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Original Article

# Influence of rocuronium on achieving optimal vagal stimulation during intraoperative nerve monitoring in thyroid surgery

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ABSTRACT

*Background:* In the present study we determine the feasibility of intraoperative neuromonitoring following the administration of a nondepolarizing neuromuscular blocking agent during thyroid operations, as well as the influence of rocuronium on the achievement of optimal vagal stimulation during intraoperative neuromonitoring in thyroid surgery. We further investigate whether accelerometry is a reliable approach to obtaining an ipsilateral vagus signal prior to recurrent laryngeal nerve dissection.
*Methods:* Included in the study were 61 thyroidectomized patients whose demographic data, indications, type of surgery, vagus, and recurrent nerve values before and after resection were obtained. We created five groups of patients based on the twitch values recorded during ipsilateral vagus stimulation prior to the recurrent laryngeal nerve dissection: (1) <10%, (2) 11–25%, (3) 26–50%, (4) 51–75% and (5) >75%.
*Results:* The average electromyography amplitudes of the vagus nerve prior to the determination of the recurrent laryngeal nerve for each group were 552 µV, 463 µV, 543 µV, 513 µV and 551 µV, respectively. No difference between the groups was observed in this regard ($p > 0.05$).
*Conclusion:* It can be expected that as soon as the effects of neuromuscular blockers on the peripheral muscles begin to abate, it will be possible to obtain the ipsilateral vagus signal prior to recurrent laryngeal nerve dissection at the desired levels. It can be concluded from this study that accelerometry using the pollicis muscle is an unreliable tool for the interpretation of the proper electromyography signals of the vagus nerve prior to the determination of the recurrent laryngeal nerve.



## 1. Introduction

One of the most feared complications among surgeons carrying out thyroid and parathyroid gland surgery is recurrent laryngeal nerve (RLN) injury. RLN injury is a significant complication that can occur after thyroid operations that can give rise to temporary or permanent paresis[1,2] with functional and psychological effects on the patient that have led in the past to medico-legal action following thyroid operations.[3–6] Although there have been studies showing that intraoperative neuromonitoring (IONM) is not that helpful in decreasing the RLN palsy rate in primary thyroid operations,[7,8] it is widely recognized as an instrument that can prevent possible RLN damage in parathyroid and thyroid operations.[9,10] IONM has been used to detect and specify the RLN, to estimate the function of the vocal cord and to clarify the RLN palsy mechanism, providing not only physical but also functional evidence of an intact RLN.[11,12] IONM can also help to predict postoperative RLN function, and can help in the staging of bilateral surgeries to avoid bilateral RLN injury and tracheostomy by detecting RLN injury intraoperatively.[13]

There are a number of pitfalls associated with IONM that can be evaluated in three groups, being technical, anatomical and complication-related. The technical pitfalls include endotracheal tube malposition, improper usage of anesthetic agents and hardware failures. Anatomical variations of RLN such as extralaryngeal branches, non-recurrent laryngeal nerve, etc. can lead to

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anatomical pitfalls in IONM. False positive (i.e. LOS with intact vocal cord mobility) and false negative (i.e. good EMG with postoperative vocal cord paralysis) results are complication-related pitfalls in IONM.[14,15]

The use of neuromuscular blocking agents (NMBA) during general anesthesia is crucial for clinically appropriate tracheal intubation and for the avoidance of laryngeal trauma. However, NMBAs may also affect EMG signals by decreasing them, which may result in a misinterpretation of IONM signals.[16] Although there have been studies showing that intubation without NMBA is possible, the use of NMBAs supports safer and easier intubation, and with less morbidity.

An acceleromyography can be applied to any muscle group whose movement or acceleration can easily be evaluated after the electrical stimulation of the nerve that innervates it. Generally, the nervus ulnaris is preferred, with acceleration evaluated using a piezo-electric sensor attached to the thumb. This technique allows for the objective evaluation of the degree of neuromuscular blockade in the adductor pollicis muscle.[17] Superficial electrodes attached to a train-of-four (TOF) guard accelerometer are placed over the ulnar nerve at the wrist, with the piezo-electric device applied to the corresponding thumb. A steady supramaximal 60 mA TOF stimulation is carried out every 15 s.[18]

In the present study, we investigate the reliability of the use of accelerometry [twitch (% TW)] for the obtaining of an appropriate ipsilateral vagus signal prior to the recurrent laryngeal nerve dissection (V1).

