

2023 American Society of Anesthesiologists Practice Guidelines for Monitoring and Antagonism of Neuromuscular Blockade: A Report by the American Society of Anesthesiologists Task Force on Neuromuscular Blockade

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ABSTRACT

These practice guidelines provide evidence-based recommendations on the management of neuromuscular monitoring and antagonism of neuromuscular blocking agents during and after general anesthesia. The guidance focuses primarily on the type and site of monitoring and the process of antagonizing neuromuscular blockade to reduce residual neuromuscular blockade.

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HIGHLIGHTS BOX

- This practice guideline provides evidence-based recommendations on the management of neuromuscular monitoring and antagonism of neuromuscular blocking agents. The objective is to guide practice that will enhance patient safety by reducing residual neuromuscular blockade. It is recommended to use quantitative neuromuscular monitoring at the adductor pollicis and to confirm a recovery of train-of-four ratio greater than or equal to 0.9 before extubation. Sugammadex is recommended from deep, moderate, and shallow levels of neuromuscular blockade that is induced by rocuronium or vecuronium. Neostigmine is a reasonable alternative from minimal blockade (train-of-four ratio in the range of 0.4 to less than 0.9). Patients with adequate spontaneous recovery to train-of-four ratio greater than or equal to 0.9 can be identified with quantitative monitoring, and these patients do not require pharmacological antagonism.

to revision as warranted by the evolution of medical knowledge, technology, and practice. They provide basic recommendations for anesthesia care that are supported by synthesis and analysis of the current literature, expert and practitioner opinion, public comment, and clinical feasibility data. Practice guidelines aim to improve patient care and patient outcomes by providing up-to-date information for patient care.

Purpose

This practice guideline provides evidence-based recommendations regarding the appropriate management of neuromuscular monitoring and antagonism of neuromuscular blocking drugs during and after general anesthesia. The guidance focuses primarily on the process of antagonizing neuromuscular blockade to reduce residual neuromuscular blockade (train-of-four ratio less than 0.9), addressing the appropriate type and site of monitoring and the use and dosing of different antagonist drugs depending on the depth

of the neuromuscular blockade. Suggestions for implementation of quantitative monitoring are included.

The appropriate use of neuromuscular blocking drugs in the context of difficult airway management is not addressed. Additionally, management of intraoperative neuromuscular blockade to optimize intubating conditions, surgical operating conditions, and patient outcomes is not addressed.

Background

Neuromuscular blocking drugs, both depolarizing (*e.g.*, succinylcholine) and nondepolarizing (*e.g.*, rocuronium, vecuronium, pancuronium, cisatracurium, atracurium), are

among the most commonly used medications in anesthesia. They are used to facilitate airway management, to improve surgical conditions, and, in some cases, to insure immobility during critical points in an operation. However, their use can be associated with sometimes-serious complications, most importantly when their paralytic effects have not disappeared or been adequately antagonized at the end of surgery. Inadequate recovery from the effects of neuromuscular blocking drugs is associated with adverse outcomes including upper airway obstruction, reintubation, atelectasis, pneumonia, prolonged stay in the postanesthesia care unit (PACU), and decreased patient satisfaction.^{1,2} While residual neuromuscular blockade is commonly unrecognized, there is convincing evidence that preventing its occurrence leads to improved patient outcomes.^{3,4}

Although peripheral nerve stimulators (which could deliver a single stimulus and sometimes a tetanic stimulus) were introduced in the 1950s, the modern era of neuromuscular blockade assessment began with the introduction of the train-of-four by Ali *et al.* in 1970.⁵ The train-of-four involves the delivery of four brief electrical pulses to a peripheral nerve at the rate of 2 Hz and assessing the “twitches” that result. With increasing paralysis, sequential twitches in the train decrease in amplitude with the progressive disappearance of the fourth, then the third, then the second, and finally the first twitch. The amplitude of the twitches can be measured quantitatively to permit the calculation of the *train-of-four ratio*: the amplitude of the fourth twitch divided by that of the first. A decreasing train-of-four ratio indicates greater degrees of paralysis.

Such quantitative measurements allowed an objective means of determining the presence of residual neuromuscular blockade after surgery. A seminal report by Viby-Mogensen *et al.*⁶ published in *ANESTHESIOLOGY* in 1979 reported a 42% incidence on arrival to the PACU in a cohort of 72 patients. These authors defined residual neuromuscular blockade as a train-of-four ratio of less than 0.7, based on earlier work showing that vital capacity and inspiratory force had recovered to near normal at this value. However, over the subsequent years, this definition has been revised upwards, as others showed that a measured train-of-four ratio of less than 0.9 was associated with clinical symptoms of weakness,^{7,8} impaired hypoxic ventilatory response,⁹ increased risk of upper airway obstruction,¹⁰ impaired airway protective reflexes,¹¹ increased risk of aspiration,¹¹ an experience of unpleasant symptoms of muscle weakness,¹² and a prolonged PACU stay.¹³ There is now a broad consensus that adequate recovery of neuromuscular function is defined as a train-of-four ratio greater than or equal to 0.9, typically measured at the adductor pollicis muscle after ulnar nerve stimulation. Since the work of Viby-Mogensen *et al.*,⁶ multiple published reports—using the current definition—have confirmed that residual neuromuscular blockade at the end of surgery and/or in the PACU remains a frequent occurrence after the use

Recommendations

Recommendation	Strength of Recommendation	Strength of Evidence
1. When neuromuscular blocking drugs are administered, we recommend against clinical assessment alone to avoid residual neuromuscular blockade, due to the insensitivity of the assessment.	Strong	Moderate
2. We recommend quantitative monitoring over qualitative assessment to avoid residual neuromuscular blockade.	Strong	Moderate
3. When using quantitative monitoring, we recommend confirming a train-of-four ratio greater than or equal to 0.9 before extubation.	Strong	Moderate
4. We recommend using the adductor pollicis muscle for neuromuscular monitoring.	Strong	Moderate
5. We recommend against using eye muscles for neuromuscular monitoring.	Strong	Moderate
6. We recommend sugammadex over neostigmine at deep, moderate, and shallow depths of neuromuscular blockade induced by rocuronium or vecuronium, to avoid residual neuromuscular blockade.*	Strong	Moderate
7. We suggest neostigmine as a reasonable alternative to sugammadex at minimal depth of neuromuscular blockade.	Conditional	Low
8. To avoid residual neuromuscular blockade when atracurium or cisatracurium are administered and qualitative assessment is used, we suggest antagonism with neostigmine at minimal neuromuscular blockade depth. In the absence of quantitative monitoring, at least 10 min should elapse from antagonism to extubation. When quantitative monitoring is utilized, extubation can be done as soon as a train-of-four ratio greater than or equal to 0.9 is confirmed before extubation.	Conditional	Very low

*Deep: posttetanic count greater than or equal to 1 and train-of-four count 0; moderate: train-of-four count 1 to 3; shallow: train-of-four count 4 and train-of-four ratio less than 0.4; minimal: train-of-four ratio 0.4 to less than 0.9.

of nondepolarizing neuromuscular blocking agents, with an incidence as high as 64% of patients.^{14,15}

Numerous factors contribute to this high incidence of residual neuromuscular blockade. Most importantly, there is the general lack of recognition of the extraordinary variability in the duration of action of neuromuscular blocking agents. This variability means that no specific amount of time (for example, “2h have elapsed after the last dose of a nondepolarizing neuromuscular blocking drug”) will guarantee adequate spontaneous recovery.^{16,17} Similarly, there is no period of time that will ensure that administration of any antagonist drug will result in complete recovery of neuromuscular function.¹⁶

A second factor is the continued use of “clinical” assessments of paralysis. Generations of anesthesiologists and other anesthesia providers have used sustained head lift or grip strength or respiratory measurements (e.g., tidal volume, inspiratory force) as markers of adequate recovery. Nevertheless, a substantial body of work has shown that these measures are insensitive to substantial degrees of paralysis. For example, Debaene *et al.*¹⁷ found that the sensitivity of a 5-s head lift to detect residual neuromuscular blockade was only 11% in patients with a train-of-four ratio less than 0.9 and 19% in patients with a train-of-four ratio less than 0.7. Kopman *et al.*⁷ found that healthy volunteers could sustain a head lift with a train-of-four ratio as low as 0.45.

Third, there is the widespread use of peripheral nerve stimulators to assess blockade with the mistaken belief that “four visibly equal twitches” to train-of-four stimulation or “sustained tetanus” indicate full recovery. Several studies have established that clinically significant weakness cannot be identified with subjective assessment of the response to a peripheral nerve stimulator.¹⁸ Using subjective assessment of the train-of-four, fade cannot be reliably appreciated until the train-of-four ratio is less than 0.4. Consequently, the lack of subjective fade in the train-of-four response represents the broad range of train-of-four ratios from 0.4 to 1.0.^{19,20}

While the quantitative assessment of blockade and the recognized value of the train-of-four ratio has existed for over 50 years, it has not gained widespread clinical use, largely because of the limitations of the measurement technology. Some monitors were complex to use, had poor user interfaces, or required startup/calibration times that are inconsistent with a busy clinical schedule. Some were limited in when they can be used (e.g., if the thumb cannot move, methods dependent on measuring the acceleration or strength of such movement are inaccurate). Fortunately, this situation is gradually changing with the recent introduction of substantially improved quantitative technology.

