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# *Intraoperative Acceleromyographic Monitoring Reduces the Risk of Residual Neuromuscular Blockade and Adverse Respiratory Events in the Postanesthesia Care Unit*

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***Background:*** **Incomplete recovery from neuromuscular blockade in the postanesthesia care unit (PACU) may contribute to adverse postoperative respiratory events. This study determined the incidence and degree of residual neuromuscular blockade in patients randomized to conventional qualitative train-of-four (TOF) monitoring or quantitative acceleromyographic monitoring. The incidence of adverse respiratory events in the PACU was also evaluated.**

***Methods:*** **One hundred eighty-five patients were randomized to intraoperative acceleromyographic monitoring (acceleromyography group) or qualitative TOF monitoring (TOF group). Anesthetic management was standardized. TOF patients were extubated when standard criteria were met and no fade was observed during TOF stimulation. Acceleromyography patients had a TOF ratio of greater than 0.80 as an additional extubation criterion. Upon arrival in the PACU, TOF ratios of both groups were measured with acceleromyography. Adverse respiratory events during transport to the PACU and during the first 30 min of PACU admission were also recorded.**

***Results:*** **A lower frequency of residual neuromuscular blockade in the PACU (TOF ratio ≤ 0.9) was observed in the acceleromyography group (4.5%) compared with the conventional TOF group (30.0%; $P < 0.0001$). During transport to the PACU, fewer acceleromyography patients developed arterial oxygen saturation values, measured by pulse oximetry, of less than 90% (0%) or airway obstruction (0%) compared with TOF patients (21.1% and 11.1%, respectively; $P < 0.002$). The incidence, severity, and duration of hypoxemic events during the first 30 min of PACU admission were less in the acceleromyography group (all $P < 0.0001$).**

***Conclusions:*** **Incomplete neuromuscular recovery can be minimized with acceleromyographic monitoring. The risk of adverse respiratory events during early recovery from anesthesia can be reduced by intraoperative acceleromyography use.**

This article is featured in "This Month in Anesthesiology." Please see this issue of ANESTHESIOLOGY, page 9A.

This article is accompanied by an Editorial View. Please see: Kopman AF: Undetected residual neuromuscular block has consequences. ANESTHESIOLOGY 2008; 109:363–4.

RESIDUAL neuromuscular blockade is commonly observed in the postanesthesia care unit (PACU) after nondepolarizing neuromuscular blocking agents (NMBAs) are administered intraoperatively. Despite the use of intermediate-acting NMBAs and antagonism of neuromuscular blockade at the conclusions of the procedure, up to 17–36% of patients arrive in the PACU with objective evidence of incomplete neuromuscular recovery.[1–3] The routine use of perioperative neuromuscular monitoring has been advocated as a method to reduce the incidence of residual paresis.[4,5] However, the effect of conventional peripheral nerve monitoring (tactile or visual assessment of train-of-four [TOF] stimulation) on postoperative neuromuscular function is uncertain, with several clinical trials demonstrating that qualitative nerve monitoring was not associated with a reduction in the frequency of incomplete neuromuscular recovery.[6–8] Quantitative neuromuscular monitoring provides a more objective measure of neuromuscular function. Acceleromyography, the most commonly used method of quantitative monitoring, allows clinicians to accurately assess the degree of neuromuscular blockade in the operating room and PACU. Few studies have examined the effect of acceleromyographic monitoring on postoperative residual paresis, however, and a recent meta-analysis suggested that intraoperative neuromuscular monitoring (qualitative and quantitative) did not reduce the incidence of this complication.[9]

An important question is whether the use of neuromuscular monitoring affects patient outcomes. Residual neuromuscular blockade impairs the function of respiratory, laryngeal, and upper airway muscles.[10] In volunteer subjects, residual neuromuscular blockade is associated with impaired airway protective reflexes,[11,12] upper airway obstruction,[13] and a decreased hypoxic ventilatory response.[14,15] In clinical studies, an association between incomplete neuromuscular recovery and postoperative hypoxemia[16–18] and respiratory complications[18] has been observed. The use of techniques to limit the degree of residual blockade, such as objective neuromuscular monitoring, may therefore reduce postoperative respira-

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tory impairment and hypoxemia in the early recovery period in the PACU.

No previous clinical trials have compared the effectiveness of qualitative and quantitative neuromuscular monitoring in reducing the occurrence of residual neuromuscular blockade after tracheal extubation. The aim of this clinical investigation was to evaluate the effect of objective neuromuscular monitoring on the incidence of postoperative residual blockade (defined as a TOF ratio $\leq 0.9$) with that of conventional qualitative monitoring. In addition, the effect of intraoperative acceleromyography on hypoxemia and airway obstruction in the PACU was examined.

## Materials and Methods

This study was approved by the institutional review board of Evanston Northwestern Healthcare, Evanston, Illinois, and written informed consent was obtained from all subjects. One hundred eighty-five patients presenting for elective surgical procedures requiring maintenance of intraoperative neuromuscular blockade were eligible for enrollment. Exclusion criteria included age younger than 18 or older than 70 yr, expected duration of the surgical procedure less than 60 min, American Society of Anesthesiologists physical status IV or V, weight greater than 30% above ideal body weight, presence of an underlying neuromuscular disease, use of drugs known to interfere with neuromuscular transmission, and preoperative chronic renal insufficiency (serum creatinine $>$ 1.6 mg/dl) or hepatic dysfunction.

