Accelerometry May be Superior to EMG for Early Evaluation of Vocal Cord Function After Nerve Injury in a Pig Model

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Objective: Vocal cord (VC) movement has been demonstrated by the use of accelerometry (ACC) to decrease in parallel with the electromyographic amplitude (EMG) during ongoing traction injury to the recurrent laryngeal nerve (RLN). When RLN function recovers, discrepancies between EMG and VC movement have been reported in clinical and experimental studies. The present study was conducted to clarify the actual relationship between EMG and VC movement measured by ACC during nerve recovery.

Methods: EMG obtained by continuous nerve monitoring (C-IONM) was compared with ACC during traction injury to the RLN, and throughout 40-min nerve recovery. A three-axis linear accelerometer probe was attached to the VC, and ACC data were registered as described. Traction damage was applied to the RLN until there was a 70% amplitude decrease from base-line EMG, or until loss of signal (LOS), that is, EMG values $\leq 100 \mu V$.

Results: Thirty-two RLN from 16 immature pigs were studied. Correlation between EMG and ACC were calculated during nerve injury and nerve recovery. The mean correlations were for the 70% and LOS group from start to end of traction: 0.82 (\pm 0.17) and 0.87 (\pm 0.17), respectively. Corresponding correlation coefficients during 40-min recovery was 0.50 (\pm 0.48) in the 70% group and 0.53 (\pm 0.33) in the LOS group.

Conclusion: There is a high correlation between EMG and VC movement during nerve injury, and a moderate correlation during early nerve recovery. EMG recovery after RLN injury ensures sufficient VC function as assessed by ACC.

Key Words: accelerometry, electromyography, intraoperative nerve monitoring, recurrent laryngeal nerve recovery, vocal cord function.

Level of Evidence: N/A

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INTRODUCTION

In thyroid surgery, the preservation of the recurrent laryngeal nerve (RLN) function is one of the primary concerns and has been studied for several years. The introduction of intraoperative nerve monitoring (IONM) did not only offer control regarding nerve function during surgery, but also prediction of nerve function at the end of surgery.¹ The possibility to predict nerve function, and thereby vocal cord function, led to the option of staged thyroidectomy in case of loss of the IONM signal on the first side of surgery,^{2,3} with the intention to reduce

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the incidence of bilateral vocal cord palsy (VCP) and the potential need for tracheostomy. However, some studies have reported relative low positive predictive values (PPV) in loss of signal (LOS),^{4–6} and some have even favored continued surgery after first side LOS, in spite of the risk of bilateral VCP.⁷ Other studies showed that in case of persistent LOS (i.e., amplitude of 100 µV or below) or an amplitude recovery <50% of baseline using continuous IONM (CIONM), the probability of VCP is as high as 50%–100%.^{8,9} This evident clinical discrepancy raised the question about the correlation between the electromyogram (EMG) measurement obtained by IONM, and the real movement of the vocal cord (VC). In an experimental study, Dahle et al. compared EMG changes with the movement of the VC assessed by accelerometry (ACC) during ongoing nerve injury.¹⁰ They found a strong correlation between changes in EMG and VC movement. This supports results described in large clinical studies.^{2,8,9} After RLN injury during surgery, intraoperative recovery of nerve function is possible, especially after less severe events like traction or pressure.¹¹ EMG recovery is defined by the International Nerve Monitoring Study Group (INMSG) as a recovery above 50% of baseline amplitude, at a minimum of 250 µV, using CIONM.¹² A waiting time of 20 min is proposed to reveal early nerve recovery before transitioning to staged thyroidectomy. These guidelines are mostly based on clinical studies, where the VC evaluation is performed on second postoperative day. This allows for longer recovery time and might influence the PPV.^{13,14}

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In contrast, Setså et al. were unable to demonstrate a strong correlation between EMG values at 20 or 40-min recovery time and the VC movement, when assessed by video-laryngoscopy directly following extubation.¹⁵ However, based on the strong correlation between EMG and VC movement obtained by ACC during nerve injury, as demonstrated by Dahle et al.,¹⁰ we would expect its existence also during the recovery phase. This study was therefore performed to thoroughly evaluate the relationship between EMG and VC movement assessed by ACC during 40-min recovery following nerve stress by traction. Not only LOS is associated with VCP. A significant risk escalation of nerve injury with postoperative VCP is already present at an EMG amplitude drop of 70% from baseline and a VCP rate of 23% is described in a clinical study.^{9,12} Nerve recovery after severe trauma without LOS is investigated to a limited scale. We therefore chose 70% amplitude decrease in addition to LOS as endpoints in this study.

