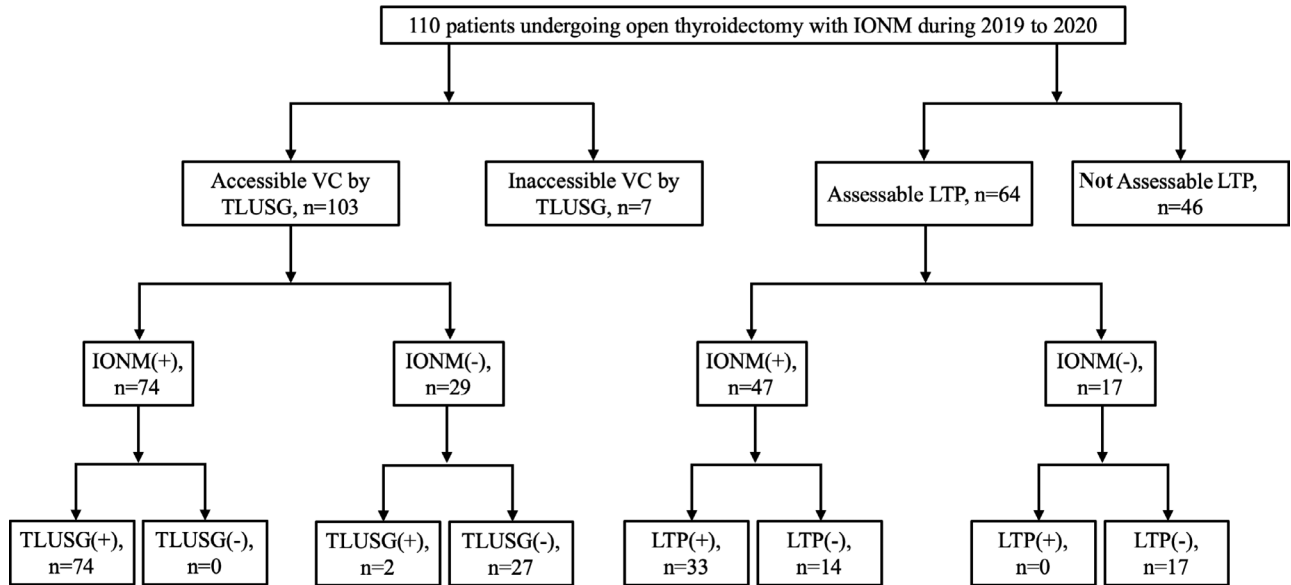


Figure 2. Flow diagram for the study. The flow diagram shows the proportion of patients during predissection vagus nerve stimulation with electromyography activity on intraoperative neuromonitoring (IONM) and vocal cord (VC) twitch response on transcutaneous laryngeal ultrasonography (TLUSG) or laryngeal twitch palpation (LTP).

monitoring of the neuromuscular block to an ideal train-of-four ratio of 40% (TOF-Watch® SX [Inmed Equipments Pvt. Ltd., Gujarat, India]) to facilitate nerve identification and smooth IONM intraoperatively. The recovery of train-of-four ratio to 90% after the last dose of rocuronium normally takes less than 3 minutes.²⁰

The position of the electrodes was routinely monitored by direct laryngoscopy after positioning with neck hyperextension to ensure that the electrodes had good contact with the true vocal cords. The electrodes from the nerve integrity monitor EMG endotracheal tube were connected to a NIM-Response™ 2.0/3.0 monitor (Medtronic Xomed, Jacksonville, Florida). A Prass Standard monopolar stimulator probe (Medtronic Xomed) was used for nerve stimulation during IONM. An EMG signal higher than the threshold of 100 μ V was considered positive. Before the identification of the RLN and resection of the thyroid lobe, the maximum evoked EMG amplitude of vagal stimulation was recorded and defined as vagal 1 (V1) signal.