Patients were randomly allocated to one of two groups according to a computer-generated randomization code. In the acceleromyography group, the degree of neuromuscular blockade was monitored with the TOF-Watch SX® (Organon, Roseland, NJ). In the conventional TOF group, standard qualitative TOF monitoring was used to guide neuromuscular management. The individual randomization assignments were concealed in opaque envelopes until the patients entered the operating room.

Anesthetic management was standardized in all subjects. Patients received 2 mg midazolam before transport to the operating room. Intraoperative monitoring consisted of electrocardiography, automatic blood pressure assessment, pulse oximetry, capnography, and core temperature *via* an esophageal probe. Anesthesia was induced with 1.2–2.0 mg/kg propofol, 100 $\mu$g fentanyl, 50 mg lidocaine, and 0.6–0.8 mg/kg rocuronium. Maintenance of anesthesia consisted of 0.5–3% sevoflurane in a 50% oxygen–air mixture. Sevoflurane concentrations were adjusted to maintain mean blood pressure within 20% of baseline values and Bispectral Index values between 40 and 60. In addition, patients received approximately 1–2 $\mu g \cdot kg^{-1} \cdot h^{-1}$ fentanyl throughout the surgical procedure. Additional opioid dosing (1–2 mg hydromorphone) could be administered for postoperative analgesia. Ventilation was controlled to maintain end-tidal carbon dioxide between 30 and 36 mmHg. Upper body forced-air warming devices (Bair Hugger®; Augustine Medical, Minneapolis, MN) were used to maintain core and upper extremity temperatures above 35.0°C. Neostigmine at 50 $\mu$g/kg and glycopyrrolate at 10 $\mu$g/kg were administered to reverse neuromuscular blockade at the conclusion of surgical closure when a TOF count of at least 3 was present.

Upon entering the operating room, group assignment was revealed to the anesthesia care providers. A research assistant applied all neuromuscular monitoring and reviewed the use of the acceleromyographic device with the clinicians providing the anesthetic. Two surface electrodes were placed over the ulnar nerve at the wrist after cleansing and rubbing the skin with an abrasive. Patients randomized to the acceleromyography group were monitored using the TOF-Watch SX®. The acceleration transducer was attached to the volar aspect of the distal phalanx of the thumb *via* a hand adapter that also applied a constant preload to the thumb and allowed a reproducible baseline thumb position (TOF-Watch Handadapter®; Organon). The evoked response of the thumb was measured after TOF stimulation (four pulses of 0.2 ms duration over 2 s at a frequency of 2 Hz). The current intensity selected was 50 mA in all subjects. Free movement of the thumb was ensured, and palmar skin temperature was maintained above 32°C. Clinicians were instructed to administer supplementary doses of rocuronium (5–10 mg) to maintain a TOF count of 2–3 (visual) during portions of the operation requiring neuromuscular blockade. No NMBAs were to be administered during the last 20–30 min of the anesthetic. When surgical relaxation was no longer required, the TOF ratio displayed on the TOF-Watch SX® was used to assess the degree of neuromuscular blockade. The primary goal of NMBA management in the acceleromyography group was to achieve a TOF ratio of greater than 0.80 at the time of tracheal extubation. Criteria for extubation included sustained head lift or hand grip for more than 5 s, the ability to follow simple commands, a stable ventilatory pattern with an acceptable arterial oxygen saturation ($Spo_2 > 95\%$), and a TOF ratio of greater than 0.80. The endotracheal tube could be removed before achieving a TOF ratio of 0.80 if the patient was unable to tolerate continued intubation.

In the conventional TOF group, the TOF-Watch SX® was applied in the same manner as in the acceleromyography subjects. However, the display panel was covered with opaque cardboard and tape so that care providers did not have access to TOF ratio data; the TOF-Watch SX® was used as a standard peripheral nerve stimulator. Dosing (5–10 mg rocuronium to maintain a TOF count of 2–3) and reversal of rocuronium were similar to the acceleromyography group. Requirements

for tracheal extubation in the conventional TOF group included sustained head lift or hand grip for more than 5 s, the ability to follow simple commands, a stable ventilatory pattern with acceptable arterial oxygen saturation, and no observation of fade during TOF stimulation (qualitative evaluation of residual neuromuscular blockade).

At the conclusion of the surgical procedure, the TOF-Watch SX® was removed from the patient, and a research assistant blinded to group assignment was called to the operating room. All subjects were administered 100% oxygen by facemask after tracheal extubation. Immediately upon transfer to a cart for transport to the PACU, a portable pulse oximetry device was attached to the patient (Rad-5; Masimo Corporation, Irvine, CA), and baseline values were recorded on a data collection sheet. No oxygen was administered during the time between transfer to the cart and admission to the PACU, as per standard practice in low-risk patients at our institution. Oxygen saturation was monitored continuously by the research assistant during transport to the PACU, and the lowest values (sustained for $> 5$ s) were noted. Episodes of hypoxemia were classified as mild ($Spo_2$ 93–90%) or severe ($Spo_2 < 90\%$). The occurrence of upper airway obstruction requiring an intervention (jaw thrust, oral airway, or nasal airway) by the clinician during the transport was also recorded.

Immediately upon arrival to the PACU, a TOF-Watch SX® device was placed on all subjects as described previously, and TOF ratios were measured and recorded by the blinded research assistant. Two consecutive TOF measurements (50-mA stimulating current, separated by 15 s) were obtained, and the average of the two values recorded. If measurements differed by more than 10%, additional TOF measurements were obtained (up to four TOF values), and the closest two ratios were averaged. The severity of residual paresis was categorized using the following criteria: TOF ratios greater than 0.9 were assessed as acceptable neuromuscular recovery; TOF ratios between 0.9 and 0.7 were considered mild to moderate blockade; and TOF ratios less than 0.7 were classified as severe neuromuscular blockade (postoperative TOF ratio associated with an increased risk of respiratory complications). All TOF measurements were obtained by researchers with more than 3 yr of experience with acceleromyographic monitoring.