Finally, like the problems associated with relaxant variability, the relationship between the depth of blockade and pharmacologic antagonism is not well understood by many

clinicians. The appropriate use of an antagonist agent (both the drug chosen and the dose given) is dependent on an accurate assessment of the depth of neuromuscular blockade. The result is frequent “fixed dose and blind” antagonism regimens (e.g., 5mg of neostigmine or 200mg of sugammadex, given without previous block assessments), which may not result in full recovery, or antagonism may take far longer than expected. While the introduction of sugammadex has clearly reduced the incidence of residual neuromuscular blockade compared with neostigmine,²¹ the problem has not been eliminated, and residual neuromuscular blockade remains an important clinical problem.

Methodology

The guideline task force included anesthesiologists, epidemiology-trained methodologists, and a patient representative, who was chosen from the contacts of the task force and who had experience as a patient. Members disclosed all relationships (industry and other entities) that might pose a conflict of interest. Members with conflicts of interest related to particular recommendations did not participate in the formulation, discussion, or approval of the relevant recommendations. The task force was responsible for developing key questions; the relevant patient populations, interventions, comparators, and outcomes; and the study inclusion/exclusion criteria to guide the systematic review. The study protocol is available as supplemental digital content (<http://links.lww.com/ALN/C924>).

- Population: all patients receiving neuromuscular blocking drugs in whom antagonism and extubation is intended. Patients receiving neuromuscular blocking drugs in the intensive care unit were excluded.
- Interventions: quantitative/objective monitoring; sugammadex or neostigmine.
- Comparators: qualitative/subjective assessment using a peripheral nerve stimulator assessment and clinical assessment without peripheral nerve stimulator; placebo and spontaneous recovery (no intervention).
- Outcomes relevant for both monitoring and antagonism questions were residual neuromuscular blockade (as assessed by train-of-four ratio and reported as such unless noted), time to recovery from neuromuscular blockade (i.e., according to depth of block at antagonism, the time to train-of-four ratio greater than or equal to 0.9), reintubation, reanalysis, pulmonary complications, hypoxia, postoperative nausea and vomiting, anaphylaxis, and cardiac events. In addition to these primary outcomes, measures of agreement for train-of-four ratio were examined across different muscle sites and monitoring devices.

Task force members rated the importance of each outcome for decision-making on a scale of 1 to 9 (1 to 3, limited importance; 4 to 6, important; and 7 to 9, critical).²² The evidence synthesis focused on the outcomes rated as important and critical.

Literature Search

Comprehensive database searches were conducted by a medical librarian using PubMed, EMBASE, and SCOPUS for literature published from 1990 through June 2022. The search start date was chosen to preserve applicability of results (the restriction is unlikely to meaningfully reduce search sensitivity²³). In addition, the Cochrane Central Register of Controlled Trials was queried; task force members provided potentially relevant studies; references from systematic reviews and meta-analyses were hand-searched; and trial registries were searched. The literature search strategy (<http://links.lww.com/ALN/C926>) and PRISMA flow diagram (<http://links.lww.com/ALN/C925>) are available as supplemental digital content.

Study Screening and Selection

Screening of titles with abstract and full text was performed using systematic review software (DistillerSR,²⁴ Evidence Partners, Ottawa, Canada) by two reviewers, with disagreements resolved by consensus. All discrepancies were resolved. Potential inclusion–exclusion discrepancies were also examined with an artificial intelligence tool, a component of the systematic review software. Eligible studies included randomized and nonrandomized trials: diagnostic (e.g., fully paired²⁵), before–after/time series, cohort, and case-control designs. Case reports and case series, conference abstracts, letters not considered brief research reports, non-English publications, and animal studies were excluded. The list of excluded studies is available in the supplemental digital content (<http://links.lww.com/ALN/C927>).

Data Extraction and Management

Study results were extracted into DistillerSR. Data extraction was performed by a single methodologist, with a second methodologist reviewing the data for quality control. Conflicts were resolved by consensus between the two methodologists after reviewing discrepancies. When the relevant data were not reported in the published work, attempts were made to contact authors. The figures were digitized as necessary to obtain quantitative results for synthesis.

Evidence Synthesis

The body of evidence was first described according to study characteristics and treatment arms. The results were then summarized in tabular form by outcome. When relevant, decision-informative, and practicable, pairwise and network random-effects meta-analyses were performed. (Note that the number of studies cited in the text may not correspond to the meta-analyses owing to no events in some studies.) Analyses were conducted in R (R Foundation for Statistical Computing, Vienna, Austria).^{26–29} Small-study effects and the

potential for publication bias were evaluated using funnel plots and regression-based tests.³⁰ (See the methods supplement for further details, <http://links.lww.com/ALN/C956>.) The subject and study characteristics are described in Appendix 1.

Risk of Bias Assessment

Risk of bias for individual studies was evaluated using tools relevant for the study design (supplemental tables S1 to S5, <http://links.lww.com/ALN/C928>; figs. S1 to S5, <http://links.lww.com/ALN/C929>): for randomized controlled trials, the Cochrane risk of bias tool was used;³¹ for nonrandomized studies, the Risk Of Bias In Non-randomized Studies of Interventions tool was used;³² for diagnostic studies, Quality Assessment of Diagnostic Accuracy Studies tool 2 was used;³³ and for the observational results (including single arms of randomized controlled trials), train-of-four confirmation was examined before extubation, a Clinical Advances through Research and Information Technology tool.³⁴

Strength of Evidence

The overall strength of evidence was rated by outcome, using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system (table 1). In this system, randomized controlled trials start as high strength of evidence, and nonrandomized studies start as low. The strength may be downgraded based on summary study-level risk of bias, inconsistency, indirectness, imprecision, and publication bias. Strength may be upgraded if the effect is large, if a dose-response is present, or if unaccounted residual confounding would likely have increased the effect.³⁵ For results obtained from network meta-analyses, the strength of evidence was assessed with the Confidence in Network Meta-Analysis tool using categories corresponding to Grading of Recommendations, Assessment, Development, and Evaluation.³⁶

Strength of Recommendations

For each key question, the results of the detailed evidence synthesis for important benefits and harms were summarized. After reviewing the evidence summary and relevant detail from the synthesis, the task force then drafted recommendations and corresponding strength consistent with the body of evidence.

The categories of recommendations in the Grading of Recommendations, Assessment, Development, and Evaluation approach include strong in favor, conditional in favor, conditional against, and strong against an intervention. Strong recommendations reflect the task force believing that all or almost all clinicians would choose the specific action or approach. Conditional recommendations are those where most, but not all, would choose the action or approach.^{37,38}

Table 1. GRADE Strength of Evidence Definitions

GRADE	Interpretation
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

GRADE, Grading of Recommendations, Assessment, Development, and Evaluation.

Neuromuscular Monitoring: Patient Outcomes

Key Question

What are the comparative effects of clinical assessment (*e.g.*, head lift), qualitative assessment (*e.g.*, peripheral nerve stimulator), and quantitative monitoring (measuring train-of-four ratios) on residual neuromuscular blockade, pulmonary complications, and other adverse events?

Recommendations

When neuromuscular blocking drugs are administered, we recommend against clinical assessment alone to avoid residual neuromuscular blockade, due to the insensitivity of the assessment.

- Strength of recommendation: Strong
- Strength of evidence: Moderate

We recommend quantitative monitoring over qualitative assessment to avoid residual neuromuscular blockade.

- Strength of recommendation: Strong
- Strength of evidence: Moderate

Summary of Evidence

Patients monitored quantitatively had less residual neuromuscular blockade compared with patients assessed qualitatively or clinically (table 2). Supplemental tables S6 and S7 (<http://links.lww.com/ALN/C928>) detail the strength-of-evidence ratings.

Clinical Assessment or Qualitative Assessment *versus* Quantitative Monitoring

Residual Neuromuscular Blockade. A total of five randomized controlled trials^{3,12,39–41} and three observational studies^{42–44} reported lower incidences of residual neuromuscular blockade with quantitative monitoring compared with qualitative assessment or clinical assessment (supplemental tables

S8 and S9, <http://links.lww.com/ALN/C928>). Although both train-of-four ratio thresholds and place (operating room or PACU) where residual neuromuscular blockade were assessed differently across the studies, there is general consistency in the estimated risk ratios. A prospective study⁴² and a retrospective cohort study⁴³ included comparisons of quantitative monitoring with clinical assessment alone; a before–after design⁴⁴ compared quantitative monitoring with peripheral nerve stimulator or clinical assessment—all defined *residual neuromuscular blockade* as a train-of-four ratio less than 0.9 assessed in the PACU. Recognizing the clinical and methodological diversity across studies, given the consistent effects reported, the results were pooled both for randomized controlled trials alone (pairwise) and in a network meta-analysis. This approach yielded similar results (moderate strength of evidence for less residual neuromuscular blockade); only in the retrospective cohort study⁴³ were some patients given sugammadex (supplemental table S10, <http://links.lww.com/ALN/C928>; fig. S6, <http://links.lww.com/ALN/C929>).