## 2. Methods

This research was approved by the Ethics Committee of Ege University Hospital with the 15–1.1/5 Institutional Review Board (IRB) serial number, and signed written consent was obtained from all patients and their families. No professional or financial association exists between the authors of the study and the commercial company whose IONM device was used in the study.

The study was conducted between January 2017 and January 2018, and included 61 patients (45 female; 16 male). All patients underwent thyroid surgery by two senior surgeons (OM-MO). The indications for thyroid surgery were multinodular goiter (primary or recurrent) and thyroid cancer (primary or recurrent) in the majority of cases. Patients under 18 years of age, and those with known neuromuscular disease or any known vocal cord dysfunction were excluded from the study. Only patients who underwent thyroidectomy with an IONM procedure were included in the study.

During the study period, IONM was performed selectively, and each patient was informed about the system and potential issues preoperatively. Since NMBAs can lead to a misinterpretation of IONM signals, details of the patients who are to undergo IONM were passed to the anesthesia department one day before the operation. Just before intubation, a suitable electrode was pasted to the appropriate part of the intubation tube by the surgical team. An Avalanche XT® (Dr. Langer Medical GmbH, Waldkirch, Germany) device was used for the IONM.

After the direct observation and checking of connections, a tap test was performed with a finger on the midline cricoid or thyroid cartilage for intubation tube position verification, while respiratory fluctuations were observed on the monitor. A bipolar probe was used for nerve stimulation, and the intensity of the electric current was set at 1 mA. V1, R1, R2 and V2 signals were recorded in all cases as routine. The V2 signal was recorded just before the midline strap muscles were closed, and after the whole resection was finished and the hemostasis was checked. The thyroidectomies were performed as described elsewhere.[19]

First, anesthesia induction was achieved with 2 μg/kg fentanyl and 5 mg/kg thiopental, and the neuromuscular blockade was monitored quantitatively using a TOF (train of four)-Guard (Biometer, Denmark) device. A finger adapter, which maintains a stable preload on the thumb with a reproducible baseline thumb position, and that prevents free movement of the thumb, was used. Accelerometry [twitch (% TW)] was routinely used for the quantative evaluation of the neuromuscular transmission of the thumb. With TOF-Guard, 0% twitch corresponded to 100% neuromuscular blockade.[20] TOF stimulation at a current intensity of 60 mA and a frequency of 2Hz every 15 s was adjusted for the monitoring of neuromuscular transmission from the inception of the complete neuromuscular blockade to the end of the operation. A single dose of rocuronium (0.3 mg/kg) was given to each patient to ease intubation, while no additional dose was applied during the operation. Nervus vagus stimulation was routinely carried out before and after the resection, with the V1 signal described as the EMG signal of the vagus nerve before the determination of the RLN. T1 was described as the time between intubation induction until the receipt of the V1 signal. The V2 signal was the EMG signal of the nervus vagus after hemostasis, and just before the termination of the operation. T2 was defined as the time between intubation induction and the receipt of the V2 signal.

We created five groups based on the TW values recorded during the V1 stimulation: (1) <10%, (2) 11–25%, (3) 26–50%, (4) 51–75%, and (5) >75%, and carried out an analysis to identify the statistical relationship.

Descriptive statistics were expressed as percentage, mean and standard deviation values. A Wilcoxon signed-rank test, analysis of variance (ANOVA) test with Bonferroni correction and Student's t-test were used for the pairing analysis. The outcomes of the study were compiled and analyzed using SPSS 22.0 statistical software, and a P-value of <0.05 was considered statistically significant.