Intraoperative laryngeal twitch response assessed by LTP

Palpation for the contraction of the posterior cricoarytenoid muscle was performed after the identification of the thyroid cartilage. A finger was subsequently inserted deep to the posterior lamina and fascia overlying the vertebral column; additionally, the posterior lamina of the posterior cricoarytenoid muscle was palpated through the wall of

the hypopharynx to detect the presence of contraction²¹ during predissection V1 stimulation.

Intraoperative laryngeal twitch response assessed by TLUSG

After applying sterile gel over the anterior neck, an US transducer was placed over the premarked line to visualize the true and false cords (Fig. 3). The real-time video was recorded and evaluated by surgeons if there was an ipsilateral vocal cord twitch response while undergoing predissection V1 stimulation (Video 1 online).

The presence of vocal cord twitch response on TLUSG and LTP was simultaneously assessed by 2 different surgeons individually to minimize the influence of each assessment. The EMG amplitude during the IONM was also recorded.

Definition of laryngeal twitch response

In this study, as per the guidelines of our institute, patients with positive EMG signals at predissection vagal stimulation as evidence of laryngeal twitching did not undergo intraoperative laryngoscopy. However, patients with a negative V1 signal, after the exclusion of possible mechanical problems, underwent laryngoscopy to check for any dislocation or rotation of sensors and adjust the position of the endotracheal intubation if needed by experienced anesthesiologists. At the same time, the surgeon would undergo vagal stimulation, and the experienced anesthesiologists

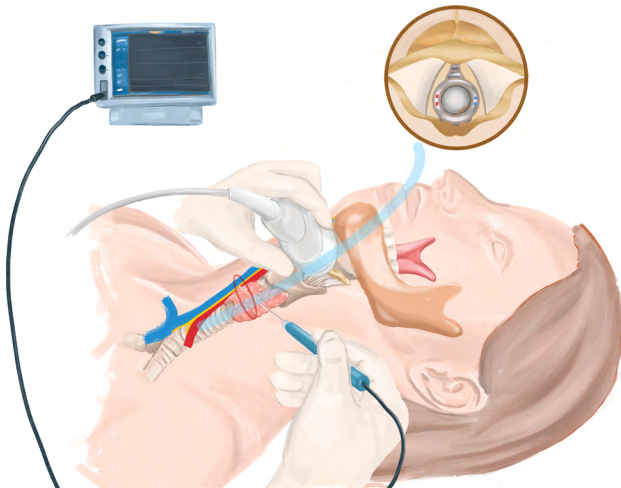


Figure 3. Illustration of how surgeons perform vocal cord twitch response assessment during predissection vagus nerve stimulation using transcutaneous laryngeal ultrasonography. The surgeon held an ultrasound transducer in one hand and stimulated using a current of 3.0 mA with the other hand. Image originally illustrated/created by Shuning L. Edited by Ting-Chun Kuo.

would confirm if there existed ipsilateral twitch response of vocal cord or not. Thus, the presence of a laryngeal twitch response during predissection vagal stimulation was based on the result of a positive EMG signal and/or positivity on laryngoscopy.

Preoperative and postoperative vocal cord movement was routinely evaluated with US for patients undergoing thyroidectomy in our institute. If voice symptoms were suspected postoperatively or cases whose nerve injuries were indicated by loss of IONM signals intraoperatively, direct laryngoscopic evaluation was performed by the otolaryngologists.

Statistical analysis

The data are summarized using descriptive statistics. Categorical variables are shown as numbers and percentages, and continuous variables are presented as means and SDs. Patient characteristics were analyzed using Student's *t*-test or ANOVA for continuous variables and the chi-square test or Fisher's exact test for categorical variables. The sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios were calculated with CIs determined at the 95% level using the Wilson score method²² and the method described by Simel and colleagues.²³ The diagnostic accuracy between tools was analyzed using McNemar's test.²³ Statistical analyses were performed using SAS (version 9.4; SAS Institute). All *p* values were 2-sided, and the significance level was set at 5%.