On arrival to the PACU, 2 l/min oxygen was applied to all subjects by nasal cannula. Baseline oxygen saturation values (Marquette Solar 8000; GE Healthcare, Portland, OR) were recorded 1 min after application of oxygen. Pulse oximetry was measured continuously throughout the PACU admission, and $Spo_2$ values were recorded automatically at 1-min intervals for the first 30 min from the initial baseline measurement. The number of episodes of mild ($Spo_2$ 93–90%) and severe ($Spo_2 < 90\%$) hypoxemia were recorded, as was the lowest $Spo_2$ during this time. In addition, PACU nurses caring for the patient documented the occurrence of any of the following events during the first 30 min of PACU admission: the lowest $Spo_2$ observed by nursing staff, the requirement for either tactile or verbal stimulation to maintain $Spo_2$ greater than 93%, and any clinical evidence of airway obstruction.

Patient demographic data that were recorded included age, sex, height, weight, American Society of Anesthesiologists physical status, and preexisting medical conditions. Details of the intraoperative anesthetic management included type of surgical procedure, duration of anesthesia, administration of blood products and crystalloids, doses of opioids provided intraoperatively, and core temperatures at the conclusion of the anesthetic and at admission to the PACU. Data collected relating to neuromuscular management included the total dose of rocuronium, the number of redoses, the TOF count at reversal, the timing from neostigmine administration until tracheal extubation and TOF measurements in the PACU, and the ability to achieve a TOF ratio greater than 0.80 before extubation in the acceleromyography group.

*Statistical Analysis*

Sample size was determined based on the two primary outcome variables: the incidence of postoperative residual neuromuscular blockade and postoperative hypoxemia. In performing the sample size calculation, we derived a conservative (smaller) estimate of the required sample size by postulating only a clinically significant 50% one-directional (*i.e.*, one-tail) change at the $P = 0.05$ level, expecting to have sufficient power to detect a much larger change at the two-tailed $P = 0.01$ level. Approximately 35% of patients given intermediate-acting NMBAs arrive in the PACU with a TOF ratio less than 0.9.[2,19] Group sample sizes of 89 (each) achieve 80% power to detect a difference of 0.175 between the null hypothesis that both group proportions are 0.350 and the alternative hypothesis that the proportion in group 2 is 0.175 (*i.e.*, a 50% reduction in the incidence of residual blockade in the acceleromyography group), using a one-sided chi-square test with continuity correction and with a significance level of 0.05. Approximately 40% of patients in the PACU will develop at least one hypoxemic episode.[20] Group sample sizes of 73 subjects each achieve 80% power to detect a difference of 0.20 between the null hypothesis that both group proportions are 0.40 and the alternative hypothesis that the proportion in group 2 is 0.20 (*i.e.*, a 50% reduction in the incidence of hypoxemic episodes in the acceleromyography group), using a one-sided chi-square test with continuity correction and with a significance level of 0.05.

Nominal data are presented as the number and percent of subjects in each category. Data were compared using the Fisher exact probability test (NCSS, Kaysville, UT).

The 99% confidence intervals (CIs) for the differences in percentages were calculated using the Farrington and Manning score.

Ordinal and continuous data found not to have homogeneous variance or to be normally distributed are presented as median and range. Ordinal data and nonnormally distributed continuous data were compared using the Mann–Whitney U test (Stats Direct, Cheshire, United Kingdom). The median differences and their 99% CIs were calculated.

Normally distributed continuous data with homogeneous variance are presented as mean and SD. These data were compared using the unpaired *t* test (NCSS). Mean differences and their 99% CIs were calculated.

The Spearman rank correlation coefficient (Rho) and its 99% CI were determined for the relationship between TOF count at reversal and the TOF ratio in the PACU for the two groups.

Given the large number of comparisons being made, the criterion for rejection of the null hypothesis was set at $P < 0.01$.

## Results

A total of 185 patients were enrolled in this clinical trial. Protocol violations occurred in 3 patients, and research assistants were unable to collect acceleromyographic data in another 3 patients. These 6 subjects were excluded from final analysis; as a result, 90 patients were included in the conventional TOF group and 89 patients were included in the acceleromyography group. The acceleromyography group and conventional TOF group were similar in terms of demographic characteristics. There were no differences between groups in age, weight, height, sex, preexisting medical conditions, or American Society of Anesthesiologists physical status (table 1). The type of surgical procedures performed did not differ significantly between the groups (table 1). Intraoperative management data are presented in table 2. The duration of anesthesia, dosing of opioids, administration of crystalloid, intraoperative blood loss, and temperature at the conclusion of the anesthetic were similar in the two groups.

