Vocal Cord Function During Recurrent Laryngeal Nerve Injury Assessed by Accelerometry and EMG

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Objective: Gradual impairment of nerve conduction is expected to be tightly associated with simultaneous gradual loss of vocal cord contractility, related to the fact that injured axons are connected to a defined number of muscle cells. In clinical studies, there is a time gap between observed adverse electromyographic (EMG) changes and examination of vocal cord function. This study evaluates the impact of intraoperative EMG changes on synchronous vocal cord contractility by simultaneous use of continuous intraoperative neuromonitoring (C-IONM) and accelerometer for registration of actual vocal cord function at a given change of EMG amplitude.

Methods: EMG was obtained following vagus nerve stimulation by use of C-IONM. A vocal cord accelerometer probe that could be attached to the vocal cords was developed based on a LIS3DH ultra low-power high performance three axis linear accelerometer (STMicroelectronics, Geneva, Switzerland). Accelerometer data were registered continuously together with EMG data during traction injury of the recurrent laryngeal nerve (RLN) until an amplitude depression ≤100 μV.

Results: Six RLN from four immature domestic pigs were studied. Vocal cord contractility assessed by vocal cord accelerometry decreased in parallel with EMG amplitude, with significant correlations ranging from 0.707 to 0.968.

Conclusion: Decrease of EMG amplitude during traction injury to the RLN injury is closely associated with a parallel drop in vocal cord contractility.

Key Words: Accelerometry, recurrent laryngeal nerve injury, vocal cord contractility, continuous intraoperative neuromonitoring.

Level of Evidence: NA

INTRODUCTION

The risk of recurrent laryngeal nerve (RLN) injury with postoperative vocal cord palsy (VCP) persists as one of the most feared complications in thyroid surgery. The ambition to preserve RLN function during surgery has led to the development of different techniques to optimize intraoperative nerve handling over time. Since its proclamation by Lahey in 1938, visualization of the RLN remains as gold standard to reduce permanent vocal cord palsy rates. The use of intermittent intraoperative neuromonitoring (I-IONM), and more recently, continuous intraoperative neuromonitoring (C-IONM), has increased worldwide since implementation in the 1990s. Both neural monitoring techniques seem to have the possibility to reduce permanent vocal cord palsy rates.

Intraoperative neuromonitoring of the RLN is performed by direct stimulation of the peripheral nerve with an electrical current and recording of the resulting vocal cord muscle depolarization. When the nerve is stimulated with supramaximal intensity, all nerve axons will be depolarized, leading to activation/depolarization of all associated muscle fibres. The intramuscular voltage, representing the activity of all muscle units, can be recorded as a compound muscle action potential (CMAP) directly by needle electrode or as surface CMAP obtained by an endotracheal tube electrode.

During surgery, the RLN can be injured by different mechanisms in which traction is the most common. In case of nerve injury, a lower number of nerve axons will transmit electrical signals to the vocal cord. Consequently, a lowered number of muscle units will depolarize, resulting in a decreased or absent amplitude of the recorded CMAP.

The loss of the neuromonitoring signal (LOS) is defined by the International Neural Monitoring Study.
Group (INMSG) as an amplitude \( \leq 100 \mu V \) after stimulating the vagus nerve, presuming a normal vocal cord function, preoperatively.\(^{10}\) However, the positive predictive value (LOS and postoperative VCP) varies considerably, and even the negative predictive value (normal signal and normal vocal cord function) may vary.\(^{11}\)

Based on the well-known model of the motor unit that an axon is connected to a defined number of muscle cells, gradual impairment of nerve conduction should result in gradual loss of contractility of the vocal cord.\(^{12}\) In all available clinical studies, there is a time gap between observed adverse electromyographic (EMG) changes and the examination of the functional status of the vocal cord. The impact of intraoperative EMG changes on synchronous vocal cord contractility has to our knowledge not been investigated so far.

Here, we present a new method to highlight functional changes of vocal cord contractility by use of accelerometry to test whether the presumed coherence between EMG signals and vocal cord muscle function really holds true.

**MATERIALS AND METHODS**

**Animals, Animal Handling, and Anesthesia**

**Procedure**

Four immature domestic pigs (Norwegian Landrace Norhybrid) with an approximate age of 3 months were studied. The study was approved by the Norwegian Animal Research Authority, Oslo, Norway (FOTS, ID 8338/2015) 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 animals were acclimated for 1 week in the laboratory housing area before the experiments. Prior to the experiments, all animals were fasted overnight but with free access to water at all times. Normothermic body core temperature was preserved by use of a heating mattress and covering blankets. Acid-base parameters and serum electrolytes were measured at the start and during the experiments. At the end of each experiment, the pigs were euthanized by an intravenous injection of 20 mL of saturated potassium chloride solution.