Table 1. Baseline Characteristics of the Study Cohort

Characteristic	All (n = 110)
Age, y, mean (SD) [range]	51.3 (13.7) [22.7–78.8]
Sex ratio, male:female (%)	25:85 (22.73:77.27)
BMI, kg/m ² , mean (SD) [range]	24.28 (3.58) [17.31–34.80]
Thyroid disease, n (%)	
Nodular goiter	37 (33.60)
Follicular adenoma	22 (20.00)
Papillary thyroid carcinoma	49 (44.55)
Follicular thyroid carcinoma	1 (0.91)
Medullary thyroid carcinoma	1 (0.91)
Type of operation, n (%)	
Hemithyroidectomy	86 (78.18)
Bilateral thyroidectomy	24 (21.82)
RLN at risk, n	134

RLN, recurrent laryngeal nerve.

RESULTS

Among 110 patients who underwent thyroidectomy with IONM with 134 nerves at risk, 85 (77.3%) were women and 25 (22.7%) were men, with an age of 51.3 years and body mass index of 24.28 kg/m². Further, 51 (46.4%) patients had malignancy, and 86 (78.2%) patients underwent hemithyroidectomy. The baseline characteristics are listed in Table 1.

In this study, no case had loss of IONM signals intraoperatively or impaired vocal cord movement on US postoperatively.

The presence of IONM V1 signal and twitch response on TLUG and LTP is shown in Figure 2. The preoperative TLUSG vocal cord identification failed in 7 patients, whereas 103 patients underwent intraoperative TLUSG assessment. A total of 74 patients showed the predissection V1 signal (190 to 970 mV) and a twitch response on TLUSG. Twenty-seven patients showed neither a V1 signal nor a twitch response on TLUSG. Two patients showed negative predissection V1 signal but positive twitch response on TLUSG, and the presence of twitch response was further confirmed by laryngoscopy.

LTP was performed in 64 patients. A total of 33 patients showed positive results for V1 signal and twitch response on both LTP and TLUSG. Fourteen patients were assessed negative of twitch response on LTP, but they showed a positive V1 signal and positive twitch response on TLUSG. Seventeen patients had negative results for V1 signal and negative twitch response on both LTP and TLUSG. The absence of twitch response was further confirmed by laryngoscopy.

The related measurement that indicates the assessment of a laryngeal twitch response using LTP and TLUSG is summarized in Table 2. For 64 patients assessable by LTP, the specificity and positive predictive value were 100%, and the sensitivity and negative predictive value were

Table 2. Related Measurement Indices for Intraoperative Laryngeal Twitch Response Assessed by Palpation and Transcutaneous Laryngeal Ultrasonography

Index	LTP (n= 64)	TLUSG (n= 103)
Sensitivity	70.21 (57.14–83.29)	100 (100–100)
Specificity	100 (100–100)	100 (100–100)
PPV	100 (100–100)	100 (100–100)
NPV	54.84 (37.32–72.36)	100 (100–100)
PLR	NA	NA
NLR	0.30 (0.17–0.43)	NA

Data presented as % (95% CI).

LTP, laryngeal twitch assessed by palpation; NLR, negative likelihood ratio; NA, not applicable; NPV, negative predictive value; PLR, positive likelihood ratio; PPV, positive predictive value; TLUSG, transcutaneous laryngeal ultrasonography.

70.21% and 54.84%, respectively. For 103 patients assessable by TLUSG, the sensitivity, specificity, and positive and negative predictive values were 100%.

The 61 patients who could be assessed by both LTP and TLUSG were summarized in Table 3. The sensitivity for LTP and TLUSG were 72.73% and 100%, respectively. The specificities for LTP and TLUSG were both 100%. The accuracies for LTP and TLUSG were 80.33% and 100%, respectively, with significant difference ($p = 0.0005$).

DISCUSSION

In this prospective observational study, we confirmed the feasibility and validity of intraoperative TLUSG in the real-time assessment of the laryngeal twitch response during thyroid surgeries. TLUSG presented a consistent correlation with the laryngeal twitch response. TLUSG had a higher assessable rate and better accuracy in the assessment of the laryngeal twitch response than LTP. In situations where IONM errors occur, the use of TLUSG may aid to avoid the routine use of laryngoscopy to exclude the possibility of EMG tube sensor dislocation.

