Pro-Con Debate: Do We Need Quantitative Neuromuscular Monitoring in the Era of Sugammadex?

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In this Pro-Con article, we debate the merits of using quantitative neuromuscular blockade monitoring. Consensus guidelines recommend their use to guide the administration of nondepolarizing neuromuscular blockade and reversal agents. A major impediment to this guideline is that until recently, reliable quantitative neuromuscular blockade monitors have not been widely available. Without them, anesthesia providers have been trained with and are adept at using a variety of qualitative neuromuscular blockade monitors otherwise known as peripheral nerve stimulators. Although perhaps less accurate, anesthesia providers find them reliable and easy to use. They have a long track record of using them with the perception that their use leads to effective neuromuscular blockade reversal and minimizes clinically significant adverse events from residual neuromuscular blockade. In the recent past, 2 disruptive developments have called upon anesthesia care providers to reconsider their practice in neuromuscular blockade administration, reversal, and monitoring. These include: (1) commercialization of more reliable quantitative neuromuscular monitors and (2) widespread use of sugammadex, a versatile reversal agent of neuromuscular blockade. Sugammadex appears to be so effective at rapidly and effectively reversing even the deepest of neuromuscular blockades, and it has left anesthesia providers wondering whether quantitative monitoring is indeed necessary or whether conventional, familiar, and less expensive qualitative monitoring will suffice? This Pro-Con debate will contrast anesthesia provider perceptions with evidence surrounding the use of quantitative neuromuscular blockade monitors to explore whether quantitative neuromuscular monitoring (NMM) is just another technology solution looking for a problem or a significant advance in NMM that will improve patient safety and outcomes. (Anesth Analg 2022;135:39–48)

GLOSSARY

AMG = acceleromyography; **EMG** = electromyography; **FVC** = forced vital capacity; **NMB** = neuromuscular blockade; **NMM** = neuromuscular monitor; **PNS** = peripheral nerve stimulator; **POPULAR** = postanaesthesia pulmonary complications after use of muscle relaxants; **PTC** = posttetanic count; **PTC** = posttetanic count; **TOF** = train-of-four; **TOFc** = train-of-four count; **TOFr** = train-of-four ratio

This Pro-Con article discusses whether quantitative neuromuscular monitoring (NMM) to guide administration and reversal of nondepolarizing neuromuscular blockade (NMB) should be used for every administration of rocuronium or vecuronium. Table 1 summarizes key arguments for and against their use. Issues surrounding NMB have come into sharp focus with the release of more effective quantitative NMMs, recent consensus statements[1] (Table 2) endorsing their use, and widespread use of a rapid and reliable reversal with sugammadex. Clinicians are left wondering why to use quantitative

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Table 1. Summary of Pro-Con Arguments for the Use of Quantitative Neuromuscular Monitors

Con	Pro
Using a peripheral nerve stimulator, a TOF count of 4/4 with sustained 5-s tetanus at eye or wrist muscles provides an adequate assessment of NMB reversal	Eye muscles do not have the same recovery profile compared to the adductor pollicis at the wrist. Eye muscles recover faster leading to assessments of adequate reversal when residual NMB persists All decisions regarding the adequacy of NMB reversal should be done at the wrist TOF count, by itself, is not an adequate measure of NMB reversal. A TOF ratio is required No patient should be extubated without first verifying that the TOF ratio is >0.9 at the adductor pollicis
Sustained head lift, strong hand grasp, following commands, and sustained tetanus using a peripheral nerve stimulator are adequate for assessing whether a patient is suitable for tracheal extubation	Clinical signs such as head lift, firm handshake, or sufficient minute ventilation of an intubated patient are misinterpreted as adequate recovery from NMB Neither qualitative NMM nor clinical tests should be used to detect residual NMB
Quantitative NMM is not needed when sugammadex is available	Sugammadex does not guarantee complete NMB recovery. Without quantitative NMM, uncertainty remains Reversal drugs should be given only if necessary. Using quantitative NMM can exclude residual NMB and can avoid unnecessary administration of reversal agent Reoccurrence of NMB may occur in vulnerable patients (eg, the elderly and obese) or after reversal of deep NMB with too low doses. Only validly applied quantitative NMM is able to detect reoccurrence in time
The incidence of clinically meaningful residual neuromuscular blockade leading to a postoperative adverse pulmonary event is very low	Although low, there is an association between residual NMB and the risk of postoperative pulmonary complications, coma, and mortality
Quantitative NMM is expensive. The devices are more expensive. There is a recurring cost for an electrode-sensor array with each use.	Residual NMB increases the incidence of critical respiratory events in the postanesthesia care unit Quantitative TOF fade by NMM is the only suitable method to identify low but clinically meaningful residual NMB
Less-expensive qualitative NMM peripheral nerve stimulators are adequate for detecting residual NMB	Even rare adverse pulmonary complications are more expensive
The use of quantitative NMM disrupt workflow. They require placement of the electrode-sensor array at the wrist, connection to a cable, and visualization of an additional monitor	The installation of the quantitative NMM is a one-time measure before anesthesia induction and, therefore, not disruptive at all. Calibration of the NMM before administration of the NMB agents is automated. These 20 s can be used to optimize conditions for laryngoscopy. In contrast to the tactile NMM, no additional measure needs to be taken in the further course until extubation
Quantitative NMMs can be difficult to interpret or fail during surgical procedures Patients may start breathing over the ventilator at deeper than expected levels of NMB	As with any monitoring device, the quantitative NMM requires user training. The quantitative NMM is not responsible for the different sensitivity of the musculature to NMB agents, but it helps to understand this phenomenon
Quantitative NMM requires unimpeded thumb movement making their use difficult when the arms are tucked	EMG quantitative NMMs do not require unimpeded thumb movement and can be used with the arms tucked (see Table 4)