MATERIALS AND METHODS

Animal Handling and Anesthesia

Thirty-two RLN from sixteen immature, domestic pigs (Norwegian Landrace, Yorkshire hybrid) were studied. Animal handling and experimental protocol was approved by the Norwegian Animal Research Authority, Oslo, Norway (FOTS, ID 13904-2018), and conducted under surveillance of the institutional Animal Use and Care Committee according to the National Institute of Health Guidelines for Care and Use of Laboratory Animals. All the animals were acclimatized in the research facility for at least five days before experiments were performed. Food was withdrawn 12 h prior to induction of anesthesia, whereas water was provided at all times.

Anesthesia was administered as previously described.¹⁶ Following pre-medication (ketamine 500 mg, diazepam 10 mg, and atropine 1 mg given as an intramuscular injection), general anesthesia was introduced via a face mask with isoflurane in oxygen supplemented by thiopentone (5 mg/kg body weight) intravenously 2 min before intubation of the trachea (Mallinckrodt, blue line oral tube, I.D 6.5, Covidien, Dublin, Ireland). General anesthesia was maintained by a continuous infusion of midazolam (0.5 mg/kg/h) and fentanyl (7.5 μ g/kg/h) and administration of isoflurane 0.5%–2.0% delivered in 50% oxygen in air via pressurecontrolled normoventilation (end-tidal carbon dioxide level of approximately 5.0 kPa) (Julian anesthesia workstation; Dräger, Lübeck, Germany). Neuromuscular blocking agents were completely avoided at all time intervals during the experiments.

Normothermic body core temperature for these animals (38°C-39°C) was preserved during the experiments by use of heating blankets. Heart rate was obtained via surface ECG electrodes. Systemic mean arterial pressure and central venous pressure were obtained by fluid-filled catheters introduced into the right femoral artery and vein connected via pressure transducers (Transact, ICU Medical, San Clemente, CA) to an IntelliVue monitor (Philips, Böblingen, Germany). Body core temperature was measured via a urinary catheter placed into the urinary bladder. Laboratory recordings (acid-base parameters and serum-potassium electrolytes) were determined at start and at the end of each experiment (OPTI CCA-TS2 Blood gas analyzer; OPTI Medical systems, Roswell, GA). After the experiments were ended, all animals were euthanized by an intravenous injection of 20 ml of saturated potassium chloride solution.

Surgical Preparation, Electromyography, and Accelerometry

After the neck and larynx were exposed by a low horizontal incision and vertical split of the upper skin and platysma, a tracheotomy was performed at the fifth tracheal ring. A single lumen cuffed endotracheal tube was then placed into the trachea to replace the oral tube initially used. Thereafter, the Vagus nerve was identified both by visualization and use of a conventional handheld monopolar stimulation probe (4 Hz, 100 µs, 1 mA (NIM 3.0 Nerve Monitoring System, Medtronic, Minneapolis, MN)). Single bipolar concentric, angle-formed needle electrodes (Dr. Langer Medical GmbH, Waldkirch, Germany) were always placed similarly, trans-ligamentary into the vocal muscle to obtain the highest possible amplitudes. EMG data were recorded following stimulation of the Vagus nerve by use of C-IONM (NIM 3.0; Nerve Medtronic, Jacksonville, FL Monitoring System; Medtronic, Minneapolis, MN). An automatic periodic stimulation electrode (APS Electrode Stimulator Probe, 2.0 mm; Medtronic, Minneapolis, MN)) was placed on the Vagus nerve. The ipsilateral RLN was identified by means of a handheld probe. Preparation was kept minimal to preserve all connective tissue surrounding the nerves. A vessel loop was wrapped around the RLN at the level of the third tracheal ring.