Pulmonary Complications. A large multinational prospective cohort study⁴⁵ did not detect a difference in a composite pulmonary complication outcome (respiratory failure, hypoxia, pulmonary infection or infiltrates, atelectasis, aspiration pneumonia, bronchospasm, or pulmonary edema) in patients with quantitative *versus* qualitative assessment (very low strength of evidence for pulmonary complications). A single-institution before–after quality improvement study reported fewer pulmonary complications using quantitative monitoring compared with qualitative assessment.⁴⁶ Three randomized controlled trials^{3,41,47} reported the incidence of hypoxia (two of the three reported a lower incidence with quantitative monitoring, one no events; low strength of evidence). A single trial⁴¹ reported episodes of bronchospasm (1 event, 72 participants), and a prospective cohort study⁴⁸ reported pneumonia (2 events, 155 participants; both very low strength of evidence). Events were uncommon, and a quantitative evidence synthesis was not performed. It should be noted that there is not one universally accepted definition of postoperative pulmonary complications.

Comment. There is convincing evidence that quantitative neuromuscular monitoring reduces the risk of residual neuromuscular blockade. The relative reductions appear consistent and substantial compared with qualitative assessment or clinical assessment. Limitations in the body of evidence include clinical and methodological aspects of study conduct (*e.g.*, train-of-four ratio threshold used to define residual neuromuscular blockade, lack of sugammadex use, device type, manner of qualitative assessment, and clinical assessment), which are reflected in the moderate strength-of-evidence rating.

An important issue with acceleromyography is that baseline (also referred to as *control*) train-of-four ratio measurements (*i.e.*, before muscle relaxation) often exceed 1.0. It is common with baseline values in the range of 1.1 to 1.15, but significantly

Table 2. Strength of Evidence for Quantitative Monitoring Compared with Qualitative or Clinical Assessment

Outcome*	Studies			Strength of Evidence	Effect (95% CI)
	Nonrandomized	Randomized Controlled Trial	Patients		
Residual neuromuscular blockade					Risk ratio
Train-of-four ratio < 0.7, < 0.8, or < 0.9					
Quantitative <i>versus</i> clinical		3	232		0.18 (0.06 to 0.50)
Train-of-four ratio < 0.9					
Quantitative <i>versus</i> qualitative		2	329		0.24 (0.13 to 0.43)
Train-of-four ratio < 0.7, < 0.8, or < 0.9 (network meta-analysis)*				Moderate	
Quantitative <i>versus</i> clinical	3	8	1,211		0.15 (0.10 to 0.22)
Quantitative <i>versus</i> qualitative					0.36 (0.26 to 0.51)
Hypoxia					Risk ratio
Quantitative <i>versus</i> qualitative or clinical		2	347	Low	0.22 (0.05 to 0.88)
Pulmonary complications (composite)†					Odds ratio
Quantitative <i>versus</i> qualitative	2		8,678	Very low	Inconsistent results‡
Any monitoring <i>versus</i> none	1		17,150	Very low	1.31 (1.15 to 1.49)§

*The network meta-analysis results (naïve pooling) are included to support pairwise results (no separate strength-of-evidence rating).

†Reintubation and upper airway obstruction lack reported events in studies; one prospective cohort study (n = 155) reported two cases of pneumonia (very low strength of evidence); one randomized controlled trial (n = 76) reported one case of bronchospasm (very low strength of evidence); and one before–after study (n = 1,810) reported fewer cases of pulmonary complications after introduction of quantitative monitors.

‡A prospective cohort (n = 6,868) did not detect a difference—adjusted odds ratio, 1.07 (95% CI, 0.90 to 1.29). A before–after study (n = 1,810) reported fewer pulmonary complications with quantitative monitoring (–0.5% [95% CI, –0.8 to –0.1%]).

§Adjusted for potential confounders. Pulmonary complications included hypoxia, suspected pulmonary infection or infiltrates, atelectasis, aspiration pneumonia, bronchospasm, or pulmonary edema.

higher baseline values have been reported. Therefore, the clinical definition of adequate recovery of neuromuscular function may vary when the results of monitoring with acceleromyography are not normalized, and the train-of-four ratio may recover to values greater than 1.0. Normalization of train-of-four ratios to the baseline (control) value obtained before neuromuscular block is accomplished by dividing the postoperative measurements by the baseline value. As an example, if the baseline train-of-four ratio is 1.15 and the raw postoperative train-of-four ratio is 0.95, then the normalized train-of-four ratio is $0.95/1.15 = 0.83$. Normalization usually yields lower train-of-four ratios, and therefore normalized observations are more likely than nonnormalized observations to be classified as positive for residual neuromuscular blockade. When neuromuscular blockade is measured with either electromyography or normalized acceleromyography, adequate recovery of neuromuscular function is a train-of-four ratio greater than or equal to 0.9.

Depolarizing Blockade. Succinylcholine is the only depolarizing neuromuscular blocking agent in clinical use. It is rapidly metabolized in the blood stream by pseudocholinesterase. Given the absence of an antagonist drug, succinylcholine blockade must resolve spontaneously. The functional half-life is typically short (less than 10 min) but may be prolonged in patients with genetic or disease-related variations in pseudocholinesterase activity. Blockade monitoring after succinylcholine reveals a different pattern of recovery than

after a nondepolarizing agent, with gradual but equal return of twitch height as blockade resolves in patients with normal pseudocholinesterase activity. However, with genetic variants such as homozygous atypical pseudocholinesterase, it is common that fade appears upon the return of muscle activity mimicking a phase 2 depolarizing block. The only way to effectively monitor both normal and abnormal succinylcholine-induced neuromuscular blockade is by measuring a single twitch baseline height and using the percentage of that single twitch to gauge return of strength. When the rate of block regression is not within the normal range, this will alert the clinician to the presence of abnormal pseudocholinesterase activity. As this is often impractical for clinicians who administer only a single dose of succinylcholine without subsequent use of nondepolarizing neuromuscular blockers, the task force suggests using neuromuscular monitoring to guide extubation when there are clinical signs of delayed recovery from succinylcholine.

Neuromuscular Monitoring: Confirmation of Train-of-four Ratio Greater than or Equal to 0.9 before Extubation

Key Question

When using quantitative monitoring, does confirming a train-of-four ratio greater than or equal to 0.9 decrease the risk of residual neuromuscular blockade?

Recommendations

When using quantitative monitoring, we recommend confirming a train-of-four ratio greater than or equal to 0.9 before extubation.

- Strength of recommendation: Strong
- Strength of evidence: Moderate

Summary of Evidence

Patients whose train-of-four ratio was confirmed before extubation experienced less residual neuromuscular blockade compared to when the train-of-four ratio was not confirmed after neostigmine or sugammadex (table 3). Supplemental tables S11 and S12 (<http://links.lww.com/ALN/C928>) detail the strength-of-evidence ratings, and supplemental tables S13 and S14 (<http://links.lww.com/ALN/C928>) describe the studies included in the analysis.

Train-of-four Ratio Confirmed *versus* Not Confirmed

Residual Neuromuscular Blockade. When sugammadex was used and a train-of-four ratio greater than or equal to 0.9 was confirmed before extubation, the pooled incidence proportion of residual neuromuscular blockade (train-of-four ratio less than 0.9) was 0.5% (95% CI, 0.0 to 6.0%). If a train-of-four ratio greater than or equal to 0.9 was not confirmed before extubation, although quantitative monitoring was used, the incidence proportion was 2.2% (95% CI, 0.5 to 9.0%). With neostigmine, the pooled incidence proportions were 5.3% (95% CI, 2.5 to 10.7%) and 44.9% (95% CI, 29.9 to 60.8%), respectively, with and without confirmation. Supplemental fig. S7 (<http://links.lww.com/>

ALN/C929) displays the entirety of the results (moderate strength of evidence for train-of-four ratio greater than or equal to 0.9 confirmation before extubation).

Comment. These results are consistent with less residual neuromuscular blockade when a train-of-four ratio greater than or equal to 0.9 is confirmed before extubation, but limitations in these analyses are important to note. Direct evidence from randomized trials that compare confirming or not confirming train-of-four ratios before extubation are lacking. The analysis is an indirect comparison that does not include potential confounding between studies such as depth of block at antagonism. However, the effects are substantive and clinically meaningful for either drug—unlikely explained by residual confounding.

Neuromuscular Monitoring: Technical Performance

Key Question

What factors affect the performance of quantitative monitoring?

Recommendations

We recommend using the adductor pollicis muscle for neuromuscular monitoring.

- Strength of recommendation: Strong
- Strength of evidence: Moderate

We recommend against using eye muscles for neuromuscular monitoring.

- Strength of recommendation: Strong
- Strength of evidence: Moderate

Table 3. Residual Neuromuscular Blockade in Randomized and Nonrandomized Studies with Sugammadex or Neostigmine According to Train-of-Four Ratio Greater than or Equal to 0.9 Confirmed Before Extubation

Outcome	Studies*	Patients	Strength of Evidence	Incidence Proportion (95% CI)
Less residual neuromuscular blockade				
Incidence by agent				
Sugammadex				
Train-of-four ratio confirmed	10	552	Low	0.5 (0.0 to 6.0)
Train-of-four ratio not confirmed	11	1,004	(Confirmed vs. not confirmed)	2.2 (0.5 to 9.0)
Train-of-four ratio not stated	7	735	Not rated	1.5 (0.0 to 11.9)
Qualitative assessment	1	29	Not rated	13.8 (5.3 to 31.5)
Clinical assessment/not stated	4	450	Not rated	8.9 (2.6 to 25.9)
Neostigmine				
Train-of-four ratio confirmed	10	486	Moderate	5.3 (2.5 to 10.7)
Train-of-four ratio not confirmed	15	1,446	(Confirmed vs. not confirmed)	44.9 (29.9 to 60.8)
Train-of-four ratio not stated	10	700	Not rated	6.5 (0.9 to 34.5)
Qualitative assessment	9	988	Not rated	35.7 (29.6 to 42.3)
Clinical assessment/not stated	10	947	Not rated	24.9 (13.2 to 42.0)

Residual neuromuscular blockade (train-of-four ratio less than 0.9) in arms of randomized and nonrandomized studies using quantitative monitoring and sugammadex or neostigmine.