Abbreviations: EMG, electromyography; NMB, neuromuscular blockade; NMM, neuromuscular monitoring; TOF, train-of-four.

Table 2. Recommendations for Use of Quantitative Neuromuscular Monitors

Anytime a neuromuscular blocking agent is administered, neuromuscular monitoring should be used to guide administration and ensure adequate reversal of neuromuscular blockade
Quantitative neuromuscular monitoring should always be used. If unavailable, departments must define a transition phase within which a peripheral nerve stimulator may be accepted yet
Adequate reversal of neuromuscular blockade is defined as a train-of-four ratio >0.9 measured at the adductor pollicis. Measurements at the face are inaccurate and should not be used to confirm adequate reversal of neuromuscular blockade
Peripheral nerve stimulators cannot confirm a train-of-four ratio >0.9
Clinical signs such has head lift for 5 s, sustained hand grasp, spontaneous ventilation, and response to peripheral nerve stimulator tetanus stimuli are unreliable and should not be used to confirm adequate reversal of neuromuscular blockade in unconscious patients
Standardized definitions of profound, deep, moderate, shallow, and minimal neuromuscular blockades should be used based on quantitative neuromuscular monitoring (see Table 3)
Professional organizations should develop and promote neuromuscular monitoring standards and guidelines
Professional organizations should develop and promote practice standards and guidelines detailing how best to manage perioperative administration of neuromuscular blocking agents

Adapted from Naguib et al.[1]

NMM when reversal with sugammadex can be effectively achieved in most patients with use of a peripheral nerve stimulator (PNS) and in some instances without any NMM?

This article will develop two opposing themes: First is the con argument: Experienced clinicians maintain that with sugammadex, reversal of NMB is fast and effective. If patients exhibit adequate strength, the consequences of imperceptible residual blockade are of little clinical consequence during the recovery period. Furthermore, if they do occur, they are likely to be of short duration as the residual blockade effect dissipates in the minutes to hours after surgery. Clinical experience indicates that a transition from qualitative assessments using a PNS to a quantitative NMM is of limited value. Second is the pro argument: Anesthesia providers are unaware of whether their patients have a residual NMB. This is largely because the clinical implications of a residual NMB are beyond the horizon of an anesthesia provider's scope of care. As such, adverse pulmonary events related to residual NMB can be erroneously attributed to other sources and thereby ignored. Consensus guidelines compiled by experts in NMM recommend their use even in the era of sugammadex. More reliable quantitative NMM are becoming widely available and should replace qualitative ones.

This Pro-Con debate will contrast anesthesia provider perceptions with evidence surrounding the use of quantitative NMB monitors in the context of: (1) what is considered effective NMB monitoring and (2) what is known of the contribution of residual NMB to postoperative adverse events. The aim of this article is to inform anesthesia providers as they consider whether quantitative NMM is just another technology solution looking for a problem or a significant advance in NMM that will improve patient safety and outcomes.

PROLOGUE

To provide a framework for this Pro-Con debate, a description of the differences between qualitative and quantitative NMMs and the occurrence of residual NMB is briefly reviewed.