Twenty anesthesia attending physicians and 50 anesthesia residents or nurse anesthetists cared for the 90 patients in the conventional TOF group, and 20 anesthesia attending physicians and 48 anesthesia residents or nurse anesthetists cared for the 89 patients in the acceleromyography group. The same attending physicians cared for the patients in both groups while 40 of 58 anesthesia residents or nurse anesthetists cared for the patients in both groups. No anesthesia attending cared for more than 8 patients in either group, and no anesthesia resident or nurse anesthetist cared for more than

**Table 1. Patient Characteristics**

| | Acceleromyography Group | Conventional TOF Group | Difference (99% CI) | *P* Value |
|---|---|---|---|---|
| Number | 89 | 90 | | |
| Sex, M:F | 50 (56.2%):39 (43.8%) | 41 (45.6%):49 (54.4%) | −10.6% (−29.0 to 8.6%) | 0.18 |
| Age, yr | 45.5 ± 13.3 | 47.7 ± 12.6 | −2.2 (−7.2 to 2.9) | 0.26 |
| Weight, kg | 82.1 ± 26.7 | 80.4 ± 22.5 | 1.7 (−7.9 to 11.3) | 0.65 |
| Height, cm | 172.0 ± 18.5 | 171.5 ± 10.0 | 0.5 (−5.3 to 6.3) | 0.83 |
| ASA physical status | | | | |
| I | 32 (36.0%) | 33 (36.7%) | −0.7% (−19.0 to 17.6%) | 1.00 |
| II | 54 (60.7%) | 50 (55.6%) | 5.1% (−13.7 to 23.6%) | 0.55 |
| III | 3 (3.4%) | 7 (7.8%) | −4.4% (−15.4 to 5.6%) | 0.33 |
| CAD | 2 (2.3%) | 4 (4.4%) | −2.2% (−11.9 to 6.8%) | 0.68 |
| Hypertension | 21 (23.6%) | 17 (18.9%) | 4.7% (−11.3 to 20.6%) | 0.47 |
| COPD | 1 (1.1%) | 2 (2.2%) | −1.1% (−9.6 to 6.9%) | 1.00 |
| Asthma | 7 (7.9%) | 7 (7.8%) | 0.1% (−11.6 to 11.8%) | 1.00 |
| Sleep apnea | 2 (2.3%) | 2 (2.2%) | 0% (−8.6 to 8.7%) | 1.00 |
| Liver disease | 1 (1.1%) | 0 (0%) | 1.1% (−5.8 to 8.9%) | 0.50 |
| Thyroid | 7 (7.9%) | 4 (4.4%) | 3.4% (−7.1 to 14.7%) | 0.37 |
| Diabetes | 7 (7.9%) | 8 (8.9%) | −1.0% (−13.0 to 10.9%) | 1.00 |
| Smoking history | 19 (21.4%) | 13 (14.4%) | 6.9% (−8.1 to 22.4%) | 0.25 |
| Drinking history | 10 (11.2%) | 11 (12.2%) | −1.0% (−14.3 to 12.3%) | 1.00 |
| Operative procedures | | | | |
| General | 13 (14.6%) | 19 (21.1%) | −6.5% (−21.6 to 8.6%) | 0.33 |
| Gynecologic | 23 (25.8%) | 23 (25.6%) | 0.3% (−16.6 to 17.2%) | 1.00 |
| Neurologic | 1 (1.1%) | 0 (0%) | 1.1% (−5.8 to 8.9%) | 0.50 |
| Orthopedic | 39 (43.8%) | 38 (42.2%) | 1.6% (−17.2 to 20.3%) | 0.88 |
| Plastic | 2 (2.3%) | 0 (0%) | 2.3% (−4.7 to 10.7%) | 0.25 |
| Urologic | 11 (12.4%) | 10 (11.1%) | 1.3% (−11.9 to 14.6%) | 0.82 |

Data are mean ± SD or number of patients (%).

ASA = American Society of Anesthesiologists; CAD = coronary artery disease; CI = confidence interval; COPD = chronic obstructive pulmonary disease; TOF = train-of-four.

**Table 2. Perioperative Variables**

| | Acceleromyography Group | Conventional TOF Group | Difference (99% CI) | *P* Value |
|---|---|---|---|---|
| Number | 89 | 90 | — | — |
| Dose fentanyl, μg | 200 (50–500) | 200 (50–500) | 0 (−50 to 25) | 0.54 |
| Dose hydromorphone, mg | 0 (0–2.5) | 0 (0–2) | 0 (0 to 0) | 0.23 |
| Anesthetic duration, min | 139 ± 66 | 142 ± 51 | −3 (−26 to 20) | 0.76 |
| Temperature at end of procedure, °C | 35.92 ± 0.57 | 36.03 ± 0.80 | −0.11 (−0.40 to 0.17) | 0.29 |
| Neuromuscular blockade–related data | | | | |
| Dose rocuronium, mg | 68.9 ± 23.7 | 71.9 ± 27.6 | −3.0 (−13.0 to 7.0) | 0.44 |
| Number of redoses | 2 (0–8) | 2 (0–8) | 0 (−1 to 1) | 0.71 |
| Patients receiving redoses within 45 min of neostigmine | 2 (2.3%) | 9 (10.0%) | −7.8% (−19.2 to 1.9%) | 0.057 |
| TOF count at reversal | 4 (1–4) | 4 (1–4) | 0 (0 to 0) | 0.54 |
| Patients with 4 twitches | 75 (84.3%) | 79 (87.8%) | −3.5% (−17.6 to 10.4%) | 0.53 |
| Patients with 3 twitches | 6 (6.7%) | 2 (2.2%) | 4.5% (−4.7 to 15.1%) | 0.17 |
| Patients with 2 twitches | 6 (6.7%) | 8 (8.9%) | −2.2% (−14.0 to 9.4%) | 0.78 |
| Patients with 1 twitch | 2 (2.3%) | 1 (1.1%) | 1.1% (−6.8 to 9.7%) | 0.62 |
| Neostigmine dose to extubation, min | 8 (1–20) | 6 (1–38) | 1 (0 to 3) | 0.082 |
| Neostigmine dose to TOF measurement, min | 15 (7–31) | 13 (6–41) | 1 (−1 to 3) | 0.37 |
| TOF ratio, % | 100 (84–127) | 100 (37–119) | 3 (0 to 10) | 0.002 |
| Degree of neuromuscular blockade* | | | | |
| Acceptable recovery | 85 (95.5%) | 63 (70.0%) | 25.5% (12.0 to 39.7%) | <0.0001 |
| Moderate | 4 (4.5%) | 15 (16.7%) | −12.2% (−25.2 to −0.4%) | 0.014 |
| Severe | 0 (0%) | 12 (13.3%) | −13.3% (−25.1 to −6.0%) | <0.001 |

Data are mean ± SD, median (range), or number of patients (%).

