Continuous Vagal IONM Prevents Recurrent Laryngeal Nerve Paralysis by Revealing Initial EMG Changes of Impending Neuropraxic Injury: A Prospective, Multicenter Study


Objectives/Hypothesis: Existing intraoperative neuromonitoring (IONM) formats stimulate the recurrent laryngeal nerve (RLN) intermittently, exposing it to risk for injury in between stimulations. We report electrophysiologic parameters of continuous vagal monitoring, utilizing a novel real-time IONM format, and relate these parameters to intraoperative surgical maneuvers that delineate nascent adverse but reversible electrophysiologic parameters to prevent nerve injury. These results are correlated with postoperative vocal cord functional outcome.

Study Design: Prospective multicenter tertiary study.

Method: Evoked vagal nerve waveform amplitude and latency changes during 102 thyroidectomies were recorded. Adverse electrophysiologic response was categorized into 1-concordant amplitude reduction and latency increase events (combined events) and 2-loss of signal (LOS). Surgical maneuvers were modified when adverse electrophysiologic findings were noted. All patients underwent preoperative and postoperative laryngoscopy; intraoperative electrophysiologic findings were correlated with postoperative laryngeal function.

Results: Continuous vagal monitoring did not result in stimulation-evoked nerve injury or intraoperative adverse cardiac, pulmonary, or gastrointestinal effects. Both intraoperative combined events and LOS were associated with development of vocal cord paralysis (VCP) ($P < 0.001$ and $P > 0.001$ respectively). Combined events had a positive predictive value (PPV) of 33%, negative predictive value (NPV) of 97%, and were reversible in 73%. LOS had a PPV of 83%, NPV of 98%, and was reversible in only 17%. Milder combined events and isolated amplitude or latency changes were not associated with VCP.

Conclusions: Continuous vagal monitoring is safe and provides real-time RLN evaluation during surgical maneuvers. Combined events and LOS, both easily identifiable intraoperatively, are related to the development of VCP. A combined event represents a largely reversible electrophysiologic change when the associated surgical maneuver is aborted. If allowed to continue, it can advance to LOS (which typically is significantly less reversible) and to postoperative VCP. Continuous vagal monitoring has utility in identifying real-time adverse concordant amplitude and latency changes (combined events), which can prompt modification of the associated surgical maneuver and may prevent RLN paralysis during thyroidectomy.

Key Words: Continuous vagal monitoring, CIONM, vagal electrodes, recurrent laryngeal nerve paralysis, recurrent laryngeal nerve injury, vocal cord paralysis, adverse EMG changes, neuromonitoring, IONM, thyroid surgery, combined events, amplitude and latency changes.

Level of Evidence: 4.

Laryngoscope, 00:000–000, 2013

INTRODUCTION

A recent analysis of 27 articles that reviewed over 25,000 patients undergoing thyroidectomy found that the average initial postoperative VCP rate was 9.8% and ranged from 0% to 18.6%.

Unilateral VCP can be associated with voice changes sufficient to alter vocation and can be accompanied by dysphagia with aspiration; bilateral VCP may result in tracheotomy.

Standard IONM

Intraoperative neural monitoring (IONM) has been routinely applied in head and neck surgery. It has been increasingly recognized as an adjunct to visual nerve identification, and as an aid in intraoperative management and in the prognostication of postoperative nerve
function over the past two decades in thyroid and parathyroid surgery.\textsuperscript{3,4} Recent studies show approximately 53\% of U.S. general surgeons and 65\% of U.S. otorhinolaryngologists use IONM in some or all of their cases. A recent survey of German surgical departments found over 92\% German surgeons routinely utilize IONM during thyroidectomy.\textsuperscript{7,9} The value of IONM information for surgeons is highlighted by its prevalent use in high volume centers by surgeons performing >100 thyroid/parathyroid surgeries per year.\textsuperscript{9}