NMM is traditionally assessed with 2 types of stimulation patterns. First is four single twitch stimuli at a frequency of 2 Hz known as the train-of-four (TOF). The TOF response is characterized by a count (TOFc) and a ratio (TOFr). The TOFr is defined as the ratio of the fourth to first response (T4/T1) and is used to quantify fade in the TOF response. Second is a posttetanic count (PTC). This consists of a tetanic stimulus at 50 Hz for 5 seconds followed 3 seconds later by a series of 20 single twitches at a frequency of 1 Hz. Responses to both patterns are used to characterize NMB depth using standardized nomenclature (Table 3).[2]

The most important difference between the qualitative and quantitative monitors occurs when TOFc = 4. A quantitative monitor can distinguish among shallow NMB (TOFr < 0.4), minimal NMB (TOFr between 0.4 and 0.9), and full recovery (TOFr > 0.9). By contrast, a qualitative NMM requires visual or tactile assessment of responses to stimulation. Experienced clinicians using PNS can detect fade with a TOFr ≤ 0.4[3] but not with a TOFr between 0.4 and 0.9. Qualitative assessment of NMB cannot distinguish minimal blockade from full recovery (Table 3).

The incidence of residual NMB has been well studied and remains an important clinical problem. In most published work, a common definition of residual NMB is a TOFr <0.9 upon arrival in the postanesthesia care unit. In a recent systematic review of 58 observational studies including >25,000 patients, Raval et al[4] describe an overall incidence of residual NMB ranging from 0% to 90%, 0% to 16% when reversed with sugammadex, 3% to 90% when reversed with neostigmine, and 15% to 89% in patients allowed to spontaneously recover from their NMB. The incidence rates vary substantially and are likely influenced by whether NMM was used; if used, the type of monitoring used (qualitative, quantitative, or physical findings such as head lift); and the level of NMB at the time of reversal. Raval et al[4] point out that approximately half of the observational studies reported using qualitative monitors.

CON: QUANTITATIVE NEUROMUSCULAR MONITORING IN THE ERA OF SUGAMMADEX: NOT NEEDED

Experienced anesthesia care providers have effectively used PNSs in combination with clinical signs of adequate NMB reversal for years with little need for more sophisticated NMM. A TOFc of 4/4 with sustained 5-second tetanus at the eye (orbicularis oris and corrugator supercilii) or wrist (adductor pollicis, first dorsal interosseous, or abductor digiti minimi) along with clinical signs of following commands, sustained

Table 3. Qualitative and Quantitative Observations With TOF Stimulation of Peripheral Nerves to Assess the Level of Neuromuscular Blockade

	Qualitative (subjective) NMB monitoring		Quantitative (objective) NMB monitoring		
Block depth	TOF count	PTC	TOF count	TOF ratio	PTC
Profound	0	0	0	-	0
Deep	0	≥1	0	-	≥1
Moderate	1–3	-	1–3	-	-
Shallow	4, fade detectable	-	4	0.1–0.4	-
Minimal	4, fade not detectable	-	4	0.4–0.9	-
Acceptable recovery	Cannot be distinguished from minimal blockade	-	4	>0.9	-

Adapted from Naguib et al.[2]
Abbreviations: NMB, neuromuscular blockade; PTC, posttetanic count; TOF, train-of-four.

head lift, and strong hand grasp is time-tested tools for assessing whether a patient is suitable for tracheal extubation.

An observation that, in part, corroborates this perception is that experienced anesthesia providers chose not to use quantitative NMM, even if readily available. Naguib et al[5] published a survey of self-reported use of quantitative NMM in Europe and in the United States. If both quantitative and qualitative NMMs were available, 19% of US respondents reported they would use quantitative NMM, whereas 63% indicated they would use a PNS. By contrast, 53% of European respondents reported that they would use quantitative NMM, whereas 17% would use a PNS. Although there are regional differences in enthusiasm for NMM, there are no reports demonstrating regional differences in adverse postoperative pulmonary events attributed to qualitative versus quantitative NMM.

As these survey results are more than a decade old, it is likely that the availability of quantitative NMMs has increased, but it remains unclear whether they are widely used among experienced anesthesia care providers. Additional work is warranted to establish their current day availability and use in the context of adverse pulmonary complications. Until more compelling evidence is available, it is reasonable to continue to use PNSs to guide administration and reversal of NMB.

There are several reasons for this position. First, residual NMB is a rare event. If patients exhibit adequate strength, the consequences of imperceptible residual blockade are of little clinical consequence during the recovery period, and the incidence of an adverse pulmonary complication is low. Furthermore, if they do occur, they are likely to be of short duration as the residual blockade effect dissipates in the minutes to hours after surgery. Clinical experience suggests that a transition from qualitative assessments using a PNS to a quantitative NMM would be of limited value in addressing this rare event.

Second, quantitative NMM is not needed in the era of sugammadex. With sugammadex, reversal of NMB is fast and effective and can be judicially used at any depth of NMB when using rocuronium or vecuronium. Recent work suggests that these 2 agents are the primary muscle relaxants of choice among US anesthesia providers. For example, Jiang et al[6] conducted a set of cost analysis simulations that explored the budgetary and clinical impact of introducing sugammadex as a routine reversal agent for a hypothetical patient cohort in the United States. Based on prior published work, they estimate that NMB is used in 19% of surgical procedures. Of those, 80% were either rocuronium or vecuronium. In addition, data from a large retrospective analysis comparing reversal of NMB with neostigmine and sugammadex found a 30% decrease in the incidence of adverse pulmonary events when using sugammadex.[7] In summary, anesthesia providers use rocuronium or vecuronium most of the time. These drugs are easily and effectively reversed with sugammadex obviating the need for quantitative NMM.