*Randomized and nonrandomized individual study arms.

Summary of Evidence

Time to reach train-of-four ratio greater than or equal to 0.9 at the adductor pollicis muscle was longer compared with eye muscles and flexor hallucis brevis. There was less residual neuromuscular blockade when patients were monitored at the adductor pollicis muscle compared to the corrugator supercilii (table 4). Supplemental tables S15 and S16 (<http://links.lww.com/ALN/C928>) describe studies comparing different muscles to adductor pollicis for monitoring and time to train-of-four ratio from different muscle groups. Supplemental tables S17 and S18 (<http://links.lww.com/ALN/C928>) detail the strength-of-evidence ratings.

Adductor Pollicis *versus* Other Muscles

Time to Train-of-four Ratio Greater than or Equal to 0.8, 0.9, or 1.0. Times to train-of-four ratio greater than or equal to 0.8, 0.9, or 1.0 were longer in patients monitored with the adductor pollicis muscles compared with the corrugator supercilii (moderate strength of evidence), orbicularis oculi (low strength of evidence), and flexor hallucis brevis muscles (very low strength of evidence).^{49–55} No difference was detected in the time to train-of-four ratio greater than or equal to 0.9 when monitoring the adductor pollicis muscle compared with the masseter (very low strength of evidence).⁵⁶

Residual Neuromuscular Blockade. One prospective cohort study reported less residual neuromuscular blockade when monitoring the adductor pollicis muscle compared

with the corrugator supercilii (very low strength of evidence).⁵⁷

No Normalization *versus* Normalization with Acceleromyography Monitors

Residual Neuromuscular Blockade. One fully paired study detected less residual neuromuscular blockade (train-of-four ratio less than 1.0) when using nonnormalized acceleromyography measures compared with normalized measures (very low strength of evidence).⁵⁸ The same study did not detect a difference in severe residual neuromuscular blockade (train-of-four ratio less than 0.7) between nonnormalized and normalized measures.

Additional Technical Performance Comparisons. Several studies compared no calibration to calibration, various arm stabilization techniques, and no preload *versus* preload. Evidence synthesis was not performed due to the diversity of outcomes reported across the studies.

Comment

Complete recovery of all muscles from neuromuscular blockade optimizes patient safety; therefore, measurements should be obtained at sites with longer times to recovery. When monitoring a muscle with relative resistance such as the eye muscles to neuromuscular blocking drugs, there is a potential for neuromuscular blocking drug overdose and for concluding that a patient is adequately antagonized when, in fact, they are not (see Appendix 2).

Table 4. Summary and Strength of Evidence for Technical Performance of Neuromuscular Monitors by Muscle and Normalization

Comparisons	Studies			Strength of Evidence	Summary
	Nonrandomized	Paired/Randomized Controlled Trial	Patients		
Train-of-four ratios					
Adductor pollicis <i>versus</i> Corrugator supercilii		4	140	Moderate	Three of four studies reported longer times to train-of-four ratio greater than or equal to 0.9 or greater than or equal to 1.0 at adductor pollicis <i>versus</i> corrugator supercilii
Orbicularis oculi		2	46	Low	Longer times to train-of-four ratio greater than or equal to 0.8 or greater than or equal to 0.9 at adductor pollicis <i>versus</i> orbicularis oculi
Masseter		1	10	Very low	Difference not detected
Flexor hallucis brevis		1	52	Very low	Longer time to train-of-four ratio greater than or equal to 0.9 at adductor pollicis <i>versus</i> flexor hallucis brevis
First dorsal interosseous <i>versus</i> flexor hallucis brevis		1	28	Very low	Longer time to train-of-four ratio greater than or equal to 0.9 at first dorsal interosseous <i>versus</i> flexor hallucis brevis
Residual neuromuscular blockade					
No normalization <i>versus</i> normalization		1	122	Very low	Less residual neuromuscular blockade (train-of-four ratio less than 1.0) detected when using nonnormalized measurements
Adductor pollicis <i>versus</i> corrugator supercilii	1		150	Very low	Less residual neuromuscular blockade (train-of-four ratio less than 0.9) detected when monitoring at the adductor pollicis <i>versus</i> corrugator supercilii

Antagonism of Neuromuscular Blockade

Key Question

What are the comparative efficacy and safety of antagonist drugs among patients receiving nondepolarizing neuromuscular blocking drugs?

Recommendations

We recommend sugammadex over neostigmine at deep, moderate, and shallow depths of neuromuscular blockade induced by rocuronium or vecuronium, to avoid residual neuromuscular blockade.

- Strength of recommendation: Strong
- Strength of evidence: Moderate

We suggest neostigmine as a reasonable alternative to sugammadex at minimal depth of neuromuscular blockade.

- Strength of recommendation: Conditional
- Strength of evidence: Low

Summary of Evidence

Table 5 defines the depths of neuromuscular blockade referred to in the recommendations. The incidence of residual neuromuscular blockade was lower and time to recovery was shorter with sugammadex compared to neostigmine (table 6). However, there were no differences in repa-lysis and reintubation rates (table 7). Supplemental tables S19 and S20 (<http://links.lww.com/ALN/C928>) detail the strength-of-evidence ratings.

Sugammadex versus Neostigmine

Residual Neuromuscular Blockade. Ten randomized controlled trials reported a lower incidence of residual neuromuscular blockade in patients antagonized with sugammadex compared with neostigmine (moderate strength of evidence; supplemental fig. S8, <http://links.lww.com/ALN/C929>).^{59–68}

Time to Train-of-four Ratio Greater than or Equal to 0.9. Times to train-of-four ratio greater than or equal to 0.9 were shorter in patients antagonized with sugammadex compared with neostigmine from deep^{65,69–71} to moderate^{62,72–85} depths of blockade (moderate strength of evidence) and from shallow^{86–90} (moderate strength of evidence) to minimal⁶⁹ depths of blockade (very low strength of evidence; supplemental figs. S9 to S12, <http://links.lww.com/ALN/C929>).

Adverse Events. Anaphylaxis was reported with neostigmine in one study⁹¹ of five (supplemental table S21; <http://links.lww.com/ALN/C928>).^{91–95} Among patients receiving sugammadex, the pooled incidence rate of anaphylaxis was 1.6 per 10,000 (low strength of evidence).^{92,93,96,97} Differences in rates of bradycardia or tachycardia were not apparent among patients who received sugammadex

Table 5. Depths of Neuromuscular Blockade by Quantitative and Qualitative Measurement

Depth of Blockade	Peripheral Nerve Stimulator and Qualitative Assessment	Quantitative Monitor
Complete	Posttetanic count = 0	Posttetanic count = 0
Deep	Posttetanic count ≥ 1 ; train-of-four count = 0	Posttetanic count ≥ 1 ; train-of-four count = 0
Moderate	Train-of-four count = 1–3	Train-of-four count = 1–3
Shallow*	Train-of-four count = 4; train-of-four fade present	Train-of-four ratio < 0.4
Minimal*	Train-of-four count = 4; train-of-four fade absent	Train-of-four ratio = 0.4–0.9
Acceptable recovery	Cannot be determined	Train-of-four ratio ≥ 0.9

*The quantitative threshold of train-of-four ratio of 0.4 cannot reliably be subjectively determined by the presence or absence of fade in the train-of-four ratio response. The absence of subjectively appreciated fade has been reported with a train-of-four ratio of less than 0.3, and the presence of fade has been reported with train-of-four ratio of greater than 0.7.¹⁴⁹

compared with neostigmine when glycopyrrolate (low strength of evidence; supplemental fig. S13, <http://links.lww.com/ALN/C929>).^{61,68,69,74,95,98} Differences were also not detected for arrhythmias irrespective of antimuscarinic used^{89,95,99–101} (low strength of evidence; supplemental fig. S14, <http://links.lww.com/ALN/C929>; table S22, <http://links.lww.com/ALN/C928>).

