

Comparison Neuromuscular Blockade Monitors

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Patients scheduled for elective surgery under general anesthesia with a supraglottic airway, not expected to require any neuromuscular blocking drugs, and with both arms available for neuromuscular monitoring, were eligible. Patients were excluded if they had known neuromuscular abnormalities.

Most patients had an electromyograph and a laboratory-built mechanomyograph placed on one arm as previously described; minor mechanical improvements in the previously described mechanomyograph were implemented for this study. Two electrocardiogram electrodes (3M Red Dot, 3M Healthcare, St. Paul MN) were placed adjacent to the stimulation electrodes of the electromyograph to detect when stimulation from the electromyograph occurred and trigger mechanomyography recording as previously described. In most cases, a third monitor (acceleromyograph or electromyograph) was placed on the contralateral arm. Hypothetically 4 devices could be studied simultaneously, under certain circumstances, such as an electromyograph electrode array on both forearms, a mechanomyograph, and an acceleromyograph sensor on the arm opposite to the mechanomyograph. Since data for the TetraGraph, TwitchView, Stimpod and Philips monitors were collected manually from the monitor display, we studied no more than 3 monitors at a time to prevent task overload in the data recording process. Train-of-four ratios were collected synchronously from the mechanomyograph and ipsilateral electromyograph, and asynchronously from the contralateral arm devices every 12-20 seconds from the induction of anesthesia to emergence; in a few instances technical difficulties with monitors or recording equipment limited the number of data points that could be collected.

Three acceleromyograph monitors were used: ToFscan (Draeger Inc, Telford, Pennsylvania, USA), Stimpod NMS450 with the acceleromyography attachment V4.0.0 (Xavant Technology, Pretoria, South Africa), and Philips NMT module (Philips, Eindhoven, Netherlands). The ToFscan accelerometer is integrated into a flexible preload device which was used according to manufacturer's instructions. The Stimpod and Philips accelerometers were secured distal to the interphalangeal joint of the thumb using medical tape. All three acceleromyographs used two electrocardiogram electrodes to stimulate the ulnar nerve. These were placed 3-6 cm apart, overlying the ulnar nerve with the negative electrode distal to the positive electrode. The hand was positioned so that the thumb was free to move. Train-of-four ratios from the Stimpod and Philips acceleromyographs were recorded manually from the display on each device. For ToFscan, a data logger provided by the manufacturer was used to record twitch amplitude, as the ToFscan monitor displays a train-of-four ratio with a maximum value of 1.0, even when the actual value is >1.0; train-of-four ratios were calculated by dividing the fourth twitch amplitude by the first twitch amplitude.

Three electromyograph monitors were used: TwitchView (software version 1.0.91; Blink Device Company, Seattle, WA, USA), Stimpod NMS450X (software version V10.4.102; Xavant Technology, Pretoria, South Africa), and TetraGraph (software version V34g.22h.12e; Senzime Inc., St. Louis, MO, USA). All three electromyographs had device-specific electrode arrays which were used according to the manufacturer's instructions. Train-of-four ratios were recorded manually from the display of each device.

Skin prep was not performed prior to attaching any electrodes. All devices were set to a stimulation current of 60 mA. Temperature homeostasis was maintained through active warming.

The effect of normalization of the acceleromyograph train-of-four ratio was examined by determining the baseline train-of-four ratio measurement for each patient, from either the first train-of-four ratio measurement or the average of up to 5 consecutive measurements. The rest of the train-of-four ratio measurements from that patient were then divided by the baseline train-of-four ratio.

Statistical analysis

A convenience sample was used for the purpose of this study. Patients were enrolled until at least 1,000 train-of-four ratio data points were collected for each device. The number of data points collected for each patient was limited by the length of the procedure, by using no more than 3 out of 7 devices per patient, and the refractory delay for train-of-four ratio measurements which was 12 seconds or greater, depending on the minimum interval available for each device. The variability in case length and the variability in the number of repeated measurements per patient resulted in train-of-four ratio data that were imbalanced.

Gauge repeatability and reproducibility analysis was chosen since it accounts for patient-to-patient variability and the variability in measurements due to each device. Patients likely introduced variability in train-of-four ratio measurements due to differences in skin impedance, body temperature, acid-base status, and other variables. Since each patient had repeated measurements that were correlated to each other which introduced a random effects

variable, we used a total of seven random effects models (one for each device) to perform gauge repeatability and reproducibility analysis. The same analysis was used for both the non-normalized and normalized train-of-four ratios when analyzing the acceleromyography-based twitch monitor data.

We used a Bayesian approach to fitting the models as suggested by Weaver et al when performing gauge repeatability and reproducibility analysis since it is more flexible for imbalanced data. The distribution of the Bayesian priors for each model fit were the default priors provided by “brms,” which were t-distributions with three degrees of freedom.

Markov Chain Monte Carlo sampling method was used to sample the prior with 50,000 iterations, 2,000 burn-ins, and 10 thinning. Larger values for iterations, burn-ins, and thinning were tried for a few of the twitch monitors but did not result in any improvements in prediction and significantly increased computation time. The number of iterations represents the number of times a sampling occurs; Markov Chain Monte Carlo produces samples that are dependent. Burn-ins represent the number of sampling iterations that are thrown away at the beginning of sampling to reduce dependence on the initial state of the Markov Chain. Thinning represents the process of keeping every n th sample to reduce dependency between samples.

Gauge repeatability and reproducibility analysis outputs three parameters that are reported for this study. The mean value for each device represents the model’s estimate of the average value measured by the device. Patient-to-patient standard deviation represents the variability from the mean value that is attributable to the patient. Gauge standard deviation is the estimated variability within each case attributable to the neuromuscular blockade monitor. We also report 95% credible intervals which are calculated by the Bayesian model. Credible

intervals are a Bayesian way of expressing a concept similar to confidence intervals with one important difference. The measured parameter value is not treated as fixed, as in the frequentist approach but rather as probability that the parameter value is in any given range. Therefore, the credible interval is interpreted as being a 95% probability (as opposed to 95% confidence) that the true value of a measured parameter is within the range of given values.

Statistical analysis was performed with R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) and RStudio version 2023.06.1 (Posit Software, PBC, Boston, MA). The R package “brms” was used to fit the random effects models.