Although effective, a remaining concern with sugammadex is recurarization after administration, especially with reversal of deep NMB. A systematic review and meta-analysis of randomized controlled trials of residual NMB for various approached to reversal of NMB suggest the incidence is low.[8] In this report, Raval et al[8] described the incidence of residual NMB as much lower in patients reversed with sugammadex compared to neostigmine or spontaneous recovery confirming that recurarization after sugammadex is a rare event. If sugammadex dosing is properly guided by a PNS in healthy patients with normal renal function, reversal is fast, reliable, and predictable. Outcomes are superb with few rare side effects.

Third, quantitative NMM is expensive, disruptive to workflow, and, at times, unreliable. It is expensive in 2 ways: (1) the devices are more expensive than PNSs and (2) for several of the available quantitative NMM, there is a recurring cost for an electrode-sensor array with each use. With rising health care costs, using more sophisticated technology, when more inexpensive and nearly as effective technology is readily available, is not wise.

In terms of workflow disruption, they require placement of the electrode-sensor array at the wrist, connection to a cable, and use of an additional monitor in a crowded workspace. This is all to be done while preparing a patient for induction of anesthesia. This can distract anesthesia providers from more important considerations such as maintaining hemodynamic stability and safe airway management.

In terms of reliability, quantitative NMMs can fail during surgical procedures. For example, cord connections to sensor arrays may come undone when the arms are tucked making it difficult to reconnect them. Selected quantitative NMMs require unimpeded thumb movement to properly assess the level of NMB making their use difficult when the arms are tucked.

Quantitative NMMs can present conflicting information. For example, they may report a TOFc of 0 in the presence of diaphragm movement prompting the administration of additional NMB. This is less of problem when monitoring patients with a PNS at the eye muscles. It is not clear how more expensive, less reliable, more distracting quantitative NMMs will improve patient outcomes when the safety profile of conventional qualitative NMM techniques is more than adequate.

Conclusions

As with other new technologies introduced into the perioperative workspace, it is premature to claim quantitative is a significant improvement over qualitative NMM. To establish the superiority of quantitative monitoring, it is reasonable to first benchmark the performance of properly used qualitative NMM. Given the wide variability in the incidence of residual NMB and associated postoperative pulmonary complications, it is likely that many patients that develop adverse postoperative pulmonary complications were either not monitored at all or not properly monitored, or NMM data were improperly interpreted or ignored. If properly used, qualitative NMM meets the clinical demands associated with NMB use. Without a benchmark describing the outcomes from proper qualitative NMM, the unique clinical advantages of quantitative NMM remain elusive.

PRO: QUANTITATIVE NEUROMUSCULAR MONITORING IN THE ERA OF SUGAMMADEX: SENSE OR NONSENSE?–SENSE

Incomplete recovery from NMB at the time of extubation is a risk that is still widely ignored by many anesthesiologists. Clinical studies clearly showed that residual NMB at the end of anesthesia increases the incidence of critical respiratory events in the post-anesthesia care unit.[9–11] Despite this overwhelming evidence of the benefits of quantitative NMM, many anesthesia providers still rely on visual or tactile assessment of twitch responses to evaluate recovery of neuromuscular function or, even worse, evaluate neuromuscular function in anesthetized or recently extubated and uncooperative patients using clinical tests. In this pro section, we will present a clear chain of reasoning that such techniques are, without any doubt and without exceptions, poor clinical practice.

The basic principle for preventing residual NMB is quantitative NMM. Quantitative assessment of the TOF fade by NMM is the only suitable method to identify low but clinically meaningful degrees of residual NMB.[11] The threshold for acceptable recovery was first set at a TOFr >0.7 based on a study in healthy volunteers with normal vital capacity and normal inspiratory force.[12] Two decades later, the level of acceptable recovery had to be increased to 0.9 based on several observations demonstrating subjective weakness,[13] decreased hypoxic ventilatory response,[14] impaired protective airway reflexes,[15] and upper airway obstruction[16] at the values of TOFr between 0.7 and 0.9. More recently, it was suggested that a TOFr of 0.95[17] or even unity might be even better, especially if neuromuscular function is monitored by acceleromyography (AMG). The higher the recommended threshold of the TOFr for indicating sufficient recovery of neuromuscular function to allow safe extubation, the more challenging the method to validly determine such values.