Pulmonary Complications. A pooled result from six randomized trials did not detect a difference in pulmonary complications (a composite of respiratory failure, hypoxia, pulmonary infection or infiltrates, atelectasis, aspiration pneumonia, bronchospasm, or pulmonary edema) in patients given neostigmine or sugammadex (low strength of evidence; supplemental fig. S15, <http://links.lww.com/ALN/C929>).^{66,82,99,102–104} A pooled estimate from seven nonrandomized studies also did not detect a difference in pulmonary complications (very low strength of evidence).^{45,93,105–109} Five randomized controlled trials^{59,61,66,104,110} and four cohort studies^{93,106,108,109} reported fewer episodes of pneumonia with sugammadex than neostigmine (low to very low strength of evidence; supplemental fig. S16, <http://links.lww.com/ALN/C929>). A difference in hypoxia was not detected between sugammadex and neostigmine in six randomized controlled trials (SaO_2 less than or equal to 90%, low strength of evidence; supplemental fig. S17, <http://links.lww.com/ALN/C929>).^{64,68,110–113} Postoperative reintubation was unreported in five randomized trials for sugammadex and neostigmine (low strength of evidence).^{81,104,110,112,114} A single trial reported postoperative reintubation with neostigmine only.¹⁰⁴ Four studies reported lower rates of reintubation with sugammadex (very low strength of evidence; supplemental fig. S18, <http://links.lww.com/ALN/C929>).^{106,115–117} As noted previously, there is not one universally accepted definition of postoperative pulmonary complications.

Table 6. Benefits and Strength of Evidence Comparing Sugammadex with Neostigmine for Incidence of Residual Neuromuscular Blockade and Time to Recovery to Train-of-four Ratio Greater than or Equal to 0.9

Outcome	Randomized Controlled Trials	Patients	Strength of Evidence	Effect (95% CI)
Less residual neuromuscular blockade				Risk ratio
Train-of-four ratio < 0.9	8	1,451	Moderate	0.18 (0.07 to 0.42)
				Risk difference
Train-of-four ratio < 0.9	8	1,451	Moderate	-21.6% (-33.8 to -9.4%)
Shorter time to train-of-four ratio \geq 0.9 from				Mean difference, min
Deep block	4	308	Moderate	-33.6 (-59.3 to -7.9)
Moderate block	17	1,114	Moderate	-10.0 (-12.7 to -7.2)
Shallow block	5	153	Moderate	-3.9 (-6.1 to -1.6)
Minimal block	1	17	Very low	-1.4 (-2.0 to -0.8)

Reparalysis. The incidence of reparable paralysis was variable across trials not occurring with either neostigmine or sugammadex in 10 of 13 randomized trials (supplemental fig. S19, <http://links.lww.com/ALN/C929>, risk difference for sugammadex versus neostigmine of -2.9% [95% CI, -8.5 to 2.7]; low strength of evidence).^{65,68,70,72,73,81,86-88,90,99,118,119}

Postoperative Nausea and Vomiting. The incidence of postoperative nausea and vomiting was reported in 16 randomized controlled trials,^{66,68,89,102,103,110,114,119-127} 1 nonrandomized trial,¹²⁸ and 4 cohort studies.^{107,129-131} In a network meta-analysis (including placebo and spontaneous arms), the incidence appeared lower with sugammadex but with low confidence in the estimate (low strength of evidence; supplemental fig. S20, <http://links.lww.com/ALN/C929>).

Postoperative nausea was reported in 31 studies (26 randomized controlled trials,^{61,62,65,67,69-71,73,74,77,79-81,84,100,102,132-141} 1 nonrandomized study,¹⁴² and 3 cohort studies^{48,143,144}). No difference was apparent between sugammadex and neostigmine (very low strength of evidence; supplemental fig. S21, <http://links.lww.com/ALN/C929>).

Postoperative vomiting was reported in 24 studies (21 randomized controlled trials,^{61,62,65,67,69-71,74,75,77,79,81,102,132,133,136,139-141} 1 nonrandomized study,¹⁴² and 2 cohort studies^{143,144}). No difference was detected between sugammadex and neostigmine (low strength of evidence; supplemental fig. S22, <http://links.lww.com/ALN/C929>).

Comment

The antagonist drugs currently available include anticholinesterases and sugammadex, a selective relaxant binding drug. Neostigmine is the most commonly used anticholinesterase and the only drug in this class of drugs that was evaluated for this guideline.

Selective use of neostigmine or sugammadex is based on identifying patients highly likely to achieve an effective antagonism with neostigmine. The degree of spontaneous

recovery at the time of antagonism has been shown to be the major determinant of successful and timely antagonism with neostigmine. Several studies have demonstrated that administering neostigmine at a train-of-four count of 4 is much more likely to yield a satisfactory and timely antagonism than neostigmine administered at a lower train-of-four count.^{145,146} However, it is also clear from several studies that an effective antagonism is not guaranteed even when spontaneous recovery has progressed to a train-of-four count of 4 if the fourth twitch is still very weak.¹⁴⁵ In one study, a cohort of patients were antagonized when the train-of-four ratio was 0.4, and all patients had a timely successful antagonism as defined by a train-of-four ratio greater than or equal to 0.9 within 10 min of neostigmine administration.¹⁴⁷ Another study compared sugammadex with neostigmine at a train-of-four ratio of 0.5 and found that both were equally effective at this depth of blockade.⁶⁸ Additional studies have confirmed that the likelihood of an effective antagonism with neostigmine is much improved when the neuromuscular blockade is minimal (*minimal block* is the proposed consensus term for a quantitatively measured block with a train-of-four ratio of 0.4 to 0.9, or a qualitatively assessed block with no subjective fade to train-of-four stimulation).^{68,148,149} The quantitative determination of train-of-four ratio greater than or equal to 0.4 is more reliable than subjective determination of no fade with train-of-four stimulation and is associated with improved predictability of neostigmine.

The evidence synthesis did not address the dosages of antagonist drugs. However, neostigmine and sugammadex both have Food and Drug Administration (FDA)-approved dose recommendations. The FDA-approved dose recommendations for antagonizing rocuronium or vecuronium with sugammadex are 2 mg/kg for train-of-four count 2 to train-of-four ratio less than 0.9, 4 mg/kg for posttitanic count 1 to train-of-four count 1, and 16 mg/kg immediate antagonism after administration of a single dose of rocuronium 1.2 mg/kg. A neostigmine dose of 30 μ g/kg

Table 7. Harms and Strength of Evidence Comparing Sugammadex with Neostigmine

Outcome	Studies		Patients	Strength of Evidence	Effect (95% CI)*
	Nonrandomized	Randomized Controlled Trials			
Anaphylaxis					Incidence proportion
Sugammadex	5	2	204,152	Low	1.4/10,000 (0.7 to 3.1)
Neostigmine	3	2	168,852	Low	0.3/10,000 (0.1 to 0.9)
Cardiac complications					Risk difference
Bradycardia					
Neostigmine/glycopyrrolate		6	663	Low	-5.0% (-11.7 to 1.7%)
Neostigmine/atropine		8	689	Moderate	-12.7% (-12.7 to -5.1%)
Tachycardia					
Neostigmine/glycopyrrolate		3	314	Low	-6.7% (-14.5 to 1.0%)
Neostigmine/atropine		1	74	Very low	-10.8% (-23.0 to -5.1%)
Arrhythmias		5	178	Low	-1.0% (-3.8 to 1.9%)
Pulmonary complications					Odds ratio
Composite	5	6	67,323	Low/very low†	0.71 (0.56 to 0.90)
Pneumonia	4	5	57,745	Low/very low†	0.59 (0.38 to 0.93)
					Risk difference
Hypoxia (SaO ₂ ≤ 90%)		6	670	Low	-6.0% (-18.2 to 6.2%)
Hypoxia (SaO ₂ > 90 to 95%)		7	792	Low	1.6% (-3.6 to 6.8%)
					Risk difference
Reintubation		5	425	Low	-0.2% (-2.1 to 1.6%)
	4		18,736	Very low	-1.7% (-4.1 to 0.6%)
					Risk difference
Reparalysis		13	705	Low	-2.9% (-8.5 to 2.7%)
					Risk ratio
Postoperative nausea and vomiting		16‡	1,536	Low	0.77 (0.61 to 0.97)
Postoperative nausea		26‡	2,781	Very low	0.94 (0.78 to 1.12)
Postoperative vomiting		21‡	2,178	Low	0.84 (0.60 to 1.18)

*Sugammadex *versus* neostigmine. †Strength of evidence for randomized and observational results considered separately. Pooled result shown for combined randomized and observational studies (consistent across designs). ‡Number of trials included in network meta-analysis.

at minimal neuromuscular blockade is consistent with the FDA-approved dosage recommendations.

The antagonist effect of neostigmine is maximal within approximately 10 min,¹⁵⁰ and therefore, there is no benefit in administering neostigmine much more than 10 min before emergence and extubation. If recovery time exceeds 10 min (*i.e.*, a train-of-four ratio greater than or equal to 0.9 has not been reached within 10 min after neostigmine administration), it is unlikely to be the result of delayed activity of neostigmine. Rather, the explanation is more likely to be that sufficient spontaneous recovery was not achieved before administration of neostigmine. When neostigmine has peaked but the train-of-four ratio is less than 0.9, three options remain to accomplish adequate antagonism: (i) allow for continued spontaneous recovery; (ii) administer sugammadex if appropriate to the relaxant given; or (iii) if a low dose of neostigmine was initially used, administer additional neostigmine (but not exceeding a total of 50 µg/kg because higher doses have not been reported as more effective).

The following factors should be considered when choosing the neuromuscular antagonist drug: the type of neuromuscular blocking drug used (*e.g.*, steroidal, benzyliisoquinolinium), depth of neuromuscular blockade, efficacy of

the antagonist drug for the class of neuromuscular blocking drug, any ceiling effect of the antagonist drug, and time required to attain full antagonism. The occurrence of residual neuromuscular blockade is affected in large part by the appropriate use of antagonist drug and monitoring equipment. Finally, for women using hormonal contraceptives (oral or non-oral) receiving sugammadex, FDA labeling states a backup contraception method must be used for 7 days.