* Degree of residual neuromuscular blockade classified as acceptable neuromuscular recovery = 0 (train-of-four [TOF] ratio > 0.90), mild to moderate = 1 (0.70 ≤ TOF ratio ≤ 0.90), or severe = 2 (TOF ratio < 0.70).

CI = confidence interval.

4 patients in either group. Because of the large number of different anesthesia providers for both cases and controls and the overlap of attending physicians, residents, and nurse anesthetists in both groups, the anesthesia provider was not considered to be a variable in our analysis.

Management of neuromuscular blockade in the operating room did not differ significantly between the groups (table 2). There were no observed differences between the acceleromyography group and the conventional TOF group in the total administration of rocuronium (68.9 and 71.9 mg, respectively), the number of redoses,[2] or the TOF count at the time of reversal (4 in both groups). The mean time from neostigmine administration until extubation was not significantly prolonged in the acceleromyography group (8 min) compared with the conventional group (6 min; $P = 0.08$). Train-of-four ratios greater than 0.80 were achieved in 88.8% of the acceleromyography subjects before tracheal extubation. Standard criteria for extubation were documented in all subjects.

The overall percentage of patients with objective evidence of residual neuromuscular blockade in the PACU (TOF ratio ≤ 0.90) was significantly higher in the conventional TOF group (30.0%) than in the acceleromyography group (4.5%; $P < 0.0001$; fig. 1). In addition, a significantly higher incidence of severe blockade (TOF < 0.70) was observed in the conventional group (13.3%) compared with the acceleromyography group (0%; $P < 0.001$). The Spearman rank correlation coefficient (Rho) for the relationship between TOF count at reversal and the TOF ratio in the PACU for all patients was 0.27 (99% CI, 0.08 – 0.44; $P = 0.0003$)

Although $Spo_2$ values were similar between groups before transport to the PACU, the nadir $Spo_2$ observed during transportation was significantly lower in the conventional TOF group (94% compared with 96% acceleromyography group; $P < 0.0001$; table 3). The percentage of patients with severe hypoxemia during transport was also higher in the conventional TOF group (21.1%) compared with the acceleromyography group (0%, $P < 0.0001$). More patients in the conventional TOF group required an active intervention to maintain a patent airway during the time interval between extubation and PACU admission (11.1% *vs.* 0%; $P = 0.002$).

On arrival in the PACU, median baseline $Spo_2$ values were lower in the conventional TOF group (95%) compared with the acceleromyography group (97%; $P < 0.0001$; table 4). During the first 30 min of PACU admission, the percentage of patients with episodes of mild (43.3% conventional TOF *vs.* 6.7% acceleromyography) and severe (21.1% conventional TOF *vs.* 0% acceleromyography) hypoxemia was significantly greater in the conventional TOF group (all $P < 0.0001$). The lowest $Spo_2$ values observed by PACU nursing staff did not differ from the lowest values automatically recorded from the Marquette pulse oximeter. Although there were no differences between groups in the observed incidence of airway obstruction, the number of patients requiring verbal or tactile stimulation to maintain $Spo_2$ values in

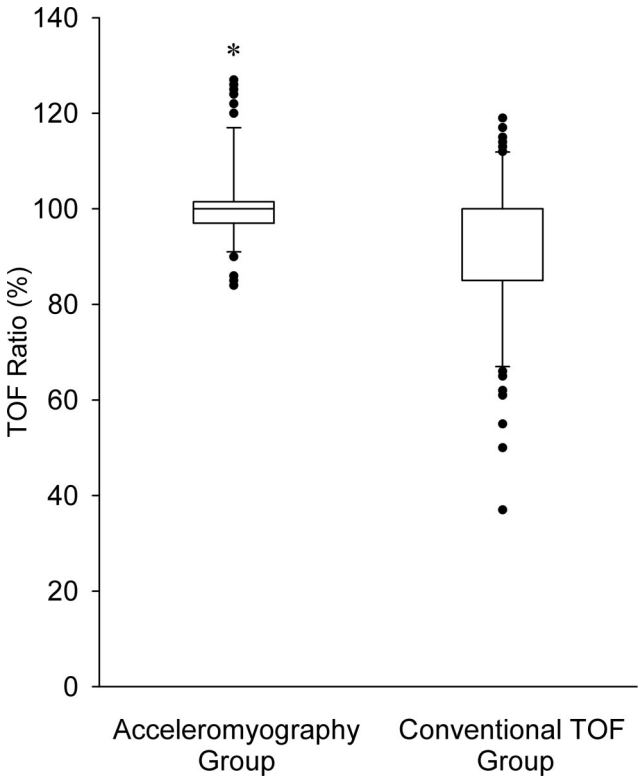


**Fig. 1. Train-of-four (TOF) ratios (%) for the 89 patients in the acceleromyography group and the 90 patients in the conventional TOF group. The *lower boundary of each box* indicates the 25th percentile, the *line within each box* indicates the median, and the *upper boundary of each box* indicates the 75th percentile. *Whiskers* above and below each box indicate the 90th and 10th percentiles. *Outlying points* are graphed above and below the upper and lower whiskers, respectively. Because both the median and the 75th percentile of the 90 patients in the conventional TOF group are 100%, the median line is not seen as a separate line within the box. * $P < 0.05$ when compared with the other group.**

the PACU was higher in the conventional TOF group (table 4).