Clinical signs such as the ability to lift the head, a firm handshake, or a sufficient minute ventilation of an intubated patient are often erroneously misinterpreted as adequate recovery from NMB. Normal tidal volume can be generated despite a TOFr <0.1, and even normal vital capacity can be achieved despite a TOFr of 0.6.[12,18] Some patients are able to lift their heads for 5 seconds at a TOFr of 0.3.[19] Figure 1 is the

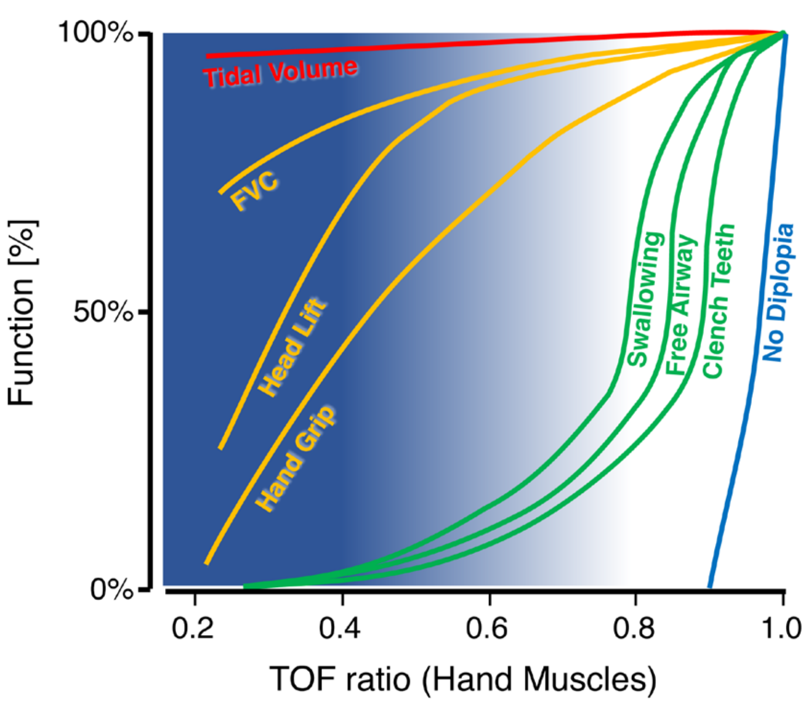

Figure 1. Average muscle-dependent functions in relation to the TOF ratio as measured at hand muscles (adapted from Donati[20]): the *x*-axis shows the TOF ratio measured at the adductor pollicis or at the hypothenar muscles. The *y*-axis shows the average function either as a percentage of the baseline value or as a percentage of patients who passed the respective test. The blue background shows the range of TOF ratios in which anesthesiologists can palpate TOF fading. From a TOF ratio >0.4, the validity of the palpation decreases, which is illustrated by the decreasing intensity of the blue background. At TOF ratios where fading can no longer be palpated, swallowing, keeping the upper airway open, and clenching the teeth may still be impaired. Data are from Eikermann et al,[16,21] Ali et al,[12] Eriksson et al,[15] Heier et al,[22] Brull and Murphy,[3] and Unterbuchner et al.[19] FVC indicates forced vital capacity; TOF, train-of-four.

updated figure by Donati,[20] in which he combined data from Eikermann et al,[16,21] Ali et al,[12] Eriksson et al,[15] Heier et al,[22] and Brull and Murphy,[3] with additional information from Unterbuchner et al.[19]

Based on the recovery profile of the displayed muscle functions in Figure 1, it is clear that clinical signs cannot be used to prove complete neuromuscular recovery. These tests are insensitive to residual NMB (tidal volume) or are not applicable to the anesthetized patient due to lack of cooperation (forced vital capacity, head raising, and handgrip) or obstruction by the recumbent endotracheal tube (swallowing, keeping the upper airway open, and clenching teeth).

Figure 1 also illustrates why qualitative NMM is also not appropriate for confirming sufficient recovery in anesthetized patients. Qualitative NMM is subjective and user-dependent because it does not enable even experienced anesthesiologists to reliably detect residual NMB of TOFr values >0.4.[23] At TOFr values of 0.6, it is completely impossible to detect a TOF fade with the sense of touch.[23] Accordingly, qualitative NMM is incapable of estimating the function of the hypopharyngeal muscles responsible for swallowing and keeping the upper airway open. Therefore, to compensate for uncertainty about the extent of neuromuscular recovery when using qualitative NMM, most protocols routinely recommend reversal agents despite lack of TOF fade. On the one hand, this practice inherently includes the administration of reversal agents, although they would not have been necessary because of a complete recovery. On the other hand, even sophisticated protocols based on qualitative NMM, restrictive use of NMB agents, and routine use of reversal agents cannot prevent any residual blockade.[24] In summary, neither qualitative NMM nor clinical tests used to detect residual NMB should, therefore, be considered an option in a patient-safety–focused anesthesia.