Preanesthetic medication with ketamine 500 mg, diazepam 10 mg, and atropine 1 mg was given intramuscularly 30 minutes prior to induction of general anesthesia. General anesthesia was introduced with isoflurane in oxygen administered via a facemask and supplemented with thiopentone (5 mg/kg body weight) intravenously 2 minutes before intubation of the trachea (Mallinkrodt, blue line oral tube, ID 6.5, Coviden, Mansfield, MA). General anesthesia was maintained with administration of isoflurane (1.5 vol. %) in oxygen/air via volume-controlled noninvasive ventilation (end-tidal carbon dioxide level of approximately 5.0 kPa) (Dräger anesthesia workstation; Dräger, Lübeck, Germany) and supplemented by an infusion of midazolam (0.5 mg/kg/hour) and fentanyl (7.5 \( \mu g/kg/hour \)), as previously described.\(^{15}\) Neurmuscular blocking agents were completely avoided at all time intervals during the experiments.

**Hemodynamic Monitoring, Body Core Temperature, Acid–Base Parameters, Serum–Potassium**

Heart rate was followed by electrocardiography (ECG) obtained by surface ECG electrodes. Systemic mean arterial pressure and central venous pressure were followed by fluid-filled catheters introduced into the right femoral artery and vein and connected via pressure transducers (Transpac, ICU Medical, San Clemente, CA) to IntelliVue monitor (Philips, Böblingen, Germany). Body core temperature was obtained via a urinary catheter placed in the urinary bladder. Acid–base parameters (pH, pCO\(_2\), and base excess [BE]) and serum–potassium were determined at start and at the end of each experiment (OPTI CCA-TS2 Blood gas analyzer; OPTI Medical systems, Roswell, GA).

**Surgical Preparation, Electromyography, and Accelerometry**

Neck and larynx were exposed by a low horizontal incision and vertical split of the upper skin and platysma after surgical disinfection. A tracheotomy was performed at the fifth tracheal ring, and a single lumen cuffed endotracheal tube was placed into the trachea after the oral tube was removed.

EMG was obtained following stimulation of the vagus nerve by use of continuous intraoperative neuromonitoring (C-IONM) (NIM 3.0; Nerve Medtronic, Jacksonville, FL Monitoring System; Medtronic, Minneapolis, MN). Needle electrodes (Dr. Langer Medical GmbH, Waldkirch, Germany) were placed transglamentary into the vocal cord. The vagus nerve was identified visually and by use of a conventional handheld monopolar stimulation probe (4 Hz, 100 \( \mu \)A, 1 mA; NIM 3.0 Nerve 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 magnifying glasses and the handheld probe. Preparation was kept minimal to preserve all connective tissue surrounding the nerves. A vessel loop was gently wrapped around the RLN at the level of the third tracheal ring.

The EMG and accelerometry recordings were started in parallel, and actual time were synchronized in both systems. After baseline EMG and accelerometer recordings were ready, traction stress was initiated by attaching a weight system to a vessel loop via a pulley yielding a constant traction force to the RLN of 1.0 N, similar to previous studies.\(^{14,15}\) Traction was continued until loss of the EMG signal, that is, to amplitude \( \leq 100 \mu V \).

**Vocal Cord Accelerometer Probe Design, Accelerometer Controller Unit**

For perioperative registration of vocal cord contraction, a vocal cord accelerometer probe was designed together with a controller unit. The probe was placed on the vocal cord through a rigid diverticuloscope (12068B, Karl Storz SE & Co. KG, Tuttinglen, Germany) and connected via a cable 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 saved to disk for postprocessing but additionally also displayed in a graphical view on the PC screen for early verification of proper probe operation.

For construction of the vocal cord probe, a LIS3DH accelerometer (STMicroelectronics, Geneva, Switzerland) was used. LIS3DH, a 3-axis sensor with a settable full-scale range in steps from \( \pm 2 \) g to \( \pm 16 \) g was controlled via an I2C interface. The chip size measured \( 3 \times 3 \times 1 \) mm, but in order to fix the interface connections (I2C) and power, it had to be soldered to a custom designed printed circuit board (PCB). For probe fixation on the vocal cord, a needle hook was additionally fixed to the PCB. The complete assembly and its placement into the vocal cord is presented in Figure 1.