Multidisciplinary organizational support for neural monitoring is also accumulating. German practice guidelines and the International Neural Monitoring Study Group recommend IONM for all cases of thyroid surgery.\textsuperscript{10,11} The American Academy of Otolaryngology and Head Neck Surgery (AAOHNS) recently published guidelines for voice optimization during thyroid surgery. It suggests that IONM is an option for patients undergoing thyroid surgery due to its proven utility in three distinct areas 1) improvement in recurrent laryngeal nerve (RLN) identification time, 2) reduction of temporary VCP rates and 3) avoidance of bilateral VCP (through prognostication of postoperative vocal cord function). These AAOHNS guidelines suggest special utility for IONM in cases of 1) bilateral thyroid surgery, 2) revision thyroid surgery, and 3) surgery in the setting of an existing RLN paralysis.\textsuperscript{12} Two recently published American Thyroid Association Surgical Affairs Committee consensus statements (on outpatient thyroid surgery and on optimal surgical management of goiter) note that neural monitoring is helpful in confirming intact neural function at the end of surgery and that this may impact on discharge planning.\textsuperscript{13,14} American Head and Neck Society guidelines for the management of invasive thyroid cancer state that IONM provides important intraoperative and postoperative functional information, which impacts on timing of contralateral surgery and the need for tracheotomy. They recommend IONM be considered in all cases of thyroid cancer, especially in the setting of preoperative RLN dysfunction.\textsuperscript{15}

Continuous Vagal Monitoring and Neural Injury Prevention

Current IONM formats allow the surgeon to intermittently stimulate and assess RLN function. While this has significant utility, such a format could potentially allow the RLN to be at risk for damage in-between stimulations.\textsuperscript{16,17} This reality may underlie the data, suggesting that current IONM formats are limited in an ability to prevent neural injury.\textsuperscript{5,10,16,18–22} An IONM format that provides information regarding impending injury would address this issue.

The advantage of continuous intraoperative neuro-monitoring (CIONM) is that it has the potential to monitor the entire vagus and RLN functional integrity in real-time throughout surgery and could identify electromyography (EMG) signals associated with early impending injury states.\textsuperscript{23–25} Initial studies on CIONM with a vagal nerve electrode have suggested such monitoring is not associated with significant adverse neural, cardiac, pulmonary, or gastrointestinal vagal side effects.\textsuperscript{17,23,26–29}

For continuous vagal neural monitoring to have proven utility, it must provide accurate detection of EMG changes, which are a) considered adverse EMG events in that they are associated with impending VCP, b) easily recognized by the surgeon intraoperatively, and c) nascent so that there is a resolution of adverse EMG changes with modification of the associated surgical maneuver. Furthermore, we must be able to segregate such EMG changes of impending neural injury from artifactual EMG changes that are associated with endotracheal tube malposition or other equipment problems.

We report one of the largest prospective continuous vagal monitoring studies investigating novel EMG outcome parameters (we define as “combined events”) associated with imminent neuropraxic nerve injury—and their relationship to intraoperative surgical maneuvers and postoperative vocal cord function.

MATERIALS AND METHODS

Informed consent was obtained from each patient in this internal review board-approved nonrandomized prospective multicenter study over a 12-month period of time. Patients with preexisting RLN paralysis or noncurrent laryngeal nerves were excluded. All patients had preoperative and postoperative laryngoscopy 2 days after surgery and repeated serially if abnormal. All IONM set-up and practices (including trouble shooting algorithm) was as recommended by the International Neural Monitoring Study Group.\textsuperscript{11}

We investigated evoked vagal nerve waveform amplitude and latency changes (alone and combined) during thyroid surgery using a size 2 or 3 vagal electrode (Suppl. Fig. 1A and 1B) and a NIM 3.0 monitor (APS vagal electrode system, Medtronic, Jacksonville, FL). These waveforms were correlated with intraoperative maneuvers and postoperative laryngeal function to determine parameters of impending and definitive nerve injury.

Definition of Adverse EMG Events

To identify clinically relevant significant adverse EMG signal changes, we categorized EMG signals based on vagal evoked signal amplitude and latency waveform characteristics. Single events were defined as EMG changes affecting either amplitude or latency. Combined events (CE) were defined as concordant changes in both signal amplitude and latency and are stratified below into mild (mCE) and severe CEs (sCE). We hypothesized that such combined events may more reliably predict impending neuropraxia, as opposed to other technical issues such as endotracheal tube malpositioning (which could affect amplitude in isolation). We defined amplitude and latency changes as follows:

- Mild Combined Event (mCE): amplitude decrease of >50% to 70\% with a concordant latency increase of 5\% to 10\%.
- Severe Combined Event (sCE): Amplitude decrease of >70\% with a concordant latency increase of >10\%.
- Loss of Signal (LOS): Complete loss of recognizable RLN electromyographic signal (amplitude < 100 \(\mu\)V) intraoperatively as defined by the International Neural Monitoring Study Group.\textsuperscript{11}

Installation of the APS electrode required exposure of less than a 1 cm segment of vagus nerve. The APS electrode was positioned on the nerve starting at a 45° angle and then sliding it over the vagus with the enclosure tabs open (see Suppl. Fig.
1A and 1B). After connecting the APS electrode to the monitor, baseline values for latency and amplitude were automatically calibrated. If the baseline amplitude was less than 500 μV, the anesthesiologist repositioned the endotracheal tube such that a waveform of greater than 500 μV was achieved as an initial baseline. If the amplitude and latency alarms engaged early in the case and were not associated with a surgical maneuver, this was felt to be artifactual and the tube was subsequently repositioned and amplitude and latency baseline was recalibrated. The APS electrode provides periodic, low-level stimulation of the vagus nerve of 1mA every 6 seconds (10 times/minute, pulse duration 100 μsec duration). The frequency of stimulation can be programmed. Amplitude and latency waveforms were displayed separately and an upper limit threshold for latency and a lower limit threshold for amplitude were defined as separate alarm lines. In addition, acoustic signals alerted the surgeon that the preset alarm threshold of amplitude or latency had been violated or that the electrode had been dislocated.

**Surgical Behavior**

As part of our surgical protocol, if significant adverse EMG changes temporally associated with a given surgical maneuver occurred, then that maneuver was immediately aborted. Subsequently, the surgical maneuver as well as the associated EMG changes were documented and observed to determine recovery. At the end of surgery, the APS electrode was removed and stimulation was performed proximal and distal to the vagal contact point, to exclude electrode induced vagal segmental injury.

**Data Analysis**

Receiver operating characteristic (ROC) curves were constructed treating the number of sCE or mCE as continuous variables in a nonparametric analysis (data distribution was skewed) with the presence or absence of VCP as the gold standard. The standard error for the area under the curve was calculated according to the algorithm described by Delong. Sensitivity and specificity were defined according to standard definitions for binary and nonbinary diagnostic tests, whereas predictive values were calculated according to Bayesian theory. Associations between the presence/absence of VCP and categories of sCEs and mCEs were evaluated with Fisher’s exact test. Statistical analysis was performed using Stata 12.0 (College Station, TX). Predictive values were calculated according to Bayes theorem with standard conditional probabilities. Pretest probabilities were estimated based on the prevalence calculations from within the study data. The intermediate pretest probability was selected as the point estimate of prevalence (5.9%). The low and high pretest probabilities were selected using the 95% CI for the prevalence point estimate (2.2%, 12.4%).

**RESULTS**

In this prospective study, 102 patients were enrolled in two tertiary thyroid cancer referral centers. The study included 73 females and 29 males, with an average age of 52.7 years (14–82 years). Almost half (47%) of the surgeries were for thyroid cancer and 21% of cases were revision thyroid cancer surgery. All patients had successful stable evoked potentials through vagal and RLN neural stimulation. Repositioning of the endotracheal tube to increase baseline EMG amplitude at the beginning of the case was required in several patients to obtain a minimum threshold of 500 μV as per our study protocol. This generally took only several minutes and was always feasible.

There were no cases of stimulation evoked nerve injury. The average number of vagal 1 mA stimulations was 602 (range of 112–2257 stimulations). In our series, we had no cases of intraoperative adverse cardiac, pulmonary, or gastrointestinal adverse effects (including bronchospasm or bradycardia).

In the majority of cases, a size 2 APS electrode was installed. On average, the APS electrode installation time was 21 seconds (10–60 seconds) and removal was safe and averaged 7 seconds (3–20 seconds). Electrode placement and removal were technically straightforward in all patients. The average number of electrode dislocations was 0.3 (range 0–3) per case. Stimulation of the proximal and distal vagal segments (relative to the electrode placement), at the end of the case after electrode removal, showed no evidence of intraoperative vagal nerve injury due to dissection of the vagus or placement of the electrode in any patients.