Finally, the clinical advantages of quantitative over qualitative NMM were proven by Murphy et al[25] comparing the effectiveness of properly applied qualitative NMM versus quantitative NMM in a prospective randomized trial. Evidence of incomplete neuromuscular recovery in the postanesthesia care unit was frequently observed in patients monitored intraoperatively with qualitative NMM. In contrast, TOFr values ≤0.9 were rarely observed in patients randomized to quantitative NMM. This was a safety-relevant finding because the risk of hypoxemic episodes and airway obstruction during the early recovery phase from anesthesia was significantly reduced using quantitative NMM.[25]

There are 2 options to reach a sufficient TOFr >0.9: waiting for spontaneous recovery or pharmacological reversal. Waiting until the patients' neuromuscular function has recovered spontaneously is a safe but seldom used option, since it might take hours to achieve adequate recovery of neuromuscular function. Alternatively, reversal can be induced by either acetylcholinesterase inhibitors or sugammadex. Acetylcholinesterase inhibitors are only effective to reverse shallow or minimal residual blocks[26–29]; however, the onset is slow, and it can take several hours before adequate neuromuscular function is present.

Sugammadex, a modified cyclodextrin, encapsulates aminosteroidal neuromuscular blocking agents in a 1:1 relation. The dose recommendations are based on reappearance of a PTC of 1 or a TOFc of 2; both findings do not necessarily require quantitative devices to be obtained. Accordingly, proponents might argue that dosing of sugammadex is possible with the use of qualitative devices, even more, because sugammadex has proven to reverse NMB fast and reliably.[30–32] In particular, the reliability of the sugammadex effect has raised discussions about the benefits of NMM and led to the misinterpretation that verification of treatment success is no longer necessary. However, solid evidence has proven this conclusion to be wrong.

First, every drug should only be given only if necessary. Using quantitative NMM, residual NMB can be excluded, and unnecessary treatment with any reversal agent can be avoided.

Second, for NMB agents other than rocuronium, vecuronium, or pipecuronium, spontaneous recovery or treatment with acetylcholinesterase inhibitors is the only alternative. Limitations of both options have been emphasized earlier in this article. In addition, both strategies are definitively less predictable than reversal of rocuronium with sugammadex. Because of its ceiling effect, reversal with neostigmine is recommended not before a TOFc of 4. Nevertheless, neuromuscular recovery is frequently slow and finally unpredictable, even when neostigmine is titrated up to the maximum dose of 70 µg/kg, and results in a time span of 5 to 150 minutes until complete recovery.[33,34]

Third, even when sugammadex given without treatment control, that is, quantitative NMM, does not guarantee complete recovery. Without verification of complete recovery following administration of sugammadex based on quantitative NMM, a degree of uncertainty remains, which cannot be solved with its routine or liberal administration.[35]

Fourth, the availability of the fast-acting reversal agent sugammadex allows for extending deep and moderate levels of NMB close to the end of surgery without an increased risk of residual NMB, an option that is not feasible using the former standard reversal with acetylcholinesterase inhibitors.[30,32] Consequently, a more liberal use of NMB agents and their reversal agents became common practice.[36–38] When reversal agents in inappropriately low doses are given at deeper levels of block, the phenomenon of reoccurrence of NMB reemerged,[39,40] a problem formerly known as "recurarization."[41] However, even after recommended doses of neostigmine and sugammadex in the absence of quantitative monitoring, reoccurrence of NMB was recently observed particularly in elderly[42] and in obese patients.[43,44]

Fifth, quantitative NMM must be performed at the wrist to avoid misinterpretation of the depth of NMB. It is true that each muscle group has different sensitivity to NMB agents and that, in particular, response of some eye muscle to TOF stimulation may wrongly indicate adequate neuromuscular recovery.[24] However, the solution is not to abandon quantitative NMM and instead continue to use qualitative NMM along with high doses of sugammadex, but to train anesthesiologists to correctly apply and interpret the results of quantitative NMM.

Conclusions

Residual NMB poses an unnecessary threat to patients that can only be prevented with a combination of reversal agents and quantitative NMM. Only quantitative NMM can guarantee a valid measurement of the recommended TOFr >0.9 before extubation irrespective of the NMB agent and/or the reversal agent used. Only quantitative NMM detects residual NMB, especially those with TOFr between 0.4 and 0.9. Additionally, quantitative NMM allows dose optimization of the reversal agents according to the actual depth of NMB.[28,29,45] Quantitative NMM embedded in a clinical algorithm (Figure 2) enables the anesthesiologist to adapt reversal drugs to the respective residual block, for neostigmine, as well as for sugammadex.[46] Furthermore, quantitative NMM indicates when neostigmine is not likely to provide neuromuscular recovery within a considerable timeframe.