Dahle et al.: Vocal Cord Function Assessed by Accelerometry
Because the probe orientation and the pig position may shift due to respiratory movements and spontaneous muscle contractions during the experiment, the gravitational impact on measurements may also shift. To remove the fluctuating gravitational component on the accelerometer data, a gliding averaging window was applied to the data. The length of the window was set to 2,000 samples (~1.5 seconds). The output of the averaging was then subtracted from the data. To suppress noise in the accelerometer datasets, a second much shorter (10 samples) moving average window was used. Random noise was reduced, whereas pulses were only moderately affected, enhancing the signal-to-noise ratio. Before peak detection, the acceleration vector was calculated using the 3-axis data. Peak pulses were detected using a gliding maximum window of 2,000 samples. As a final step, the maximum values were resampled to a 10-second rate using the average of the maximum values, suppressing any remaining effect of unwanted movements during the measurements. This last processing step was also applied to the EMG data. The two datasets were then normalized and compared. Because the data included a majority of samples with normal EMG and accelerometry, this made direct unadjusted correlation between all EMG and acceleration amplitudes misleadingly strong. For a more balanced comparison, all data were therefore categorized in bins based on intervals of 10% decrease of EMG amplitude before Pearson correlation coefficients were calculated.

For comparison of laboratory parameters during the experiments, simple parametric and nonparametric tests were used. Data were presented as mean (standard deviation [SD]). $P < 0.05$ was considered significant.

**RESULTS**

Four immature domestic pigs aged 104 (12) days (mean [SD]) and with a body weight of 41.1 (4.6) kg were studied. Of the available eight RLNs, six nerves were included, whereas two nerves were excluded due to technical failure. Hemodynamic parameters, body core temperature, acid-base balance, and serum electrolytes remained within normal range for these animals during the study. pH, pCO$_2$, BE, and serum-potassium were at start of the experiments 7.52 (0.04), 5.5 (1.4) kPa, 5.5 (3.4) mmol/L, and 3.8 (0.4) mmol/L, respectively; and at end of the experiments were 7.52 (0.04) ($P = 0.99$), 4.8 (0.4) kPa ($P = 0.37$), 4.8 (2.6) mmol/L ($P = 0.76$), and 4.5 (0.3) mmol/L ($P = 0.31$), respectively. Body core temperature was at start 38.8 (0.4) °C and at the end was 39.1 (0.6) °C ($P = 0.44$).

Figure 2 (A–F) shows the time-related changes observed in normalized values for EMG amplitude (blue lines) and corresponding accelerometry (red lines) obtained during sustained traction stress to the RLN for each of the six nerves studied.

Figure 3 (A–F) displays the covariance between normalized EMG data and normalized acceleration data for each single nerve studied. A high correlation between the changes of acceleration and EMG amplitude during traction injury to the RLN was observed in all six experiments with calculated correlation coefficient ($r^2$) ranging from 0.707 to 0.968 (Table I). All correlations were statistically significant.

Vocal cord velocity and displacement data were also calculated and behaved essentially as the vocal cord acceleration data.
DISCUSSION
Intraoperative visual identification remains the gold standard for preservation of the RLNs during thyroid surgery; however, visually apparently intact nerves do not necessarily guarantee full functional integrity. The introduction of I-IONM and C-IONM has contributed to improved understanding of the pathogenesis of nerve dysfunction and development of vocal cord paralysis, and in addition seem to have improved surgical safety by reducing permanent vocal cord palsy rates.

The justification behind the use of intraoperative neuromonitoring requires a monitoring system reliably predicting the functional integrity of the RLN continuously during surgery, especially when staged thyroidec- tomy is implemented in surgical practice. In the present study, accelerometry was for the first time introduced to...
access vocal cord contractility in an experimental model during sustained stress to the RLN. Gradual impairment of nerve function, accompanied by well-known EMG changes, resulted in corresponding deterioration of vocal cord contractility.

In five of our experiments, a 50% decrease of EMG amplitude from baseline revealed a similar reduction in vocal cord contractility, whereas in one experiment the vocal cord contractility remained at about 80% of baseline activity despite an EMG amplitude depression of 50%, as demonstrated in Figure 2A. One explanation for a certain deviation between the acceleration data and the EMG data may be due to differences in placement of the EMG needle electrodes into the vocal cord through the cricothyroid ligament from one experiment to another. The placing of the needle electrodes was performed the same way as described in the Materials and Methods.