Depth of Neuromuscular Blockade and Choice of Antagonist Drug.

When neostigmine is used at minimal blockade (train-of-four ratio greater than or equal to 0.4 and less than 0.9), the dose should not exceed 40 µg/kg. The shallower the blockade, the lower the neostigmine dose required—when the train-of-four ratio exceeds 0.6, 15 to 30 µg/kg is usually adequate. Higher doses may have the paradoxical effect of causing weakness with neostigmine when a dose exceeding 30 µg/kg is administered after spontaneous recovery to train-of-four ratio greater than or equal to 0.9. This can be avoided if quantitative monitoring is used.¹⁶ When quantitative monitoring is not available and spontaneous recovery has progressed to a train-of-four count of 4 without fade, it is advisable to routinely administer a small dose of 15 to 30 µg/kg neostigmine. The reason

is that, as has been discussed above, it is not possible to rule out residual neuromuscular blockade with the use of a peripheral nerve stimulator. When quantitative monitoring is not available, and to be relatively sure that the block is adequately recovered, a minimum of 10 min should pass after neostigmine-induced antagonism before extubation is performed. With quantitative monitoring, extubation can be performed as soon as the train-of-four ratio is greater than or equal to 0.9. Depending on clinical judgment and in the context of quantitative monitoring, neostigmine may be considered for a depth of block deeper than minimal (train-of-four ratio of 0.4 to 0.9), with the understanding that deeper blocks will require more time to attain a train-of-four ratio greater than or equal to 0.9.

Adverse Effects of Antagonism. The adverse effects of sugammadex and neostigmine (coadministered with glycopyrrolate) do not favor either drug. The strength-of-evidence ratings do not support differences in rates of anaphylaxis, bradycardia, or tachycardia when glycopyrrolate is used with neostigmine, postoperative nausea and vomiting, postoperative nausea alone, and postoperative vomiting (table 7).

Economic Considerations. Although outside the scope of this guideline, many raise concerns regarding the cost of sugammadex. It is important to note that regardless of the perspective, the decision calculus for an economic evaluation of sugammadex is complex.^{151,152} Factors beyond drug costs require consideration—*e.g.*, time to recovery and operating room costs, residual neuromuscular blockade and reparation, as well as the costs associated with adverse events caused by residual neuromuscular blockade. Finally, in discussions regarding costs during guideline development, the patient representative noted to the panel the rather small proportion added by sugammadex to overall operative charges.

Pancuronium. The systematic review did not identify published clinical trials of antagonism of pancuronium by sugammadex. It also did not identify published studies comparing the antagonism of pancuronium-induced neuromuscular blockade by sugammadex *versus* neostigmine. Therefore, no recommendations were developed. Sugammadex has a lower affinity for pancuronium, and higher doses may be required.^{153,154}

Key Question

What are the antagonism strategies for benzyliisoquinolinium (*e.g.*, cisatracurium) neuromuscular blockade?

Recommendations

To avoid residual neuromuscular blockade when atracurium or cisatracurium are administered and qualitative assessment is used, we suggest antagonism with neostigmine at minimal neuromuscular blockade depth. In the absence of quantitative monitoring, at least 10 min should

elapse from antagonism to extubation. When quantitative monitoring is utilized, extubation can be done as soon as a train-of-four ratio greater than or equal to 0.9 is confirmed before extubation.

- Strength of recommendation: Conditional
- Strength of evidence: Very low

Benzyliisoquinolinium Neuromuscular Blockade Antagonism Time to Train-of-four Ratio Greater than or Equal to 0.9.

Times to train-of-four ratio greater than or equal to 0.9 after neostigmine administration ranged from 1 to 143 min reported in six studies as shown in supplemental fig. S23 (<http://links.lww.com/ALN/C929>; very low strength of evidence).^{77,145,147,155–157} Time to train-of-four ratio greater than or equal to 0.9 for neostigmine antagonism of cisatracurium and atracurium is shown in table 8. Supplemental tables S19 and S20 (<http://links.lww.com/ALN/C928>) detail the strength-of-evidence ratings.

Comment. Benzyliisoquinolinium neuromuscular blocking drugs (cisatracurium and atracurium) can be antagonized only with an acetylcholinesterase inhibitor such as neostigmine—sugammadex is ineffective. However, neostigmine can be accompanied by a longer time to recovery than may be recognized. Assuming that (i) neostigmine is given once a muscle relaxant is no longer required for surgery, (ii) there is some spontaneous recovery from neuromuscular blockade, and (iii) emergence from anesthesia is expected in approximately 10 min, antagonism success depends primarily on the depth of block at the time of administration. Full antagonism within 10 min is most likely when neostigmine is given with four twitches and no visible or tactile fade. Success is unlikely when given with fewer than four twitches. Under these circumstances limited evidence is consistent with a median time to antagonism less than 10 min, but with a wide range in time to recovery from a train-of-four ratio of less than 0.4 to a train-of-four count 2 to 3 blockade (table 8). Therefore, verifying adequate recovery necessitates measuring train-of-four ratio with a quantitative monitor.

Research Gaps and Major Uncertainties

- Train-of-four ratio cutoff for acceleromyography *versus* electromyography in the context of patient outcomes. Are there additional improved patient outcomes if an acceleromyography train-of-four ratio greater than or equal to 1.0 is used instead of 0.9? Studies are needed to directly confirm that an electromyography train-of-four ratio greater than or equal to 0.9 is associated with improved patient outcomes.
- This guideline did not examine sugammadex dosing. Lower-than-recommended doses are potentially

associated with rep paralysis. Sugammadex has a greater affinity for rocuronium than vecuronium. Therefore, a lower dose of sugammadex is required for rocuronium when compared with vecuronium at the same depths of blockade. The appropriate mg/kg dose and use of ideal *versus* total body weight at various depths of blockade should be determined for rocuronium and vecuronium separately to ensure full antagonism without rep paralysis.

- There is a need for additional studies comparing sugammadex and neostigmine at minimal blockade, including effectiveness, safety, and pharmacoeconomic analysis.
- There is a need to evaluate the routine avoidance of pharmacological antagonism for patients with spontaneous recovery to a train-of-four ratio greater than or equal to 0.9, including clinical outcomes, safety, adverse outcomes, and economic implications.
- The relationship between residual neuromuscular blockade and postoperative pulmonary complications requires further investigation. Patient comorbidities (e.g., morbid obesity, chronic pulmonary diseases) and site of surgery (abdominal/thoracic *versus* other sites) strongly influence postoperative pulmonary complications. Intraoperative ventilation strategies using lung protective ventilation, extubation strategies using pressure support ventilation with positive end-expiratory pressure, and emergency procedures all are strong predictors of postoperative pulmonary complications. The effects of residual neuromuscular blockade need to be further studied, focusing upon higher-risk surgical patients.

Implementation

Routine quantitative monitoring for patients receiving neuromuscular blocking agents represents a change in clinical practice. As demonstrated in recent surveys,^{158,159} quantitative monitors are infrequently available, and peripheral

nerve stimulators used in less than 50% of anesthetics when patients receive neuromuscular blockers.¹⁵⁹ Many clinicians continue to use clinical indicators such as sustained head lift to guide their decision on when to extubate patients.^{20,159–161} There is no clinical test that is predictive of adequate neuromuscular recovery, and clinical tests are not sensitive to the presence of residual neuromuscular blockade. Clinical tests are also not applicable to the patient still under anesthesia. The clinician needs reliable information as to the patient's neuromuscular function before emergence from anesthesia. Therefore, opportunities to accelerate adoption of quantitative monitoring and improve patient outcomes need to be identified.

The benefits of complete recovery include increased patient satisfaction,^{12,162} decreased length of PACU stay,^{13,163} decreased postoperative pulmonary complications,³ and decreased mortality.¹⁶⁴ Because of these benefits, there have been multiple calls to develop guidelines to monitor depth of neuromuscular block.^{149,159,165–167}

Champions for adoption of routine quantitative monitoring must educate fellow anesthesia clinicians of the benefits of monitoring: increased understanding of the patient's physiologic condition, more effective antagonism of blockade, decreased need for PACU airway interventions, and decreased morbidity. Increasing local acceptance of monitors will require multiple approaches (table 9), as well as constant oversight and feedback.⁴⁴

There have been quality improvement projects aimed at bringing the advantages of this technology to patients. Projects previously described strategies such as placing quantitative neuromuscular monitoring equipment in all anesthetizing locations, departmental education, and departmental feedback. One project reduced residual paralysis in the PACU over 9 years (1995 to 2004) from 62 to 3.5% of patients as a result of increasing quantitative neuromuscular monitoring in the operating room from 2 to 60% of patients.¹⁶⁸ Another project resulted in a reduction of residual paralysis in the PACU from 31 to 15%

Table 8. Time to Train-of-four Ratio Greater than or Equal to 0.9 for Neostigmine Antagonism of Benzylisoquinolinium Drugs Cisatracurium and Atracurium