For perioperative registration of VC movement, an accelerometer probe was used. A complete presentation of the instrumental construction, design, and setup was recently presented.¹⁷ The accelerometer probe was placed into the VC via a rigid diverticuloscope (12068B, Karl Storz SE & Co. KG, Tuttlingen, Germany) and cable-connected to the controller unit. The controller unit read the probe values at a regular rate and streamed the data to a PC. During operation, all data were not only saved to disk for post-processing, but also displayed in a graphical view on the PC screen for early verification of proper probe operation. Experimental setup is displayed in Figure 1.

After all baseline EMG recordings were registered, traction stress of 1.0 N was initiated via a pulley yielding a constant traction force to the RLN. This was continued until the EMG amplitude decreased to 70% below baseline value (70%-group) or went on to LOS (LOS-group), respectively. Block randomization was used to determine the desired amplitude reduction and order of nerve studied.

EMG and ACC data recordings were started in parallel, and actual time was synchronized in both systems.

After the desired level of stress was reached, traction stress was removed, and the nerve was allowed 40-min recovery. EMG amplitude, latency, and VC movement were recorded for the next 40 min.

Thereafter, the nerve on the contralateral side was studied, using the same protocol.

Signal Processing

All data from the controller unit were streamed and stored for post-processing. The post-processing procedure consisted of the following steps: (1) data conversion, (2) removal of gravity influence, (3) filtering, and 4) peak detection. The raw data were stored in several files in a binary format with checksums. All analyses were performed in Python (Python Software Foundation, www.python.org). A Python script converted these files into comma separated values data files for further assessment.

The processing was necessary because the orientation of the probe and the position of the pig could shift for different reasons during the experiment. The program removed gravitational influence by applying a gliding average of the readings that was then subtracted. This was repeated with a second shorter moving window to suppress the noise in the ACC datasets. This helped



Fig. 1. A schematic view of the experimental setup before traction was initiated. (A) frontal view. (B) lateral view. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

to enhance the signal-to-noise ratio. Vectors were calculated and peak pulses detected. The data processing were discussed in more detail by Dahle et.al. 17

Statistics

Data analysis was carried out by using Graph-Pad Instat (Graph-Pad Software, San Diego, CA). Hemodynamic parameters at start and end of the experiments were compared by use of paired t-test with two-tailed p-value. Similarly, paired t-test with two-tailed p-value was used for analysis of recovery of the EMG amplitude from 20 to 40 min after release of nerve traction in both study groups. For between-group comparison of changes of the EMG amplitudes at 20 and 40 min, unpaired t-test was applied. Significance level was defined as p < 0.05. The correlation between EMG and ACC was calculated using Pearson correlation coefficient, using Python software (Python Software Foundation, www.python.org).

RESULTS

We studied 32 nerves from 16 immature domestic pigs, aged 88^{18} days (mean (SD)), and with a body weight of 43.4 (5.0) kg. During the study hemodynamic and laboratory parameters as well as body core temperature remained stable. Mean arterial blood pressure was at start 58.5 (5.3) mmHg (mean(SD)) and at end 55.9 (8.6) mmHg. Corresponding heart rates were 89.6 (10.8) beats per min and 95.3 (13.8) beats per min.

To reach the defined endpoints of the respective groups (70%-group versus LOS-group), duration of traction lasted 12 (6–41) min (median (IQR 10%–90%)) and 27 (2–110) min, respectively.

Figure 2A displays the amplitude (μ V) at start (BL), at end of traction (70/LOS) and following 20- and 40-min

recovery in the 70%-group and the LOS-group, respectively. Significant between-group differences were present at 20 min (p = 0.01), as well as at 40 min (p = 0.026). Within-group differences were obtained in the LOS-group between 20 and 40 min (p = 0.01), but not in the 70%-group (p = 0.32).