**TABLE I.**
The Correlation Coefficient ($r^2$) Between Acceleration and EMG Amplitude During Traction Injury Applied to the Recurrent Laryngeal Nerve Calculated in Each Single Experiment.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>$r^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.878</td>
</tr>
<tr>
<td>B</td>
<td>0.707</td>
</tr>
<tr>
<td>C</td>
<td>0.905</td>
</tr>
<tr>
<td>D</td>
<td>0.968</td>
</tr>
<tr>
<td>E</td>
<td>0.946</td>
</tr>
<tr>
<td>F</td>
<td>0.951</td>
</tr>
</tbody>
</table>

Values were categorized in bins based on intervals of 10% decrease of EMG amplitude before the calculations. EMG = electromyographic.

Fig. 3. The correlation between normalized EMG amplitudes and normalized acceleration data during traction stress to the recurrent laryngeal nerve from six experiments (A–F). EMG = electromyographic.
section, but exact placement could not be visually verified. Therefore, the position of the needle electrodes within the vocal cord might have varied between the experiments. Consequently, if the needle electrodes were placed within the muscle fibers innervated by axons injured first, the EMG would tentatively be lower than global vocal cord motility. This assumption is in accordance with and supports the motor unit model previously described. According to this viewpoint, the use of an intramuscular needle electrode seems less robust than an EMG recorded by surface electrode and may therefore represent a limitation of the present study. In line with previous studies, intramuscular needle electrodes reveal a wide range of amplitudes dependent on placement of the needle electrodes within the vocal cord. Unlike the summation that occurs with surface electrode recording, the intramuscular needle electrodes may sample only a fraction of the total motor units.

In newly published experimental and clinical reports, surface electrodes placed on the thyroid cartilage seem superior to tube electrodes, with higher and more stable EMG signals. This type of electrodes would not influence the vocal cord movement and should be introduced in further experimental setups. The use of surface electrodes seems superior due to the intramuscular needle electrodes’ higher sensitivity detecting fibrillations, fasciculation potentials, and polyphasic waveforms as seen after nerve injury.

The predominantly parallel evolution of the changes in EMG and vocal cord contractility, as assessed by accelerometry, differs in one of the six experiments (see Figure 2B). The lowered values in acceleration, as observed initially, may be due to restrictions to movement of the acceleration probe for some reason because a slight rotation of the probe underway contributed to a numeric increase in acceleration to expected levels. In the further course of the experiment, acceleration and EMG changed similarly over time with reasonable correlation.

In the literature, the positive predictive value (PPV) of intraoperative nerve monitoring is reported to range from 12% to 88%. The correlation between EMG amplitudes and vocal cord contractility, as demonstrated in this study, should be expected to result in high PPVs. Lower PPVs reported in some studies may be explained by technical failure, mainly related to malposition of the tube electrodes during surgery. After LOS has occurred, the troubleshooting algorithm should always be implemented as suggested by the INMSG. One should, however, also bear in mind that the time gap between intraoperative LOS and postoperative laryngoscopy to some extent may explain false positive results.

Both the concept of staged thyroidecemy, for example, in case of LOS on the first side not to continue with the other side in planned bilateral surgery, as well as the concept of C-IONM by alerting the surgeon to impending nerve injury with the possibility to release intraoperative nerve stress, require reliable interpretation and accurate prediction of postoperative vocal cord function. Definitions of clinically important signal changes in C-IONM vary in the literature. The INMSG defines an impending adverse EMG as an amplitude decrease above 50% from initial baseline combined with latency increase of ≥10%. Furthermore, C-IONM can provide the prediction of postoperative vocal cord function after intraoperative recovery of LOS. Amplitude recovery of >50% of initial baseline is accompanied with normal postoperative vocal cord function. Interestingly, Schneider et al. could reveal differences in relative and absolute recovery values regarding segmental LOS type 1 (49% and 449 μV) and global LOS type 2 (44% and 253 μV). As confirmed by our study, EMG values above 50% are combined with vocal cord contractility values ranging essentially from 50% to 90% of baseline values.

In a recent experimental study, Brauckhoff et al. found that amplitude decreases of more than 50% below baseline resulted in a more unpredictable outcome of nerve function. From the actual study, EMG below 50% of baseline is closely followed by parallel decreases of vocal cord contractility. However, prognostic conclusions cannot be drawn from the actual study because recoveries were not investigated.

Previous clinical and experimental studies revealed differences in evolution of EMG and recovery of nerve function dependent on injury mechanism. The results from the actual study refers only to traction injuries to the RLN and should be confirmed following other injury mechanisms.

CONCLUSION
Changes in EMG amplitude during C-IONM highly reflect the actual contractile function of the vocal cord during traction injury to the RLN.

BIBLIOGRAPHY

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