## 3. Results

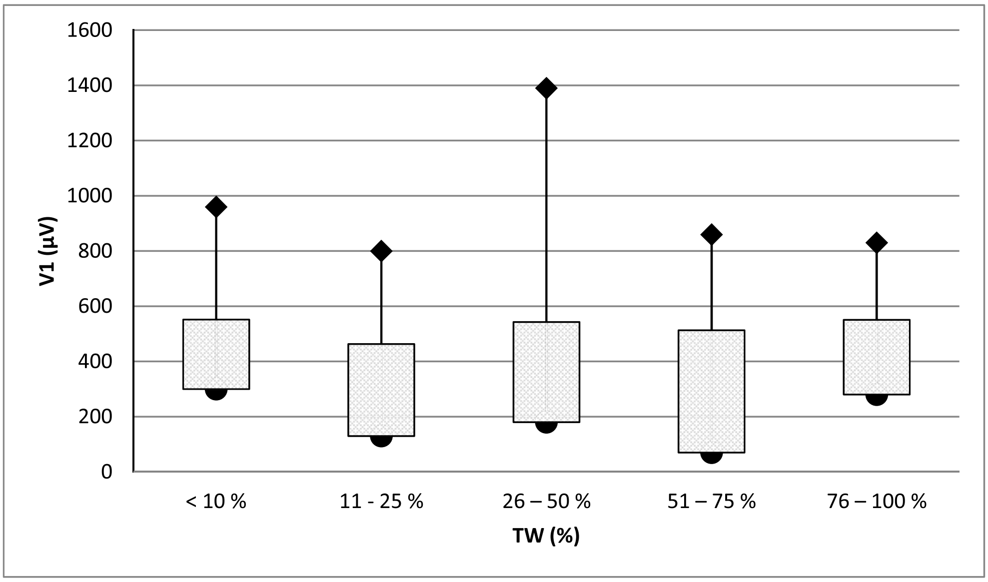
The study included 61 patients who underwent an IONM-based thyroidectomy (45 female; 16 male). The mean age of the study group was 50.9 (21–74); 32 (52%) of the 61 operations were primary procedures, and 29 (48%) were secondary procedures. The demographic characteristics of the patients are presented in Table 1. The average T1 value of the patients was 39.7 ± 13.7 min (6–82), and the mean V1 amplitude was 521 ± 243 μV (70,00–1390,00). The average V1 values for the groups were as follows (Table 2). The V1 signal was obtained from all patients, none of our which experienced a loss of signal. The mean TW value during the V2 stimulations was 81.1% (5%–100%); the average T2

**Table 1**
Characteristics of patients.

| Characteristics | |
|---|---|
| **Sex (n = 61)** | |
| Female | 45 (74%) |
| Male | 16 (26%) |
| **Indication for surgery** | |
| Recurrent multinodular goiter | 23 (37%) |
| Thyroid cancer | 17 (29%) |
| Multinodular goiter | 8 (13%) |
| Recurrent thyroid cancer | 6 (10%) |
| Thyroiditis and others | 7 (11%) |
| **Type of surgery** | |
| Total thyroidectomy | 32 (52%) |
| Completion thyroidectomy | 19 (31%) |
| Total thyroidectomy + CLND* | 8 (13%) |
| Hemithyroidectomy | 2 (3%) |

* Central lymph node dissection

**Table 2**
The average V1 values for the groups.




value of the patients was 91.9 ± 37.4 min (40–252), and the mean V2 amplitude was 647 ± 365 μV (150,00–1820,00).

## 4. Discussion

There is a common belief among surgeons that NMBAs should not be used in cases where IONM will be implemented due to the possibility that it will affect the IONM signals, leading to an incorrect interpretation.[2] In contrast, some researchers recommend using succinylcholine when using IONM due to its rapid onset and short duration. But serious undesired effects of the succinylcholine like cardiac dysrhythmia, hyperkalemia, malignant hyperthermia, myalgia, elevated intracranial and intraocular pressure, myoglobinemia, myoglobinuria made rocuronium most preferable among anesthetists. Some researchers have proposed the use of rocuronium, and the reversal of its effects with sugammadex.[21] Rocuronium is widely used as part of a standard intubation premedication approach.