**Vagus and RLN Normative Amplitude and Latency Values in Patients with Normal Postoperative Vocal Cord Function**

The average vagal initial baseline amplitude was 1185 μV (496–3542 μV). The amplitudes and latencies for patients with normal postoperative vocal cord function are illustrated (See Suppl. Table 1). There was no significant difference between presurgery and postsurgery amplitude or latency of the vagus or RLN, suggesting that repetitive vagal stimulation and surgical dissection were not associated with nerve injury. Left vagal latency was significantly longer than right vagal latency and vagal latency was significantly longer overall than RLN latency. This is consistent with prior work—and suggests that timed vagal evoked waveforms at the completion of lobectomy could serve documentation purposes in that the characteristic left and right vagal latency implies that entire vagal-RLN neural circuit is functioning.

**The Relationship Between Adverse EMG (CE and LOS) and Postoperative Vocal Cord Function**

Of the six cases that developed VCP, there was no significant correlation between the RLN having >1 branch or a specific dorsoventral relation to the inferior thyroid artery. VCP did not develop in any of the cases with isolated amplitude or isolated latency changes.

**A. Severe Combined Events (sCE)**

ROCs were created for both sCE and mCE. The area under the ROC curve for sCE was 0.84 (95% CI 0.65, 1.0; Suppl. Fig. 2), suggesting overall accuracy of the sCE test result. At the threshold value of one event, the sensitivity of sCE was 83.3%, with a specificity of 79.2% for VCP. At the threshold value of 7 sCEs, the sensitivity and specificity are 66.7% and 91.7%, respectively, for VCP. sCE as a test for VCP showed a PPV of 33% and a NPV of 97%. When evaluating sCE according
to categories of VCP, there was a significant association between the number of sCE and VCP (Fisher's exact \( P = .001 \)) (see Table 1). In the 80 patients without sCEs, there was only one VCP, whereas in the remaining 22 patients with multiple sCEs there were five cases of VCP. Of the six cases who developed a temporary VCP, 83% developed sCE during surgery, and the average number of sCEs for this VCP group was 29 (1–124 events). Of the remaining 96 cases that had a normal postoperative vocal cord examination, only 20% developed sCEs during surgery. The average number of sCEs for this group was 3.5 (range 1–79) (Table 1).

The area under the ROC curve (not shown) for mCE was only 0.74 (95% CI 0.54, 0.94) suggesting a low accuracy for this test relative to VCP. Even at a threshold of 19 mCE events, the sensitivity and specificity of mCE was only 66.7% and 82.3%, respectively.

### B. Loss of Signal (LOS)

If LOS is considered as a binary test for VCP, its sensitivity is estimated at 83.3% (95% CI 35.9%, 99.6%), with a specificity of 99% (95% CI 94.3%, 100%). LOS showed a PPV of 83% and a NPV of 98% for VCP. Thus, a positive LOS indicates that VCP is highly likely. When evaluating LOS according to categories of VCP, there is a significant association between LOS and VCP (Fisher's exact \( P < .001 \)) (Table 1).

There were six (5.9%) cases of postoperative temporary VCP (no cases of permanent VCP). Of these six cases of VCP, five cases (83.3%) developed LOS. One temporary VCP had no combined events or LOS recorded intraoperatively (Suppl. Fig. 3). We hypothesize that neural injury in this case occurred after the vagal electrode was removed; thus, the adverse EMG changes were not recorded. Of the six patients who developed LOS, one case had recovery of signal and five cases did not recover signal by the end of surgery. Of these five VCP cases that did not resolve at the end of the surgery, the majority resolved within 8 weeks, with the longest being 12 weeks postsurgery. For the normal postoperative glottic function group, only 1% had LOS (and this recovered).

LOS therefore was found to be a grave finding—only 17% of those with LOS exhibited recovery intraoperatively. In the one case where LOS recovered intraoperatively, the LOS was felt to be due to a global type 2 injury secondary to traction, and vocal cord movement was normal postoperatively. When LOS occurred, it was localized to a discrete segment of RLN (the RLN entry site/ligament of Berry region) in one case (i.e., Type I neural injury) (Suppl. Fig. 4), and a global lesion in four cases (i.e. Type II neural injury). \(^\text{11}\)

The suspected mechanisms of injury to the RLN in the LOS cases was believed to be due to nerve traction in two cases, coagulation in one case, cold irrigation in one case, and unknown in two cases. Of interest, in the irrigation case, initial amplitude and latency changes were seen only after the completion of surgical maneuvers during irrigation of the surgical field with cold saline. This patient had VCP for nearly 3 months.

