Workflow Eats Optimum Care for Lunch

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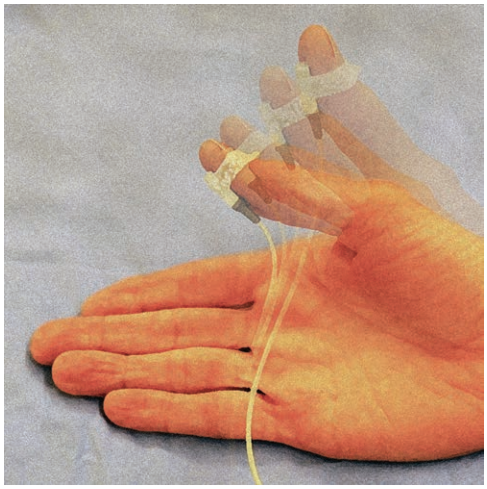
"It is not the strongest of the species that survives, nor the most intelligent, but the one most responsive to change."

— Charles R. Darwin (1809–1882)



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EDITORIALS are meant to place scientific findings in the appropriate clinical context, and this editorial is no exception. It is important to note several limitations of any new technology, particularly when it is meant to replace an older one. Acceleromyography, since its introduction into clinical use by Viby-Mogensen *et al.* in 1988,[1] has become the most widely used method of monitoring (measuring) neuromuscular function, and the initial TOF-Guard (Biometer, Denmark)[2] morphed into the TOF-Watch (Organon, Ireland) that, at the time of its production demise in 2016, had a total worldwide installed base of just more than 50,000 units (personal communication, Michael Rosenheimer, MIPM, Germany, May 20, 2016). Despite this miniscule uptake, the TOF-Watch had somehow succeeded in becoming the "standard" (read: "most-used") device for conducting clinical studies on neuromuscular blockade and its pharmacologic antagonism—a problematic state of affairs, given that the device is disappearing rapidly.

In this issue of the journal, Murphy *et al.*[3] present a seemingly straightforward study comparing assessment of neuromuscular function recovery with TOF-Watch SX (which requires calibration and normalization) and TOF-scan (idMed, France; a new device, which ostensibly does not require calibration or normalization). Given the documented struggles anesthesiologists have getting themselves to use any kind of quantitative monitoring system,[4,5] one wonders, "Why bother"? Murphy *et al.* themselves set the stage for this question:

> *"Several factors may account for this reluctance to use these monitors, which include the need for additional operating room time (attachment of sensors, initial signal stabilization), requirement for calibration and obtaining baseline measurements before muscle relaxant administration, and lack of accuracy and precision of first-generation quantitative monitors when an initial set-up is not performed"*[3]

Reading further into their article, one learns from the Methods section that at least 2 min (and more likely, about 5 min) of additional induction time were devoted to application and stabilization of the quantitative neuromuscular monitor. And, reading the description of the manipulations, it is also quite possible that two operators were involved at the start of each case, with one dedicated to the application of the monitor.

Workflow is paramount in fee-for-service procedural medicine. Quantitative neuromuscular monitors insert themselves into the critical path of the anesthesia induction workflow. They must be applied and activated (and calibrated) before neuromuscular blocking drug administration. The induction of general anesthesia (time from "wheels in" to "ready for surgery," including monitor application, preoxygenation, tracheal intubation) can have mean times as short as 10 to 13 min in American academic medical centers,[6] but this workflow does not include a break for quantitative neuromuscular monitor setup. Inserting 2 to 5 min into this workflow seems like a small feat, until one considers that the anesthesia team is delaying progress of the rest of the operating room team for these steps, and that this time really adds up over the course of a five- to seven-case operative day.

In contrast, current practice using qualitative monitors (peripheral nerve stimulators) typically involves a first assessment of neuromuscular blockade *after* intubation, after most other anesthesia tasks have been accomplished, and while the surgical team is at work on their own tasks.

Image: J. P. Rathmell.

Corresponding article on page 880.

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Neuromuscular assessment is outside the main workflow path. Off-line processing (work done outside—often in parallel with—the main workflow path) is inherently more efficient. Converting an efficient parallel process into an obligate linear process must have a clear benefit (such as pulse oximeter application) or be unavoidable (such as tracheal intubation prior to the start of surgery). Such a benefit is not obvious for the case of quantitative neuromuscular monitoring in most operating rooms.

Moreover, all stand-alone quantitative neuromuscular monitors available at the present time require unrestricted movement of the monitored digit. The exception is the electromyography-based E-NMT module (GE Healthcare, USA) that is integrated in the GE anesthesia workstation. The requirement for unencumbered movement of the monitored muscle (or digit) is a serious liability for two reasons. First, the extremities are commonly moved during surgical positioning, and this likely interferes with calibration. Second, access to the patient for surgery increasingly requires the arms to be tucked at the patient's side, restraining digit movement. Negotiating for unrestricted thumb movement puts the anesthesia team into competition for access to the patient in a way that might (potentially or actually) compromise the surgical conditions.