Given that the proportion of subjects in the TOF monitoring group arriving at the PACU with a TOF ratio less than 0.9 was 30% whereas that in the acceleromyography group was 4.5%, using the two-sided Fisher exact test with a significance level of 0.01, our group sample sizes of 90 in the TOF monitoring group and 89 in the acceleromyography group achieved 98% power to detect the observed difference in group proportions. Given that the proportion of subjects in the TOF monitoring group experiencing an episode of $Spo_2$ less than 90% in the PACU was 0.211 whereas that in the acceleromyography group was 0.001, using the two-sided Fisher exact test with the significance level of 0.01, our group sample sizes of 90 in the TOF monitoring group and 89 in the acceleromyography group achieved 100% power to detect the observed difference in group proportions.

## Discussion

Previous studies that have examined the effect of neuromuscular monitoring on the incidence of residual neuromuscular blockade have yielded conflicting results. Most clinical trials have evaluated the usefulness of perioperative visual or tactile assessment of the response to TOF stimulation using standard peripheral nerve monitors (qualitative or conventional neuromuscular monitoring).[9] A randomized controlled trial by Pedersen *et al.*[6] demonstrated that the use of tactile evaluation of TOF stimulation did not influence the dosing of NMBAs intraoperatively or the degree of residual block detected clinically or objectively with mechanomyography in the PACU. In contrast to these findings, a randomized study by Shorten *et al.*[21] established that the use of a conventional peripheral nerve stimulator resulted in a reduction in the incidence of residual block from 47% (no monitoring group) to 15% (TOF monitoring). Observational trials have noted that the use of qualitative TOF monitoring was not associated with a reduction in the incidence of residual block.[7,8] It is not surprising that visual or tactile assessment of TOF responses may not reduce the severity of postoperative residual blockade significantly. Even experienced observers are unable to manually detect fade at TOF ratios greater than 0.4.[22] Although the TOF count may be a useful parameter in predicting the success rate of neostigmine-induced recovery, qualitative monitoring is insufficient to ensure acceptable neuromuscular recovery (TOF ratio $> 0.9$) at the conclusion of the surgical procedure.

The use of intraoperative quantitative neuromuscular monitoring may influence the incidence of residual paresis. Portable acceleromyographic devices are relatively easy to use and allow anesthesiologists to objectively

**Table 3. Transport Variables**

| | Acceleromyography Group | Conventional TOF Group | Difference (99% CI) | *P* Value |
|---|---|---|---|---|
| Number | 89 | 90 | — | — |
| No. with episodes of $Spo_2$ 90–93% during transport | 9 (10.1%) | 17 (18.9%) | −8.8% (−23.0% to 5.1%) | 0.14 |
| No. with episodes of $Spo_2 < 90\%$ during transport | 0 (0%) | 19 (21.1%) | −21.1% (−34.0% to −12.2%) | < 0.0001 |
| Lowest $Spo_2$ during transport, % | 96 (90–100) | 94 (78–100) | 2 (1 to 4) | <0.0001 |
| No. requiring airway maneuver during transport | 0 (0%) | 10 (11.1%) | −11.1% (−22.4% to −3.8%) | 0.002 |

Data are median (range) or number of patients (%).

CI = confidence interval; $Spo_2$ = arterial oxygen saturation measured by pulse oximetry; TOF = train-of-four.

**Table 4. Postanesthesia Care Unit Variables**

| | Acceleromyography Group | Conventional TOF Group | Difference (99% CI) | *P* Value |
|---|---|---|---|---|
| Number | 89 | 90 | — | — |
| Dose fentanyl, μg | 0 (0–200) | 0 (0–100) | 0 (0 to 0) | 0.09 |
| Dose hydromorphone, mg | 1 (0–4) | 1 (0–5) | 0 (−0.5 to 0.5) | 0.75 |
| Temperature on PACU arrival, °C | 36.35 ± 0.57 | 36.50 ± 0.67 | −0.14 (−0.39 to 0.10) | 0.12 |
| $Spo_2$ on PACU arrival, % | 97 (90–100) | 95 (72–100) | 2 (1 to 3) | <0.0001 |
| No. with $Spo_2$ 90–93% on arrival in PACU | 5 (5.6%) | 22 (24.4%) | −18.8% (−32.9 to −5.5%) | <0.001 |
| No. with $Spo_2$ < 90% on arrival in PACU | 0 (0%) | 9 (10.0%) | −10.0% (−21.1 to −2.7%) | 0.003 |
| No. with episodes of $Spo_2$ 90–93% in PACU | 6 (6.7%) | 39 (43.3%) | −36.6% (−51.2 to −21.1%) | <0.0001 |
| No. of $Spo_2$ 90–93% episodes in PACU | 0 (0–4) | 0 (0–12) | 0 (−1 to 0) | <0.0001 |
| No. with episodes of $Spo_2$ < 90% in PACU | 0 (0%) | 19 (21.1%) | −21.1% (−34.0 to −12.2%) | <0.0001 |
| No. of $Spo_2$ < 90% episodes in PACU | 0 (0–0) | 0 (0–6) | 0 (0 to 0) | <0.0001 |
| Lowest $Spo_2$ in PACU, % | 96 (90–100) | 93.5 (80–100) | 3 (2 to 4) | <0.0001 |
| No. requiring airway maneuver in PACU | 0 (0%) | 4 (4.4%) | −4.4% (−13.8 to 2.7%) | 0.12 |
| No. requiring stimulation to maintain $Spo_2$ in PACU | 0 (0%) | 7 (7.8%) | −7.8% (−18.3 to −0.5%) | 0.014 |

Data are mean ± SD, median (range), or number of patients (%).