Study	Drug	Depth at Neostigmine Administration	Neostigmine Dose, µg/kg	Time to Train-of-four ≥ 0.9	
				Mean, min (SD)	Median, min (range)
Goldhill <i>et al.</i> ¹⁵⁵	Atracurium	Train-of-four count 2	35	10.3 (1.3)	
Flockton <i>et al.</i> ⁷⁷	Cisatracurium	Train-of-four count 2	50		7.3 (4.2 to 28.2)
Kirkegaard <i>et al.</i> ¹⁴⁵	Cisatracurium	Train-of-four count 4	70		16.5 (6.5 to 143.3)
Song <i>et al.</i> ¹⁵⁷	Cisatracurium	Train-of-four count 4	70		11 (2 to 28)
Song <i>et al.</i> ¹⁵⁷	Cisatracurium	Train-of-four count 4 no fade	70		8 (1 to 25)
Fuchs-Buder <i>et al.</i> ¹⁴⁷	Atracurium	Train-of-four ratio 0.4	30		4 (3 to 6)
Preault <i>et al.</i> ¹⁵⁶	Cisatracurium	Train-of-four ratio 0.4	40		3.8 (2.3 to 7)

after introducing quantitative monitoring in all operating rooms.⁴⁴ This accompanied a 2-year period without any PACU reintubations associated with residual paralysis (two to four reintubations occurred per year before the project). A more recent project benefitted from a broader range of commercially available equipment choices and leveraged that by involving the department end users in the equipment purchasing decision. This decision was supplemented by communication regarding acquisition and ongoing disposable cost projections. Educational efforts included equipment instructional videos, and alerts were built into the electronic medical record for real-time reminders to record train-of-four ratios. Additionally, performance feedback was provided on an individual level. These efforts led to a cultural shift that saw 93% of patients with a documented train-of-four ratio greater than or equal to 0.9 in December 2020, which increased to 97% by March 2022.⁴⁶ Merely placing a quantitative monitor in each anesthetizing location will not by itself reduce the incidence of residual postoperative neuromuscular block. A substantial and sustained educational effort is also necessary.⁴⁴

The exact strategies employed by any given practice will vary, but a systematic approach may include restructuring the clinical environment by placing monitors in all anesthetizing locations, educational efforts on the departmental and individual levels utilizing different mediums, and performance feedback on the departmental and individual levels.

Conclusions

This practice guideline makes clinical recommendations about monitoring and antagonism of neuromuscular blocking agents with the aim of preventing residual neuromuscular blockade. It is recommended to use quantitative neuromuscular monitoring at the adductor pollicis and to confirm recovery of a train-of-four ratio greater than or equal to 0.9 before extubation. Sugammadex is recommended for deep, moderate, and shallow depths of neuromuscular blockade induced by rocuronium or vecuronium. Neostigmine is a reasonable alternative for minimal blockade (train-of-four ratio ranging from 0.4 to less than 0.9). Patients with adequate spontaneous recovery to train-of-four ratio greater than or equal to 0.9 can be identified only with quantitative monitoring, and these patients do not require pharmacological antagonism.

Appendix 1. Study and Patient Characteristics

Neuromuscular Monitoring: Patient Outcomes

The body of evidence included 16 studies (10 randomized controlled trials,^{3,12,39–41,47,169–172} 2 before–after design,^{44,46} 3 prospective cohort studies,^{42,45,48} and 1 retrospective cohort study⁴³) comparing the effects of quantitative monitoring with qualitative assessment or clinical assessment on patient outcomes. Studies enrolled a median of 135 participants (range, 30 to 17,150). The mean age was 46.6 years, 56% were

Table 9. Strategies for Implementation and Acceptance of Routine Quantitative Monitoring

Educate clinicians on the prevalence and consequences of residual neuromuscular blockade in routine care; provide key references.
Provide in-service training on quantitative monitoring technology, emphasizing the increasing ease of use and interpretation.
Work with the operating room value-based-purchasing committee (or local equivalent) to define appropriate indications and contraindications for quantitative monitoring. Include all patients receiving neuromuscular blocking drugs, with particular focus on patients receiving nondepolarizing neuromuscular blocking drug.
Ensure that monitors are readily available.
Seek opportunities to document and promote results within your group and institution to enable:

- A decrease in incidence of postoperative respiratory complications.
- A decrease in ICU and hospital length of stay.
- An increase in patient satisfaction.
- Changes in the use of antagonist drugs.

Provide team and individual feedback on appropriate use of quantitative monitoring.

ICU, intensive care unit.

female, and the average body mass index was 26.2 kg/m². Six studies (40%) enrolled participants rated ASA Physical Status I to II, and seven (47%) included participants rated ASA Physical Status I to III (unreported in two studies [13%]).

Neuromuscular Monitoring: Confirmation of Train-of-four Ratio Greater than or Equal to 0.9 before Extubation

The body of evidence included 41 studies (26 randomized controlled trials,^{41,59–63,65–68,71,73,86,118,139,145,147,173–181} 1 before–after design,⁴⁴ 4 nonrandomized trials,^{142,182–184} 6 prospective cohort studies,^{105,117,185–188} 3 retrospective cohort studies,^{43,189,190} and 1 fully paired study⁵⁸) using quantitative monitoring and sugammadex or neostigmine and reporting residual neuromuscular blockade (train-of-four ratio less than 0.9). For studies stratifying randomization, the arms were considered independent. In studies reporting results by subgroup, the subgroups were combined to remove dependence (subgroup differences were not of interest). Studies enrolled a median of 120 participants (range, 20 to 624). The average mean or median age was 53.6 years, 54% were female, and the average body mass index was 26.1 kg/m².

Sugammadex was administered for antagonism in 28 studies (supplemental table S13, <http://links.lww.com/ALN/C928>). Based on the available information (reported in the publication or obtained from authors), the train-of-four ratio was confirmed greater than or equal to 0.9 before extubation in 10 studies,^{60,62,68,73,86,118,139,142,179,180} greater than or equal to 0.8 or not stated in 2 studies,^{128,191} and unconfirmed in 11 studies.^{59,63–66,105,176,184,186,187,189}; in 6 studies (1 had two strata), whether train-of-four ratio was confirmed could not be determined.^{43,61,67,117,182,190} Neostigmine was administered as the antagonist drug in 40 studies (supplemental

table S14, <http://links.lww.com/ALN/C928>). A train-of-four ratio greater than or equal to 0.9 was confirmed before extubation in 10 studies,^{41,60,62,68,73,86,118,173–175} greater than or equal to 0.8 or not stated in 5 studies,^{3,12,191–193} and unconfirmed in 15 studies^{58,59,63,65,66,71,105,181,183–189}; in 9 studies, whether train-of-four ratio was confirmed could not be determined.^{43,44,61,67,117,145,147,177,182}

Neuromuscular Monitoring: Technical Performance

The body of evidence included 22 studies (17 fully paired,^{49–51,53–56,58,194–202} 4 randomized controlled trials,^{52,203–205} and 1 prospective cohort study⁵⁷) evaluating various factors that may affect the performance of neuromuscular monitors. Studies enrolled a median of 36 participants (range, 8 to 150). The mean age of participants was 47.8 years, 50% were female, and the average body mass index was 26.3 kg/m². Fifteen studies (68%) enrolled participants rated ASA Physical Status I to II, 4 studies (18%) enrolled participants rated ASA Physical Status I to III, and 1 study (4%) included participants rated ASA Physical Status I to IV (unreported in 2 studies). Eight of the studies focused on comparing time to recovery at the adductor pollicis with other muscles. Supplemental tables S15 and S16 (<http://links.lww.com/ALN/C928>) describes this subset of studies.

Antagonism of Neuromuscular Blockade

The body of evidence enrolling adults included 191 studies (133 randomized controlled trials,^{4,59–90,92,95,98–104,110–114,118–127,132–141,145–148,155–157,163,173–181,206–254} 11 nonrandomized trials,^{17,128,142,182–184,191,255–258} 45 cohort studies,^{15,42,86,91,93,94,96,97,105–109,116,117,129–131,143,144,186–190,227,259–277} and 2 before–after designs^{115,168}) evaluating efficacy and safety of antagonist drugs for neuromuscular blockade. The randomized controlled trials enrolling only adults had a median of 88 participants (range, 16 to 350). The mean age was 47.6 years, 52% were female, and average body mass index was 28.7 kg/m². The remaining studies enrolled a median of 187 participants (range, 17 to 45,712). The mean age was 54.0 years, 56% were female, and average body mass index was 30.5 kg/m². Industry supported 21% of the randomized controlled trials, and 17% of the studies were limited to adults.

Appendix 2. Technical Performance of Quantitative Neuromuscular Monitors

Although not directly informing the strength of evidence for quantitative monitoring to reduce postoperative pulmonary complications, the evidence synthesis considered the clinical validity of quantitative monitoring to reduce residual paralysis (supplemental tables S23 to S26, <http://links.lww.com/ALN/C928>). This appraisal relates to both device–diagnostic performance and the reduction of residual

neuromuscular blockade. Mechanomyography, which measures twitch strength using a force transducer, is considered the most appropriate reference standard. As a tool to measure underlying residual neuromuscular blockade, measurement error is apparent with all quantitative monitors. The limits of agreement for train-of-four ratio between devices or even with measurements of the same device (including mechanomyography) often approach $\pm 10\%$ at the adductor pollicis muscle. Proper device use, including calibration and muscle selection, may help limit measurement error. Despite these limitations, quantitative monitoring has a large effect in reducing residual neuromuscular blockade so that measurement error is unlikely to have clinical consequences. The evidence concerning the comparative diagnostic performance of different device types suggests that the preferred device is the one that a clinician uses appropriately.