EPILOGUE

This Pro-Con debate has been smoldering for decades. Although evidence clearly established improved outcomes with quantitative NMM, enthusiasm for adopting it into routine clinical practice remains underwhelming. The debate has been refreshed by the arrival of sugammadex and by newer more accurate electromyography (EMG)-based quantitative NMMs. That sugammadex allows a means of reliable reversal from any depth of NMB has perhaps pushed the debate for some in favor of conventional NMM with PNS. Furthermore, although the latest generation of quantitative EMG-based NMMs is reliable and convenient, they have been available for <2 years and, in many institutions, do not meet priority for purchase.

New medical technologies require on average 10 to 15 years for widespread adoption once practice guidelines are established.[47] Many new medical devices do not have the staying power to last that long. As described by the Rogers Innovation Adoption Curve, new technologies are quickly embraced by innovators and early adopters. The clinicians are motivated by new ideas, are willing to try new technology, and require minimal evidence before using it. They represent

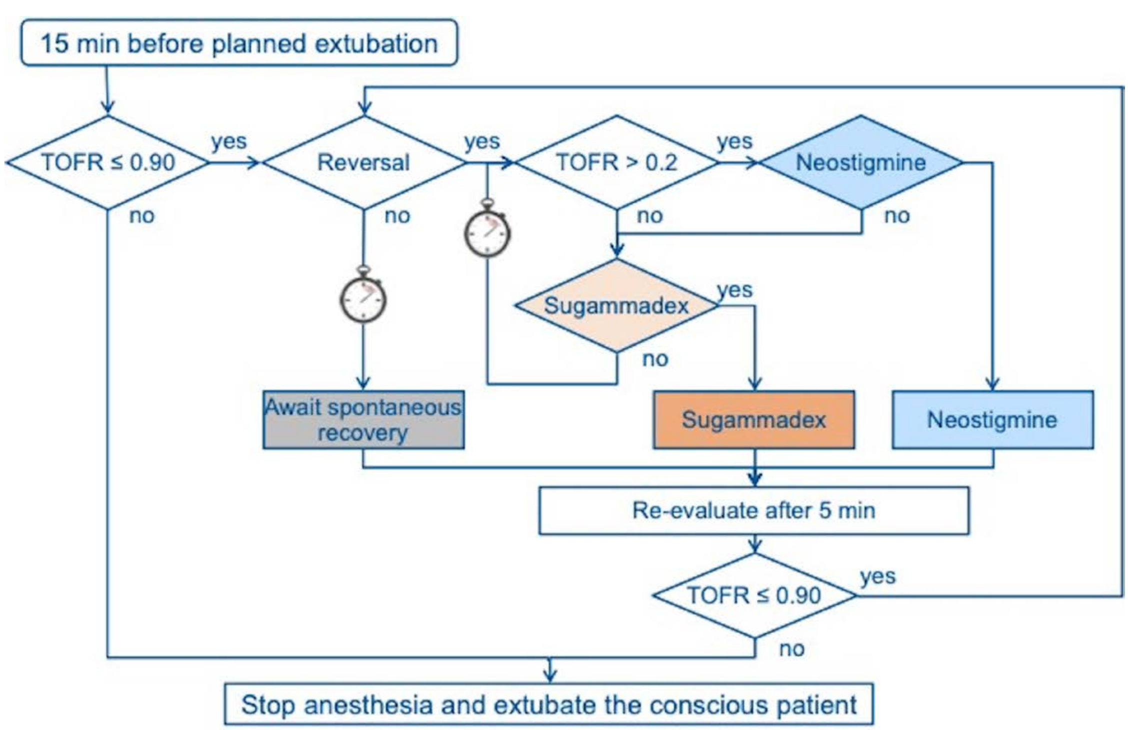

Figure 2. Clinical pathway based on quantitative neuromuscular monitoring to avoid residual neuromuscular blockade (adapted from Ripke et al.[46]). A TOFr is measured once the train-of-four count reaches 4 out of 4. TOFr indicates train-of-four ratio.

only 16% of clinician users. The early majority (34%), however, require more evidence. Late majority (34%) and laggards (16%) not only require more evidence but personal experience that confirms new devices (eg, EMG-based quantitative NMM) meet expectations. A marker of successful adoption is crossing the "chasm" from early adopters to early majority. Once across, new technologies enjoy more widespread adoption.