Corresponding values for latency changes during the experiments are depicted in Figure 2B. No significant difference was found at 40-min recovery, although there was an allover trend to higher values during the experiments in the LOS-group.

Figure 3 visualizes six typical plots comparing normalized values for EMG and ACC in selected experiments. The nerve stress was released at EMG values corresponding to the desired levels, either 70% of baseline (A–C) or LOS (D–F), as described in Materials and Methods.

The combined mean graph correlation from all 32 experiments (Pearson correlation coefficient) for the 70%- and LOS-group was from start to end of traction: 0.82 (\pm 0.17) and 0.87 (\pm 0.17), respectively. When comparing the correlation of EMG versus ACC from end of traction (ET), throughout 40-min recovery, the correlation coefficient was 0.50 (\pm 0.48) in the 70%-group, and 0.53 (\pm 0.33) in the LOS-group.

Figure 4 illustrates the normalized EMG and ACC values of each experiment in the 70%-group and in the LOS-group. In the 70%-group, the EMG amplitude recovered to or above 50% of baseline in seven of the 16 nerves, whereas recovery to or above 50% of baseline occurred in 15 of the 16 nerves assessed by ACC. Corresponding values in the LOS-group were three of 16 nerves and eight of 16 nerves, respectively.

The calculated mean value of the normalized data at 40-min recovery (Fig. 4), were in the 70%-group for EMG 0.52 (± 0.24) (mean (SD)) and for ACC 0.71 (± 0.18).



Fig. 2. (A) The electromyography (EMG) amplitude at baseline (BL), at end of sustained recurrent laryngeal nerve (RLN) traction (LOS/70%) and following 20 (R20 min) and 40 min (R40 min) recovery. RLN traction was continued to either LOS (LOS-group) (black columns) or amplitude decrease below 70% of BL (70%-group) (white columns). (B) The latency increase (in per cent) from BL in the LOS-group (black columns) and the 70%-group (white columns) are displayed. Significant differences were absent.

Corresponding values for the LOS-group were for EMG 0.25 (± 2.19) and for ACC 0.41 (± 0.3), respectively.

Duration of traction until the defined endpoints in the respective groups, varied from 4 to 50 min (min-max) in the 70%-group and 2–137 min in the LOS-group. No signs of correlation regarding duration of traction to injury and degree of nerve recovery were observed.

DISCUSSION

Intraoperative nerve monitoring is accepted among thyroid surgeons worldwide as the gold standard for predicting RLN function at the end of surgery.¹² Early nerve recovery after nerve injury is described both in experimental and clinical studies^{15,18,19} and intraoperative recovery of the electrophysiological signal after LOS may indicate normal VC function. Complete EMG signal recovery is defined as absolute amplitude $\geq 250 \ \mu V$

and $\geq 50\%$ of baseline amplitude.¹² In a large prospective multicenter study, Schneider et al. were able to show that all patients with complete EMG recovery had normal postoperative VC function.¹⁸ On the other hand, in case of persistent LOS. VCP was most likely. Our experimental study is in accordance with these findings. In all nerves with complete recovery (≥50% of baseline amplitude), the VC movement was restored to or above 50% of the original measurement by ACC, whereas, in case of persistent LOS, movement of the VC showed impairment with relative ACC values below 50% of the original baseline. However, incomplete EMG recovery ($\geq 100 \mu V$, < 50%baseline) seems to be accompanied with more unpredictable VC function as described in both clinical and experimental studies.^{13,15} That may also explain the high variability of PPV, ranging from 10 up to 90%, in clinical practice. This lack of diagnostic precision has raised doubt on the strategy of staged thyroidectomy.⁷