RLN IONM provides essential information for surgeons about accurate nerve identification and functional integrity.²⁴ IONM errors, with incidence rates ranging

from 3.8% to 23.0%,⁵ exert significant psychological pressure on operators. On the causes and solutions of ordinary IONM errors, prevention of false no signal from contact failure of EMG tube electrodes and the troubleshooting algorithm may ensure a safe and steady operation.²⁵ In our series, the percentage of patients without predissection V1 signal was as high as 28.16% (29/103). If the IONM signal is absent and when the mechanical problems are excluded, the most possible causes can be (1) an improper type or dosage of muscle relaxant and (2) recording electrode displacement or dislodgement due to repositioning of the head or body during the operation.

Assessment of the laryngeal twitch response by palpation by the surgeon is recommended as one of the first steps for intraoperative no signal evaluation in the current guideline statement.² However, the twitch response and interpretation by palpation vary among patients and surgeons. Furthermore, a smaller incision restricts the accessibility of LTP before the retraction or resection of the thyroid gland in the era of minimally invasive procedures. In this study, the interpretation of LTP could be achieved in only 64/110 (58.18%) patients. This situation can be diverse in various institutes because the skin incision for thyroidectomy varies between surgeons, and the size of the thyroid differs between patients. However, even when the specificity was as high as 100%, the negative predictive value was only 54.84% for LTP. This means that if the laryngeal twitch response cannot be palpable, we cannot assume that there is no twitch response. This implies that LTP is (1) not always feasible before the dissection of the whole gland, especially in thyroidectomies with small incisions, (2) subjective and poorly correlated with real vocal cord movements during the operation, and (3) not a reliable tool for the differentiation of the reasons for IONM errors without laryngoscopy confirmation.

Traditionally, if the initial IONM was negative, the ongoing procedure would be rechecked with laryngoscopy, and the IONM sensor location would be adjusted if needed. Once there is no dislocation of the IONM sensors, it is recommended to wait until the muscle relaxant wears off or use a proper dose of a muscle relaxant antagonist. Laryngoscopy is the most common and simple technique for directly checking the vocal fold movement. However, laryngoscopy checkups for patients undergoing thyroidectomies with IONM and receiving limited doses of muscle relaxants are not always easy and may cause unpredictable trauma. In our study, only 2/29 (6.9%) patients had predissection V1 negativity caused by improper electrode displacement and would benefit from a laryngoscope checkup. Thus, a noninvasive method that can accurately evaluate real-time vocal cord movement is important. In this study, the presence

Table 3. Comparing 61 Patients with Assessable Laryngeal Twitch Response by Both Palpation and Transcutaneous Laryngeal Ultrasonography

Method	LTP		p Value
	Yes	No	
TLUSG			0.0005
Yes	32	12	
No	0	17	

Accuracy: TLUSG 100% (100%–100%), LTP 80.33% (70.35%–90.30%).

LTP, laryngeal twitch assessed by palpation; TLUSG, transcutaneous laryngeal ultrasonography.

of a twitch response on TLUSG was correlated with the real vocal cord movement in all patients. Because of the nature of the study, we did not manipulate the evoked IONM value and study whether there were threshold level IONM values for detecting the presence of a twitch response on TLUSG. Thus, we cannot assume that negative TLUSG findings would always be a perfect indicator to ensure that there will be no vocal cord twitch response in the future. This should be studied in experimental settings. We only included patients in whom preoperative TLUSG evaluation was possible. The assessable rate of 93.6% in our study is much higher than that reported previously (73.9%)²⁶ but is in accordance with that reported in other studies in Asian populations (82% to 87%).^{19,27} This may be due to the high female/male ratio and low BMI (24.28 kg/m²) in our patients as previously proposed factors that may influence vocal cord visualization²⁶ and may vary in different patient groups, especially for those with a high BMI and long anterior–posterior distance.