Newer EMG-based quantitative NMM may be on the cusp of crossing the chasm. To get across the chasm, more evidence and clinical and economic validation may be warranted to build anesthesia care providers confidence to the point where they will share their clinical experiences and insights with others. To that end, we recommend filling knowledge gaps with sufficiently powered randomized clinical trials to develop a rationale strong enough to refute the clinician' perception that a PNS is sufficient in the era of sugammadex. They include the following.

Gap 1: Evidence That a Train-of-Four Ratio >0.9 Reflects Adequate Recovery

Recommendation of restoring TOFr to >0.90 as a marker of NMB reversal is based on 2 small sample size studies in awake healthy volunteers.[13,15] Doubts about whether this threshold of the TOFr indicates sufficient neuromuscular recovery were raised not only by functional studies in volunteers[21] but also by the results of observational outcome studies.[17] Importantly, effects of residual NMB may persist even after recovery to a TOFr of 1 due to the occupation of up to 80% of receptors (iceberg phenomenon).[48]

Gap 2: Evidence That Quantitative NMM Optimizes Sugammadex Dosage

Sugammadex provides effective reversal of any rocuronium-induced NMB. However, the patent holder only provides approved dose recommendations for NMBs that can also be measured with qualitative NMM. Therefore, there are no dose recommendations for shallow and minimal NMBs, although dose finding studies are available.[28,29,45] Postanaesthesia pulmonary complications after use of muscle relaxants (POPULAR) data suggest that European anesthesia providers who are using quantitative NMM optimize sugammadex doses by titration of the drug along its reversal effect,[17,49] a finding that is supported by data of Iwasaki et al.[50]

Gap 3: Anesthesia Care Provider Knowledge Deficits Will Impair Adapting to and Proper Use of Quantitative NMM

Anesthesia care providers continue to believe they can safely manage NMB using time-tested clinical heuristics because that has been how they were taught and there has been no compelling reason to change.[51] Selected education priorities aimed at improving clinician awareness of NMB pharmacology and principles in NMM are needed to properly implement quantitative NMM. These include an understanding of the levels of NMB depth, the implications of monitoring eye muscles versus the wrist, the importance of achieving a TOFr >0.9 before tracheal extubation, and the advantages and disadvantages of available modalities in quantitative NMM (Table 4). In addition to further training of anesthesia providers, binding

Table 4. Quantitative Neuromuscular Blockade Monitor Modalities

Modality	Acronym	Description	Technology	Advantages	Disadvantages
Acceleromyography	AMG	Measures thumb acceleration in response to ulnar nerve stimulation	Accelerometer	Provides continuous assessment of NMB	Requires unencumbered thumb movement Requires calibration Significant overshoot of the baseline TOF ratio (reverse fade)
Mechanomyography	MMG	Measures force thumb movement in response to ulnar nerve stimulation	Force transducer		Requires unencumbered thumb movement Requires a constant preload Sensitive to repetitive stimulation and temperature
Kinemyography	KMG	Measures thumb movement with a mechanosensor placed between the base of the thumb and base of the index finger in response to ulnar nerve stimulation	Piezoelectric polymer strip	Simple to apply Reliable	Requires unencumbered thumb movement The mechanosensor strip may dislodge with repeated stimulation The use of tape to hold sensor strip in place may alter accuracy
Electromyography	EMG	Measures electrical activity at neuromuscular junction of the adductor pollicis muscle in response to ulnar nerve stimulation	EMG recording electrodes	Does not require unencumbered thumb movement Stable over time Stable over wide range of temperatures	

Adapted from Naguib et al.[2]
Abbreviations: NMB, neuromuscular blockade; TOF, train-of-four.

recommendations on the use of quantitative monitoring need to be adopted by professional societies. They must include statements as suggested in Table 2.

In summary, we have explored arguments for and against the use of quantitative neuromuscular monitors. We conclude that even in the era of sugammadex, residual NMB remains a threat to patient safety, and quantitative NMM can effectively manage this threat. Selected gaps remain in our understanding of quantitative NMM, but sufficient evidence exists in support of using quantitative NMM. Perhaps the most significant gap is that of anesthesia care provider knowledge deficits regarding NMM. We call upon anesthesia department leadership and professional anesthesia societies to actively address this education gap and endorse quantitative NMM.

DISCLOSURES

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Name: Markus W. Hollmann, MD, PhD, DEAA.
Contribution: This author helped review the literature, prepare the manuscript, coauthor the manuscript, and review and approve the final manuscript.
Conflicts of Interest: M. W. Hollmann is Executive Section Editor "Pharmacology" with *Anesthesia & Analgesia* and serves as Section Editor "Anesthesiology" for the *Journal of Clinical Medicine* and as Editor for Frontiers in Physiology. In addition, he has received consultancy fees from IDD and Eurocept BV and speakers' fees from CSL Behring.
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