#### Modification of the Surgical Maneuver and EMG Change Resolution

For patients with significant adverse EMG changes of multiple sCEs, immediate modification of the surgical maneuver resulted in resolution of those EMG changes in nearly 73% of cases (Fig. 1). Typically, during a case in which adverse EMG events (i.e., CEs) occurred, a surgical maneuver could be implicated. Subsequently, a relatively short period of alteration of the surgical maneuver—which we termed “relaxation time”—resulted in prompt improvement in the EMG waveform, usually over a few minutes. However when LOS was present, modification of the
surgical maneuver was associated with resolution of the EMG changes in only 17%.

DISCUSSION

This series represents two thyroid cancer tertiary care units, with nearly 50% of patients undergoing surgery for thyroid cancer and 20% undergoing revision surgery. In all 102 patients, a continuous vagal monitoring format successfully allowed safe vagal data recording. With stimulation levels at 1 mA, the vagal electrode yielded supramaximal stimulation in all patients. Endotracheal tube repositioning to obtain an initial amplitude baseline > 500 μV (from which decreased amplitude changes can be readily appreciated) was occasionally necessary and was readily achieved. Repetitive neural stimulation, vagal dissection, and vagal electrode placement were safe in all patients.

CIONM Efficacy in Prevention of RLN Injury

Impending nerve injury to the facial nerve during skull base surgery may result in dramatic evoked EMG changes. In thyroid surgery, however, EMG changes are not reliably present during RLN trauma related to various surgical maneuvers.6 This inherent disadvantage of current formats of intermittent IONM may be in part underpinning (along with issues of statistical power) the inability to diminish RLN paralysis rates with current IONM formats.33,34 CIONM of the vagus nerve, on the other hand, offers real-time, ongoing intraoperative assessment of the entire length of the vagal-RLN neural circuit at risk for intraoperative injury. Although various vagal electrodes are available for CIONM, there is still uncertainty regarding the electrophysiologic thresholds indicative of imminent RLN injury.23–25,35

For the CIONM format to be of surgical utility, it must meet several criteria: 1) It must incorporate existing monitoring standards of preoperative and postoperative laryngeal examination, routine vagal stimulation, recognition of standard normative recording parameters, and the application of a standard equipment trouble shooting algorithm—as outlined by the International Neural Monitoring Study Group Guidelines.11 2) It must differentiate artifactual EMG changes (such as those occurring with intraoperative endotracheal tube displacement) from EMG changes truly reflective of impending neuropraxic injury. 3) EMG changes must track with impending neuropraxic injury and must be clearly recognizable intraoperatively. Of importance, these changes must be nascent and completely reversible once the associated surgical maneuver is aborted.

We feel our definition of a severe combined event (sCE = amplitude reduction > 70% with concordant latency increase of > 10%) appears to meet this last criteria.

Adverse EMG Events Tracking with VCP Are Identifiable With CIONM

Our study showed certain intraoperative EMG changes are “adverse” in that they are associated with VCP. The two adverse EMG parameters we found are sCE as well as LOS. We found that both had a statistically significant association with VCP. It should be noted that these EMG changes are easily recognizable intraoperatively. The evidence is as follows:

a. sCE: The area under the ROC curve for sCE is 0.84 (95% CI 0.65, 1.0: Suppl. Fig. 2), suggesting an overall accuracy of the sCE test result. At a threshold value of seven events, the sensitivity and specificity for VCP is 66.7% and 91.7%, respectively, with a PPV of 35% and a NPV of 97%. When evaluating a number of sCEs according to VCP categories, there is a significant association between the number of sCE and VCP (Fisher’s exact P < .001). The total number of sCEs in the VCP group was 29, and in the no VCP group it was 3.5. The percent of patients having sCEs in the VCP group was 83% and only 20% in the no VCP group. Milder forms of combined events (i.e., mCE) in isolation, as well as isolated amplitude and latency changes, were not associated with VCP. In the 80 patients without sCEs there was only one VCP, whereas in the remaining 22 patients with multiple sCE there were five VCPs. Thus, sCE represents a robust adverse EMG event tracking with VCP.

b. LOS: If LOS is considered as a binary test, then its sensitivity for VCP is estimated at 83.3% (95% CI 35.9%, 98.6%), with a specificity of 99% (95% CI 94.3%, 100%), with a PPV of 83%, and with a NPV of 98%. Evaluation of LOS with respect to VCP and no VCP categories shows a significant association between the number of LOS cases and VCP (Fisher’s exact p < 0.001). Thus, LOS is a good test for VCP, with a PPV of 83% and a NPV of 99% (assuming our groups prevalence of VCP).