A total of 27/103 (26.2%) patients showed neither pre-dissection V1 signal nor twitch response on TLUSG, which was further confirmed by laryngoscopy. The effect of a muscle relaxant was suspected, the signal became positive after minutes of waiting, and the twitch response presented on TLUSG. As suggested, the anesthesiologists in our series currently use single induction dose of nondepolarizing neuromuscular blocking agents for

patients undergoing open thyroidectomy with IONM. It was recommended as an optimal dose for IONM during thyroid operation for providing high EMG amplitude at an early stage of operation and satisfactory intubating conditions.²⁸ During thyroidectomy with IONM under train-of-four monitoring, the anesthesiologist could use sugammadex to reverse the patients at any time. There is another strategy of neuromuscular blockade management for IONM using depolarizing neuromuscular blocking agent (succinylcholine), with respect to rapid onset and short duration of muscular relaxation.² However, many anesthesiologists avoid succinylcholine because of its side effects, such as cardiac dysrhythmia, hyperkalemia, and malignant hyperthermia.^{29,30} In addition, buckling during minimally invasive thyroidectomies with IONM may cause serious complications, and we would like to keep adequate muscle relaxation to achieve the best surgical field of vision. However, the choice of muscle relaxant use may vary in different institutes. A high percentage of patients in our current settings may show a false absence of IONM signal initially caused by the muscle relaxant, and the dose should be further justified.³¹ Therefore, direct evaluation of vocal cord movement seems to be a more reliable tool for surgeons when encountering pre-dissection V1 negativity during IONM.

There was no false presence of twitch response on TLUSG, implying its clinical application. In cases where

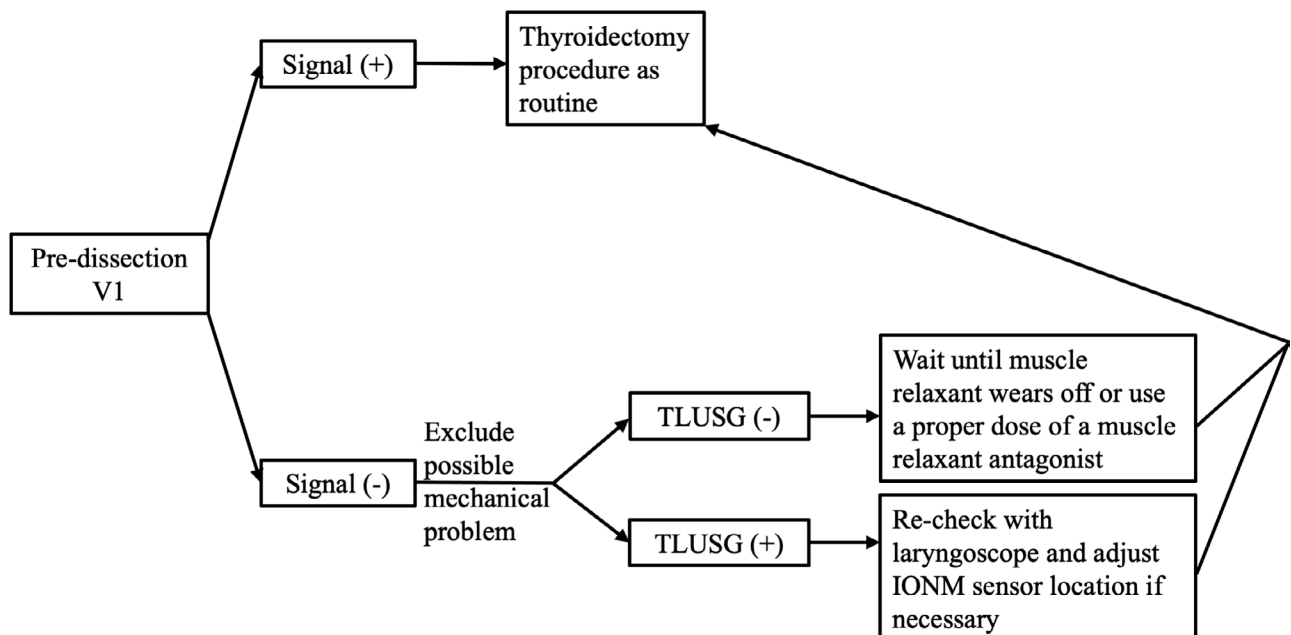


Figure 4. Proposed algorithm for patients when encountered with no intraoperative neuromonitoring (IONM) signal during pre-dissection vagus nerve stimulation in thyroid operation. TLUSG, transcutaneous laryngeal ultrasonography; V1, vagal 1.