CI = confidence interval; PACU = postanesthesia care unit; $Spo_2$ = arterial oxygen saturation measured by pulse oximetry; TOF = train-of-four.

quantify the TOF ratio in daily clinical practice. Only two randomized trials have examined the role of acceleromyographic monitoring in preventing or reducing residual block. Mortensen *et al.*[23] randomized 40 patients to receive either acceleromyographic monitoring or no neuromuscular monitoring. A total intravenous anesthetic with pancuronium was administered to all subjects. Fifty percent of patients in the no monitoring group had TOF ratios less than 0.7 immediately after tracheal extubation, compared with only 5% in the acceleromyography group. In a larger investigation by Gätke *et al.*,[1] 120 patients undergoing a propofol–opioid anesthetic were randomized to an acceleromyographic monitoring group or a group monitored using clinical criteria without a peripheral nerve stimulator. After tracheal extubation, TOF ratios less than 0.8 were measured in 3% of subjects in acceleromyography group *versus* 16.7% in the control group ($P = 0.029$). A recent meta-analysis that included studies using both qualitative and quantitative monitoring was unable to demonstrate that neuromuscular function monitoring decreased the risk of residual paresis.[9] The authors concluded, however, that the analyzed studies were very heterogeneous and of varying quality, which limited interpretation of the findings. A subsequent analysis of only studies using quantitative monitoring was unable to demonstrate any significant reduction in the incidence of postoperative residual blockade when compared with qualitative monitoring or no monitoring at all.[24]

The studies of Mortensen *et al.*[23] and Gätke *et al.*[1] compared subjects receiving acceleromyographic monitoring with those receiving only clinical assessment with no neuromuscular monitoring. The purpose of the current investigation was to determine whether acceleromyographic monitoring reduced the incidence and degree of residual block when compared with conventional qualitative TOF monitoring. In particular, we assessed whether acceleromyographic monitoring would provide any additional benefit when applied in the setting of "optimal" neuromuscular management, as defined by Kopman *et al.*[25] (use of intermediate-acting NMBAs, avoidance of total twitch suppression, anticholinesterase reversal of blockade at a TOF count of 3–4). Our findings demonstrate that use of intraoperative acceleromyography resulted in a significant reduction in the incidence and severity of residual paresis, even when principles to reduce the risk of incomplete neuromuscular recovery are used.

Several factors may be associated with postoperative residual paresis, which include duration of surgical procedure, type and dosing of NMBAs, anesthetic technique (volatile anesthetic *vs.* total intravenous anesthetic), and use of anticholinesterase reversal.[8,9,26] These management factors did not differ between the conventional TOF and acceleromyography groups in the current study, nor were the groups different in any other measured intraoperative variable, which suggest that the differences in residual block were attributable to use of quantitative monitoring. We observed a relatively high incidence of residual block (30%) in subjects monitored with conventional peripheral nerve stimulators. However, the percentage of control patients with TOF ratios of 0.9 or less was similar to the incidence reported in other recent studies using qualitative monitoring.[2,16] The frequency of residual block in the conventional TOF group was higher than that measured in the control group by Gätke *et al.* (16.7%). Difference in study design (use of total intravenous anesthesia *vs.* volatile agents, redosing of NMBAs based on clinical criteria *vs.* TOF count, residual block defined as TOF ratio of 0.8 *vs.* 0.9) likely accounted for variations in findings. Despite important differences in study design, the percentage of patients with residual block monitored with acceleromyography was comparable in the current investigation (3%) to the incidence reported in other randomized (3–5%)[1,22] and observational (3%) trials.[26]

The effect of quantitative monitoring on clinical outcomes and early recovery from anesthesia has not been previously assessed. Partial neuromuscular blockade may impair the function of respiratory, laryngeal, and upper airway muscles and contribute to adverse respiratory events in the PACU. An association between residual paresis and postoperative hypoxemia and upper airway obstruction has been observed in clinical studies,[8,16,17,18] and a TOF ratio less than 0.7 has been demonstrated to be a risk factor for postoperative pulmonary complications.[18] The mechanisms by which residual neuromuscular blockade can produce adverse respiratory events have been examined in volunteer studies. Significant reductions in respiratory muscle strength (maximum inspired pressure) have been observed in awake subjects with TOF ratios less than 0.7.[27] Upper airway obstruction and impaired inspiratory flow occurs frequently in subjects at a TOF ratio of 0.83.[13] Volunteer studies have also demonstrated pharyngeal dysfunction with aspiration at TOF ratios less than 0.90.[11,12] Furthermore, studies in healthy, nonanesthetized subjects have demonstrated a marked attenuation of the hypoxic ventilatory response at a TOF ratio of 0.70.[14,15]

We hypothesized that the use of acceleromyographic monitoring, by reducing the risk of incomplete neuromuscular recovery after tracheal extubation, would also decrease the incidence of hypoxemia and airway obstruction during transport to the PACU and during the first 30 min of PACU admission. The time between extubation and recovery of TOF ratios to greater than 0.9 represents a particularly vulnerable period for adverse respiratory events.[28] Although $Spo_2$ values were similar between groups before transport to the PACU, the percentage of patients with episodes of mild or severe hypoxemia during transport was significantly less in the acceleromyography group compared with the conventional TOF group. In addition, the nadir in measured $Spo_2$ values during this time was significantly higher in patients randomized to acceleromyographic monitoring. Fewer episodes of airway obstruction requiring active interventions during transport were also observed in the acceleromyography group during the interval between extubation and PACU admission.