LOS was highly associated with postoperative VCP, with 83% of VCP being associated with preceding LOS, as opposed to only 1% of the no VCP group. In the single case of VCP without LOS, we hypothesize a poststimulation injury. Also of interest, in the single case of recovery
of LOS, VCP did not occur postoperatively. While sCEs may be reversible, the development of LOS is significantly more worrisome: LOS was reversible in only one of six individuals (17%), whereas sCE was reversible in nearly 73%. Other workers have disputed this finding; however, their findings may be explained by less strict definitions of LOS. Furthermore, the application of the IONM troubleshooting algorithm is important in the accurate delineation of LOS intraproactively. Therefore, we think it is reasonable to consider LOS, in general, as a nonreversible adverse EMG event—and when present, highly predictive of VCP. True LOS represents a robust adverse EMG forecaster of VCP.

VCP is the outcome of neural injury, which can be identified by an intraoperative progression of increasingly severe, adverse evoked EMG-events. The most typical sequence of adverse EMG events leading to VCP was multiple sCE with evolution to complete LOS. Again, sCEs (generally reversible) and LOS (generally irreversible) track robustly with VCP and are easily identifiable intraoperatively.

We propose that the presence of sCEs suggests impending RLN injury and should warrant modification of the associated surgical maneuver whenever possible. With the implementation of such an algorithm, we estimate that 73% of VCP, which would result from the evolution of sCEs to a complete LOS and VCP, could be prevented. The authors feel that it is intuitive that CIONM would not evade transection nerve injury, yet it was multiple sCE with evolution to complete LOS. VCP reliably occurred if multiple CEs were associated with ensuing LOS intraoperatively. However, in patients with initial adverse EMG changes, modification of the surgical maneuver averted VCP in 70% cases, which is very similar to our findings.

The vagal electrode we utilized meets many CIONM requirements including electrode geometry, applicability, easy removal, low stimulation current, and signal stability—rendering it a potential useful instrument for CIONM. However, a number of issues need to be addressed. Latency measurement can be hampered by latency “jumping,” which represents an artificial system measurement error caused by atypical triphasic-evoked waveforms and may also be associated with low amplitude waveforms below 350 µV. Baseline amplitude changes may also occur during the surgery and be associated with slowly evolving changes in endotracheal tube placement through surgical manipulation and retraction. Such changes may require recalibration of amplitude and latency baseline during the surgery.

**Studies on Type and Method of Injury**

Injury to the RLN can result from transection, compression, stretch, or thermal trauma to the main trunk or its branches. Nerve injuries may be divided into three categories: neuropraxia, axonotmesis, or neurotmesis, according to the Seddon classification. Of our five cases of nonreversible LOS, one case was a Type I segmental injury at the ligament of Berry/nerve entry site, and four cases were Type II global injuries. Two of the five injuries were thought to be caused by traction; one of the five injuries was by coagulation; and interestingly, one of the five injuries was thought to be associated with cold irritation. In this case, the onset of adverse EMG changes was coincident with the irrigation of cold saline into the operative field after all surgical maneuvers had been completed. As a result, we now ensure irrigation with body temperature saline at our institution.

**Literature**

In 2007, Lamadé et al. noted in a pilot study that stretch or tension on the nerve during manipulation of the thyroid gland resulted in signal depression of up to 60%, which resolved within seconds after removal of the force. Lamadé et al. suggested that such trauma to the RLN may be recognized early by use of CIONM, and thus allow the surgeon to react accordingly. Lamadé et al. concluded in a study on 55 patients with CIONM that the new system offered five advantages. Schneider et al. recognized the limitations of conventional hand-held stimulation electrodes and conducted a CIONM feasibility study on 23 pigs using a specially designed vagal electrode. During applied trauma, EMG changes such as amplitude reduction and/or latency increase were recorded. Schneider et al. did not correlate amplitude changes, latency changes, or LOS to postoperative VCP.