IONM is used, if there is no signal during predissection vagus stimulation, the use of TLUSG can help better identify true vocal cord twitch and potentially mitigate the need for IONM troubleshooting or laryngoscopy. This procedure may be a more practical and objective initial step than LTP. Data on a total of 29 of 103 (28.2%) patients with predissection negative V1 signal in the study can provide perfect guidance about who would need further laryngoscopy and who should be kept waiting until the muscle relaxant wears off or in whom a proper dose of a muscle relaxant antagonist should be used as the algorithm for clinical practice (Fig. 4). However, it is possible that accessibility or accuracy of TLUSG may decrease during or after thyroid dissection. In addition, the accessibility and accuracy of LTP may improve once thyroid dissection is started or completed, narrowing the gap of accuracy between TLUSG and LTP.

Preoperative and postoperative TLUSG, as used in this study for assessing of vocal cord function, has been reported with high sensitivity, specificity, and accuracy up to 100%, 70.0%, and 70.5%, respectively.¹⁷ Precision of IONM in correctly predicting postoperative vocal fold palsy³² and almost 100% correlation between standardized IONM EMG signals and true vocal cord function had been proposed by Chiang and colleagues.¹¹ Though invasive procedure for assessing of vocal cord function as laryngoscopy might not be used in all institutes or worldwide as Chai and colleagues recently reported routine rigid laryngoscope for assessing of vocal cord mobility.³³ Generally, assessment of the vocal cord function by laryngoscopy could be used. In our study, the vocal cord function was confirmed by combined modalities such as TLUSG visualization, IONM, and laryngoscopy in symptomatic patients.

This study has several limitations. First, we enrolled only patients who could be assessed by TLUSG preoperatively, and this meant that the method might only be applicable to these patients. Second, the assessment of the twitch response on TLUSG and LTP, and by laryngoscope, as a yes or no was still a relatively subjective method. We attempted to record IONM data and the movement of TLUSG by different surgeons using a standard workflow to minimize the influence of each assessment. Future quantitative measurements of TLUSG are necessary to improve the assessment of vocal cord movement objectively.

CONCLUSIONS

TLUSG, with a high assessable rate, is useful in evaluating the real-time laryngeal twitch response intraoperatively

and providing practical guidance in troubleshooting in patients with no IONM signals during predissection vagus nerve stimulation.

Author Contributions

Study conception and design: Kuo, Wu

Acquisition of data: Kuo, Chen, Lai, Wang, Lin, Wu

Analysis and interpretation of data: Kuo, Wang, Chang, Lin, Wu

Drafting of manuscript: Kuo, Chang, Wu

Critical revision: Kuo, Wu

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Invited Commentary

Intraoperative Percutaneous Ultrasound Examination of the Larynx: A New Adjunct to Intraoperative Recurrent Laryngeal Nerve Monitoring

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Recurrent laryngeal nerve (RLN) injury occurs in 5% to 10% of patients undergoing thyroidectomy. Most RLN injury is transient, but some can be permanent. Unilateral RLN injury causes vocal cord paralysis and voice impairment. Bilateral RLN injury is a devastating complication that may require a tracheotomy.

Knowing the usual anatomy and common variations and visually identifying the recurrent laryngeal nerve during thyroidectomy are the most important ways to avoid RLN injury.¹ In addition, intraoperative nerve monitoring (IONM) has been shown to lower the risk of recurrent nerve injury by studies using large registry databases, such as the American College of Surgeons NSQIP² and the European registry EUROCRINE.³

The most common IONM technique uses an endotracheal tube that incorporates electrodes for real-time assessment of the electromyographic (EMG) signal of