There are other limitations to most neuromuscular monitors. The "control" indirectly evoked train-of-four ratio measured at the adductor pollicis muscle by acceleromyography exceeds unity,[1,7] and in fact, can be as high as 147%.[8] This "reverse fade" can be a significant limitation of the acceleromyography technology; it can be explained by a failure of the monitored digit (the thumb) to return to its prestimulation baseline, although the exact mechanism has not been elucidated. In cases where the "baseline" train-of-four ratio was 147%, the return of the train-of-four ratio to a value of 0.90 (90%) will not ensure adequate recovery of neuromuscular function. To ensure minimum (safe) recovery, the train-of-four ratio would need to reach 90% of the 147% baseline, or a train-of-four of 132%. Investigators have sought to diminish the effects of reverse fade while minimizing train-of-four ratio variability associated with acceleromyography-based monitoring by adding pretension to the thumb *via* a hand adapter. This has improved, but not eliminated, the reverse fade.[9] To further address this limitation, if the second twitch of the train-of-four (T2) is greater than the first twitch (T1), some acceleromyography monitor manufacturers used algorithms to calculate the train-of-four ratio as T4/T2, rather than the accepted T4/T1 ratio.[10] Other manufacturers simply ignore any train-of-four ratio values greater than 100%, and report "baseline" ratios of 100% (while presenting the absolute amplitudes of the train-of-four responses graphically, but not numerically).[3]

Obfuscating measurements in order to "fit to normal physiology" may make some clinicians skeptical. It appears that recently introduced three-dimensional acceleromyography-based monitors, such as the TOFscan, further improve the accuracy and repeatability of measurements; however, the TOFscan also uses a T4/T2 rather than the accepted standard of T4/T1 algorithm to calculate the train-of-four ratio if T2 is greater than T1, and it will not display train-of-four ratio numbers greater than 100%. The astute clinician may therefore ask whether the comparison between the TOF-Watch SX (that does not limit train-of-four ratio to 100%) and TOFscan (that both limits the train-of-four ratio to 100% and uses T4/T2 ratio calculation if T2 is greater than T1) is a reasonable comparison. Previous work suggested poor agreement between the two devices at deep block levels, and better agreement during recovery.[11] From a scientific standpoint, the two monitors are not interchangeable: the mean baseline train-of-four ratios were significantly higher when measured with the TOF-Watch (110.0 ± 5%) than TOFscan (100.0 ± 1%); and, despite starting from a higher train-of-four baseline, the time to complete block (defined as train-of-four count of 0) was more than 1 min faster when measured with the TOF-Watch. Practically, however, the bias between the two monitors was minimal, the limits of agreement were narrow, and the train-of-four ratios at extubation were clinically similar. We are indebted to Murphy *et al.* for the clinically relevant comparison, and for showing that the TOFscan, as a TOF-Watch replacement, is a reasonable monitor of neuromuscular block that nevertheless retains the limitations inherent in acceleromyography. Future studies must confirm that clinical decisions based on TOFscan data result in optimal surgical conditions and a lower incidence of residual neuromuscular block and critical respiratory complications.

Two other points are worth mentioning in contextualizing of Murphy *et al.*'s article. First, the version of the TOF-Watch SX device used by Murphy *et al.* is considered the best available device for quantitative neuromuscular block monitoring, yet it is no longer commercially available! This fact alone suggests that quantitative neuromuscular monitoring is so thoroughly neglected as to negate the business case for device manufacturers. It also jeopardizes future research and development of neuromuscular monitors, to the extent that valid comparison measurements are required to assess future technologies.

Second, clinicians were blinded to the train-of-four data and judged recovery from neuromuscular block solely on clinical signs (without even a qualitative monitor). One wonders how the authors got their study past the local institutional review board unless the proposal is in equipoise with current institutional clinical practice. Nevertheless, the authors state that neostigmine/glycopyrrolate reversal was administered to patients "who potentially did not spontaneously recover to a train-of-four ratio greater than or equal to 0.9."[3] Again, one wonders how the clinicians made that determination guided solely by clinical signs, such as head lift or acceptable pulse oximetry readings. This is not meant to impugn the investigators' clinical practice, but, rather, to highlight that this is exactly the current state of practice,

not only extant in the United States, but is also the practice presented to institutional review boards, defended to institutional review boards by anesthesiologists, and accepted by institutional review boards as "reasonable."

In summary, we commend Murphy *et al.*[3] for doing the thankless work of cross validating a "new" monitor against an accepted standard. However, we are concerned that the most important question has not been answered: is the TOFscan a reasonable quantitative monitor that can be used in both research and clinical care? In other words, is the TOFscan likely to become the new "standard" monitor? This still unanswered question will require additional trials and comparisons; such future comparisons must validate the TOFscan (or any other monitor) against a technology (such as electromyography or mechanomyography) that has been shown to be free from the "reverse fade" that has plagued acceleromyography. To quote Kopman, "It is clear that one major limitation of [acceleromyography-derived] values has not been solved."[10] The TOFscan's other claimed advantage is that it does not require calibration before first measurement. However, support for such claims is still missing; it remains to be proven whether the TOFscan can be applied to anesthetized patients after the neuromuscular blocking agent was administered, and whether the data obtained can be used for making clinical decisions. In the current study, Murphy *et al.* applied both devices before induction of anesthesia, and neuromonitoring with both devices was started before a neuromuscular blocking agent was administered. Given that most anesthesiologists seem to think it's okay to essentially not monitor neuromuscular function at all, it is unrealistic to think they will compete with the other operating room personnel over patient access or add substantial time to the induction phase of anesthesia in order to apply a neuromuscular monitor (and calibrate it). Three things are still categorically needed to advance neuromuscular monitoring: (1) a monitor that requires fewer than 1 to 2 min for application and that does not require free motion of a digit to work (such as electromyography); (2) a study demonstrating that such a monitor is free from reverse fade (*i.e.*, one that calculates T4/T1 ratios) and effectively detects recovery from neuromuscular block with no required baseline measurement when applied mid-case (*e.g.*, after the procedure has begun); and (3) most important, we need our specialty organization, the American Society of Anesthesiologists, to finally acknowledge what other specialty organizations already have recognized: without advocacy, education and guidelines, physician anesthesiologists will continue to ignore what we know is an important patient safety issue.

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