The commercial intraoperative nerve monitoring devices use the EMG of the vocal muscle as a surrogate for RLN function and indirectly for VC movement. However, movement of the VC is a balanced interaction of different larvngeal muscles. The RLN innervates four of these five muscles, and the only abductor (posterior cricoarytenoid muscle (PCM)) contributes mainly to glottis opening, whereas the vocal muscle makes only small adjustments to the tension of the VC. Liddy et al. could demonstrate that the EMG signals of the PCM were comparable with signals from the vocal muscle during thyroid surgery.²⁰ In a canine model, Puram et al. confirmed that EMG from the PCM and the vocal muscle during traction injury behaved similarly.²¹ Dahle et al. could demonstrate that EMG changes by IONM were highly correlated to the impairment of the VC movement during nerve injury.¹⁷ These findings suggest that almost all the intrinsic muscles in the larynx are affected simultaneously by the degrading function of the RLN's ability to transmit motor signals.

Nerve recovery, however, seems to be more complex than EMG changes by IONM may indicate. Our observed divergence between the EMG and the movement of the VC during recovery is difficult to explain. The complex structure of the RLN, where the different sensory, motor, and autonomic fibers are diffusely arranged within the nerve,²² must also be considered. Gacek et.al. found that the motor nerve fibers in the RLN, after exiting the Vagus nerve and before entering the larvnx, convenes into abductor and adductor halves. However, the axons innervating the two muscle groups have no topographic segregation within the RLN itself.^{22,23} This may potentially lead to less severe damage to motor fibers that innervate muscles other than the vocal muscle and might explain that VC movement shows better recovery than could be expected from the EMG of the vocal muscle, as found in our study. In their experimental study, Sung et al. investigated the movement of the VC using piezoelectric effect from a pressure sensor during nerve injury.²⁴ Signals from the pressure sensor after a 20-min recovery time were better than the EMG from the vocal muscle. These findings are similar to the results from our study and cements the possibility that lack of early EMG



Fig. 3. Six typical plots from a series of 32 experiments. Values are normalized for electromyography (EMG) and accelerometry (ACC). Figure 3A–C are plots from experiments in the 70%-group, and Figure 3D–F are from the experiments in the LOS-group. Red graphs: EMG and blue graphs: ACC. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

recovery is not directly correlated with impaired VC movement in real time. Earlier discussions regarding the PPV variations^{4,5,7} have either not gone in depth as to why or correctly focused on the delay between LOS and the postoperative laryngoscopy. In this study, we have seen that recovery of the VC movement is superior to the recovery of the EMG recordings from the vocal muscle after RLN injury, well below the 50% threshold. Incomplete EMG recovery despite adequate VC function, may lead to unnecessary staged thyroidectomies in clinical practice. There is a need for further research to improve the evaluation of nerve recovery during surgery more

precisely and thus strengthen the concept of staged thyroidectomy using results from nerve monitoring.

Limitations: To warrant unrestricted movement of the VC during the experiment, the use of endotracheal tube electrodes, as common in clinical settings, to record the EMG was not possible. This explains to some extent the relatively high standard deviation in the EMG recordings. The trans-ligamentary placement of the EMG needle electrode into the vocal muscle was performed the same way as described in Materials and Methods. However, exact placement might have varied through the series. The ACC probe was placed in the same manner for each



Fig. 4. Normalized values for electromyography (EMG) amplitude at baseline (BL), at end of sustained recurrent laryngeal nerve (RLN) traction (ET) and following 10-, 20-, and 40-min recoveries. RLN traction was continued to loss of signal (LOS-group) or 70% amplitude decrease below BL (70%-group) and following 10-, 20-, and 40-min recovery for each single experiment. Corresponding normalized values for accelerometry (ACC) are presented for comparison.

experiment, but small variations in the placement might occur intraexperimentally and result in small variations in the length and speed of the probe movement. The postprocessing steps as described in Material and Methods are designed to remove registered movement from breathing, accidental movement of the pig, and lessen this impact on the data by running "peak detection". Some degree of interference could still lead to a small difference in the ACC vs EMG graphs.

CONCLUSION

There is a strong correlation between EMG and VC movement during nerve injury. Similarly, a moderate correlation is also present during the early nerve recovery. ACC seems to indicate a better recovery of the VC movement than expected from the EMG data.

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