Schneider et al. in their series of 52 patients, defined combined events as amplitude changes of >50% and latency changes >10% from baseline. They found, consistent with our data, no cases of VCP with isolated amplitude or latency changes. All CEs occurred during either traction or cautery, with almost 80% being attributable to traction injury. Multiple CEs occurred in 13 patients. VCP reliably occurred if multiple CEs were associated with ensuing LOS intraoperatively. However, in patients with initial adverse EMG changes, modification of the surgical maneuver averted VCP in 70% cases, which is very similar to our findings.

The vagal electrode we utilized meets many CIONM requirements including electrode geometry, applicability, easy removal, low stimulation current, and signal stability—rendering it a potential useful instrument for CIONM. However, a number of issues need to be addressed. Latency measurement can be hampered by latency “jumping,” which represents an artificial system measurement error caused by atypical triphasic-evoked waveforms and may also be associated with low amplitude waveforms below 350 µV. Baseline amplitude changes may also occur during the surgery and be associated with slowly evolving changes in endotracheal tube placement through surgical manipulation and retraction. Such changes may require recalibration of amplitude and latency baseline during the surgery.

**Safety**

Our series demonstrates that continuous IONM is safe. Despite the average number of vagal stimulations being 602 for patient (with a maximum in one patient of 2300) at 1 mA with a pulse duration of 100 µsec, there were no cases of adverse amplitude or latency changes or VCP resulting from neural stimulation injury, and no cases of adverse cardiac, pulmonary or gastrointestinal side effects.

Electrode installation on the vagus was technically straightforward, taking an average of 21 seconds—with removal taking an average of 7 seconds. Testing the vagus proximal to the segment occupied by the electrode after its removal showed no adverse effects from either vagal dissection or vagal electrode placement in any patient. The electrode was easily managed during surgery within the operative field, with the average number of dislocations being <1 per case (0–3).

Groves and Brown demonstrated that it takes more than 2 mA or more to elicit a cardiopulmonary response from the C fibers of the vagus nerve. Low-level vagal stimulation at frequencies less than 30 Hz have not been
associated with subsequent adverse vagal effects such as central headache and numbness, cardiac arrhythmias, bradycardia, pulmonary bronchospasm, or gastrointestinal side effects of nausea and vomiting.\textsuperscript{23,40–42}

CONCLUSION

VCP is the outcome of neural injury, which can be identified by an intraoperative progression of increasingly severe adverse evoked EMG events. Our study shows that CIONM allows identification of the EMG changes (sCE), heralding imminent RLN injury that empowers the surgeon to promptly initiate corrective action that preserves the nerve’s functional integrity by reversing the surgical maneuver associated with these early but adverse EMG changes. Our initial data suggests that in nearly 73% of cases of such adverse EMG changes, modification of the surgical maneuver results in a resolution of the adverse EMG changes and averts VCP. The identification of such EMG events is therefore of great importance.

In conclusion, this study demonstrates the potential usefulness of a CIONM device to monitor the RLN and potentially warn the surgeon of impending RLN injury. Our findings would suggest that sCE represent a clear but reversible adverse EMG change, and when allowed to continue may progress to LOS (which is significantly less recoverable) and to postoperative VCP. Such monitoring is well-tolerated and unassociated with vagal/RLN injury, pulmonary, gastrointestinal, or cardiac adverse sequel.

Isolated EMG changes in either amplitude or latency, which may derive from endotracheal tube malposition or equipment related problems, did not predict VCP.

Clearly, further work is required to optimize a CIONM definition of meaningful warning threshold values. The NPV and PPV of various adverse EMG parameters are strongly related to the underlying prevalence of VCP in our study population. We recognize that our adverse EMG parameters of sCE and LOS are applied to different surgical populations and must be taken into account. Also, we appreciate that the development and temporal course of the adverse EMG changes as a result of surgical trauma will likely vary with the nature of the given surgical maneuver and its force and duration. Our study was limited in the forms of trauma that were identified and studied in this series of patients.

BIBLIOGRAPHY