IONM is becoming a standard tool in thyroidectomy. Although the contributions of IONM to traditional thyroidectomy are still controversial, the procedure can certainly benefit from IONM in clinical practice (reductions in RLN injury, intra-operative diagnosis of RLN injury, supporting the identification and dissection of the RLN, enhancing the completeness of a total thyroidectomy, tumor involvement of the RLN, use in endoscopic thyroidectomy), in education (benefiting the resident in training and less-experienced surgeons, monitoring of surgical performance), in research (neurophysiology and pathology of the RLN), and in medico-legal issues associated with thyroid surgeries.[22] However, no meta-analysis has yet been able to show that IONM is superior to traditional thyroidectomy for primary thyroidectomies. But in a recent meta-analysis, Wong et al have shown that selective use of IONM during high-risk thyroidectomy decreases the rate of RLN palsy and should be recommended during re-operation or thyroidectomy for malignancy.[23]

IONM is of utmost importance in intraoperative decision making, and is based on good communication between the surgeon and the anesthetist.[24] The International Neural Monitoring Study Group (INMSG) guidelines suggests the use of succinylcholine in doses of 2–2.5 mg/kg, or smaller doses of a nondepolarizing NMBA (e.g., rocuronium and atracurium at 0.5 mg/kg) at intubation to allow for the normal return of spontaneous respiration and the resumption of normal muscle twitch activity within a few minutes. The INMSG also suggests that it should be kept in mind that a preoperatively unknown pseudocholinesterase deficiency will lead to prolonged paralysis after a depolarizing NMBA like succinylcholine, and will invalidate an EMG monitoring system.[25]

Lu et al reported that only 30 min after an intubation dose of rocuronium (i.e. 0.6 mg/kg), when the neuromuscular blockade on the adductor pollicis muscle had reached a 5% twitch height, achieving a signal was possible in 53% of the patients at the adductor muscle of the larynx.[9] As soon as the effect of neuromuscular blockers on the peripheral muscles begins to vanish, it is possible to obtain V1 values at the desired level of >500 μV. Marusch et al found the average summed action potential to be 1.27 mV at time point 0% TW, 2.68 mV s at 10% TW, and 5.08 mV s at 25% TW. They further reported that the adductor pollicis muscle had a longer recovery period than the laryngeal muscles as a complete neuromuscular blockade effect of the administered rocuronium.[2] Meistelman et al showed the difference in blockade after administration of rocuronium in a bolus dose of 0.5 mg/kg, so the higher blockade was at the adductor pollicis muscle 98% (±1%), whereas blockade for a larynx was 77% (±5%).[26] It is interesting to note that the recovery period for the laryngeal muscles (22 ± 3 min) was notably shorter when compared to the adductor pollicis muscle (37 ± 4 min).[27]

In the present study, the cases were divided five groups based on their TW values (TW <10%, 11–25%, 26–50%, 51–75% and 76–100%). A V1 signal was obtained from all patients in each group, with the average V1 values for the groups recorded as 552 μV, 463 μV, 543 μV, 513 μV and 551 μV, respectively. When the V1 values of the groups were compared using Wilcoxon and Npar tests, no statistical difference was observed. It was possible to achieve reasonable signals regardless of the TW value of the adductor pollicis muscle, which is partly due to the better blood supply to the larynx muscles, and partly due to the faster fiber types in the larynx muscles.[28] Non-depolarizing neuromuscular blockers tend to make more blockade at slow-twitch than fast-twitch fibres.[29] It can be understood that there is no need to wait for full neuromuscular recovery of the adductor pollicis muscle during IONM.

One of the important points is also the time passed from intubation induction to V1 signal and is proposed that after 40 min, at which most of the effect of rocuronium vanishes. In the present study, the average T1 value of the patients was 39.7 ± 13.66 min (6–82 min), for what can we say that the sufficient time passed from intubation induction so that V1 values may be achieved properly. The time of the initiation of the neuromuscular blockade in the laryngeal adductor muscles after rocuronium 0.50 mg/kg (1.5 ± 0.1 min) is close to that recorded for succinylcholine (0.9 ± 0.1 min). These findings indicate that rocuronium can be utilized when enough intubating conditions are required rapidly, with maximum blockade being achieved in 1.5 min.

This study has some limitations, one of which is related to the low number of cases included in the study, and we also neglected to take into account the BMI of the patients. Furthermore, previous uses of corticosteroids, or antibiotics such as tetracycline, polymyxin B or lincomycin, which may enhance the action of NMBDs, were ignored.[30] Another drawback is that no distinction was made between right- and left-side thyroid operations in the study. Despite these limitations, our study shows that accelerometry [twitch (% TW)] using the pollicis muscle should be considered unreliable for the obtaining of accurate V1 signals.

## Declaration of competing interest

The authors report no potential financial and non-financial conflicts of interest.

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