Hypoxemia occurred less frequently in the PACU when acceleromyography was used. Initial median $Spo_2$ values recorded on arrival to the PACU were significantly higher in these patients (97%) compared with the conventional TOF subjects (95%). During the first 30 min of PACU admission, the percentage of subjects with at least one episode of mild or severe hypoxemia was significantly reduced in the acceleromyography group, as was the number of hypoxemic episodes, whereas the lowest recorded $Spo_2$ was higher.

Several important patient demographic (obesity, preexisting lung disease) and intraoperative management (type and duration of surgery, use of opioids) factors may contribute to postoperative hypoxemia.[29–31] However, the two study groups were similar in all measured preoperative and intraoperative variables. In addition, the only factor clearly associated with postoperative respiratory events when the data were stratified for the presence or absence of an episode of $Spo_2$ less than 90% in the PACU and reanalyzed was the use of acceleromyographic monitoring. Of interest, the majority of recorded hypoxemic events occurred within the first 5 min of recovery in the PACU. Previous data have demonstrated that when an intermediate-acting neuromuscular block is reversed at a TOF count of 3–4, the median time required for TOF ratios to recover to greater than 0.9 is 16–17 min.[32] This time course corresponds to the period of greatest risk for hypoxemia and airway obstruction in the current investigation (20 min after reversal).

The mechanisms by which quantitative monitoring improves postoperative neuromuscular recovery have yet to be clearly defined. We hypothesize that the use of acceleromyography allowed for more rational and accurate titration of rocuronium toward the conclusion of the anesthetic. However, our study was insufficiently powered to identify specific factors that would be indicative of more rational and accurate titration of rocuronium in the acceleromyography patients toward the end of the anesthetic. Although less rocuronium was used in the acceleromyography group, this difference (3.0 mg, or 6.7% less on a mg/kg basis) was not statistically or clinically significant. A lack of effect of acceleromyographic monitoring on total dosing of NMBAs is consistent with the observations from other studies using quantitative monitoring.[1,23,33] Because similar levels of neuromuscular blockade were maintained throughout most of the surgical procedures in both groups, these results are not surprising. In fact, fewer patients received a redose of rocuronium during the final 45 min of the anesthetic in the acceleromyography group (two in the acceleromyography group *vs.* nine in the conventional TOF group), but this difference was also not significant ($P = 0.06$). The time from neostigmine administration until extubation was slightly, but not statistically significantly, prolonged (1–2 min) in subjects randomized to receive quantitative monitoring. A requirement for a recovery to 0.9 would likely have resulted in longer extubation times (2.5–5 min), as observed in other acceleromyographic studies.[1,23] Although the differences between groups in total NMBA administration, redosing during the final 45 min of the anesthetic, and neostigmine-to-extubation times were small and not statistically significant, these findings suggest a more careful management of neuromuscular blockade in patients receiving acceleromyographic monitoring.

Our clinical trial has several limitations. First, the degree of residual neuromuscular blockade was measured

in the PACU using acceleromyography. Clinical studies have demonstrated that acceleromyographic data and mechanomyographic data (the accepted standard technique to quantify residual block) are not interchangeable. Viby-Mogensen *et al.*[34] observed average control TOF fade ratios of 1.16 ± 0.12 with acceleromyography, and an uncalibrated acceleromyographic TOF ratio of 0.97 has been shown to correspond to a mechanomyographic TOF of 0.9.[35] Evidence suggests that TOF ratios should recover to 1.0 to ensure complete recovery of pulmonary and upper airway function.[13] Therefore, our study is likely to have underestimated the true incidence of residual paresis in both groups. Second, the accuracy of acceleromyography in awake postoperative patients has been questioned.[36] We applied several principles to increase the reliability of our TOF-Watch SX® measurements, including use of higher stimulating currents, obtaining TOF values in duplicate with less than 10% variation, use of a hand adapter, and maintaining core and peripheral temperatures with an upper extremity forced-air warming device.[37,38] Third, blinding of clinicians treating patients intraoperatively was not possible. However, all postoperative data were collected by investigators blinded to group assignment. Finally, patients were only followed for the first 30 min of the PACU admission. We have previously observed that residual paresis and hypoxemic episodes usually occur within the first 20 min of PACU admission, as was observed in the current investigation. The effect of incomplete neuromuscular recovery, hypoxemic episodes, and airway obstruction during the early phases of anesthetic recovery on long-term morbidity was not assessed. Larger-scale investigations in low- and high-risk patient populations are required to examine this important safety issue.

Because conventional neuromuscular monitoring and standard clinical tests (*e.g.*, 5-s head lift) are unreliable in detecting residual neuromuscular blockade, several recent editorials and reviews have stated that acceleromyographic monitoring should be used routinely to reduce the risk of residual block and associated complications.[4,5,38] Our findings support these opinions. Evidence of incomplete neuromuscular recovery in the PACU was commonly detected in patients monitored with conventional peripheral nerve stimulators intraoperatively. In contrast, TOF ratios of 0.9 or less were rarely observed in subjects randomized to acceleromyographic monitoring. Furthermore, the risk of developing hypoxemic episodes and airway obstruction during early recovery from anesthesia was reduced significantly by the use of acceleromyography. To exclude with certainty the possibility of residual paresis and reduce associated adverse respiratory events, clinicians should use quantitative neuromuscular monitoring.

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