Regarding specific quantitative monitors, the reference standard has generally been mechanomyography, despite the aforementioned measurement bias of train-of-four ratio of approximately 0.1. Electromyography has some advantages; immobilization of the muscle to be monitored is not necessary, and therefore, it also works well when arms and hands are tucked for surgical positioning. No preload is needed, and because of good agreement with mechanomyography with baseline values close to train-of-four ratio 1.0, there is no need for normalization. The electromyography response is less influenced by temperature changes than mechanical techniques. The advantages with electromyography compared to acceleromyography comes at a cost; all FDA-approved stand-alone electromyography monitors require proprietary, single-use electrodes that often cost \$15 to \$20 each. Acceleromyography can be *normalized* (the train-of-four ratio as a fraction of the baseline train-of-four ratio, which is often greater than 1.0) or *nonnormalized* (no baseline measurement). Nonnormalized acceleromyography measures the train-of-four ratio approximately 0.1 higher than mechanomyography, but normalized acceleromyography is fairly similar to mechanomyography.⁵⁸ Acceleromyography units can measure acceleration of the thumb in one direction (uniaxial) or in three directions (triaxial), the latter of which is more common in newer devices. There are limited data comparing uniaxial and triaxial acceleromyography (see supplemental table S24, <http://links.lww.com/ALN/C928>). Some manufacturers of acceleromyographs have incorporated their own proprietary algorithms to the displayed train-of-four ratio values. This includes either suppressing any value higher than 1.0 (*i.e.*, displaying 1.0 when the value is actually higher) or calculating the ratio as T4/T2. It is important for the clinician to be aware of these modifications.

Preload is defined as the application of a set resistance to thumb movement that has been used with mechanomyography and acceleromyography. Preload may improve acceleromyography precision, but the data are limited.

In studies comparing devices, the time to a specified train-of-four ratio offers some indirect insight regarding the safety of the device (supplemental table S26, <http://links.lww.com/ALN/C928>). Technologies that show longer time to recovery to a specified train-of-four ratio are thought to offer greater safety. This is in the context of no known devices that provide erroneously low train-of-four ratios. The literature suggests that the time to train-of-four ratio of 0.9 is as follows, in order of longest to shortest (highest to lowest margin of safety): mechanomyography \approx electromyography $>$ acceleromyography.

Monitoring Sites

While different eye muscles have different characteristics, distinguishing the evoked responses from orbicularis oculi and corrugator supercilii muscles is often difficult.^{39,51} We therefore make the same recommendations for all eye muscles. The adductor pollicis muscle recovers more slowly than the corrugator supercilii or orbicularis oculi muscle. There are higher simultaneous train-of-four ratios at the corrugator supercilii and orbicularis oculi muscles compared with the adductor pollicis. *Residual neuromuscular blockade* is defined as a train-of-four ratio less than 0.9 at the adductor pollicis muscle, and it is therefore optimal to confirm adequate recovery by obtaining a valid measurement at this site. A valid measurement of the depth of the neuromuscular blockade is also essential to guide selection of the pharmacological antagonist drug and dosage. Therefore, if intraoperative neuromuscular monitoring has been performed at the eye muscles because no other site was easily accessible intraoperatively, then we recommend changing the site to the adductor pollicis muscle before antagonism. Dosage recommendations for pharmacological antagonist drugs are based on the adductor pollicis muscle responses. When monitoring at the corrugator supercilii muscle, dosage recommendations approved by the FDA for sugammadex are not applicable.⁵⁴ For these reasons, the adductor pollicis muscle is a safer option than the orbicularis oculi or corrugator supercilii. The time to recovery is similar between the adductor pollicis and masseter muscles, although the data are very limited.

In the hand, there are three muscles most commonly monitored using electromyography. These muscles are the adductor pollicis (palmar portion of the thumb), the first dorsal interosseous (posterior aspect of hand between the thumb and index finger), and the abductor digiti minimi (medial aspect of palm proximal to the pinky finger). The reference site of measurement is the adductor pollicis muscle. Train-of-four ratios at the adductor pollicis and first dorsal interosseous muscles are similar when measured simultaneously, and therefore, it appears reasonable to use data interchangeably between these sites, especially if the adductor pollicis muscle is not available or signal quality is poor. Train-of-four ratios at the adductor pollicis muscle are lower than the abductor digiti minimi when measured simultaneously, indicating a relative resistance to neuromuscular blockade at the abductor digiti minimi. Therefore,

data from the abductor digiti minimi muscle should be used with caution to guide neuromuscular blockade management (understanding the patient is more deeply paralyzed than the monitor indicates). Direct comparisons of the two alternate muscles, the first dorsal interosseous and the abductor digiti minimi, reveal the same pattern of relative resistance at the abductor digiti minimi muscle, reinforcing that measurements at the adductor pollicis and the first dorsal interosseous offer a higher margin of patient safety.

The time to recovery is similar between the adductor pollicis and masseter muscles, although the data are very limited. The data on the flexor hallucis muscle are inconsistent; however, the time to recovery is more similar between the adductor pollicis and flexor hallucis than between adductor pollicis and the eye muscles.

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Address correspondence to American Society of Anesthesiologists: 1061 American Lane, Schaumburg, Illinois 60173. kdomino@uw.edu. This Practice Guideline, as well as all published ASA Practice Parameters, may be obtained at no cost through the Journal Web site, <https://pubs.asahq.org/anesthesiology>.

Supplemental Digital Content

Systematic Review Protocol, <http://links.lww.com/ALN/C924>
PRISMA Diagram, <http://links.lww.com/ALN/C925>

Search Strategy, <http://links.lww.com/ALN/C926>
 Excluded Studies, <http://links.lww.com/ALN/C927>
 Supplemental Tables, <http://links.lww.com/ALN/C928>
 Supplemental Figures, <http://links.lww.com/ALN/C929>
 Methods Supplement, <http://links.lww.com/ALN/C956>

References

- Kopman AF, Brull SJ: Is postoperative residual neuromuscular block associated with adverse clinical outcomes? What is the evidence? *Curr Anesthesiol Rep* 2013; 3:114–21
- Murphy GS, Brull SJ: Residual neuromuscular block: Lessons unlearned. Part I: Definitions, incidence, and adverse physiologic effects of residual neuromuscular block. *Anesth Analg* 2010; 111:120–8
- Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS, Nisman M: Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. *ANESTHESIOLOGY* 2008; 109:389–98
- Sauer M, Stahn A, Soltesz S, Noeldge-Schomburg G, Mencke T: The influence of residual neuromuscular block on the incidence of critical respiratory events: A randomised, prospective, placebo-controlled trial. *Eur J Anaesthesiol* 2011; 28:842–8
- Ali HH, Utting JE, Gray C: Stimulus frequency in the detection of neuromuscular block in humans. *Br J Anaesth* 1970; 42:967–78
- Viby-Mogensen J, Jørgensen BC, Ording H: Residual curarization in the recovery room. *ANESTHESIOLOGY* 1979; 50:539–41
- Kopman AF, Yee PS, Neuman GG: Relationship of the train-of-four fade ratio to clinical signs and symptoms of residual paralysis in awake volunteers. *ANESTHESIOLOGY* 1997; 86:765–71
- Heier T, Caldwell JE, Feiner JR, Liu L, Ward T, Wright PMC: Relationship between normalized adductor pollicis train-of-four ratio and manifestations of residual neuromuscular block: A study using acceleromyography during near steady-state concentrations of mivacurium. *ANESTHESIOLOGY* 2010; 113:825–32
- Eriksson LI, Sato M, Severinghaus JW: Effect of a vecuronium-induced partial neuromuscular block on hypoxic ventilatory response. *ANESTHESIOLOGY* 1993; 78:693–9
- Eikermann M, Groeben H, Hüsing J, Peters J: Accelerometry of adductor pollicis muscle predicts recovery of respiratory function from neuromuscular blockade. *ANESTHESIOLOGY* 2003; 98:1333–7
- Eriksson LI, Sundman E, Olsson R, Nilsson L, Witt H, Ekberg O, Kuylenstierna R: Functional assessment of the pharynx at rest and during swallowing in partially paralyzed humans: Simultaneous videomanometry and mechanomyography of awake human volunteers. *ANESTHESIOLOGY* 1997; 87:1035–43
- Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Marymont JH, Vender JS, Gray J, Landry E, Gupta DK: Intraoperative acceleromyography monitoring reduces symptoms of muscle weakness and improves quality of recovery in the early postoperative period. *ANESTHESIOLOGY* 2011; 115:946–54
- Butterly A, Bittner EA, George E, Sandberg WS, Eikermann M, Schmidt U: Postoperative residual curarization from intermediate-acting neuromuscular blocking agents delays recovery room discharge. *Br J Anaesth* 2010; 105:304–9
- Fortier LP, McKeen D, Turner K, de Médicis E, Warriner B, Jones PM, Chaput A, Pouliot JF, Galarneau A: The RECITE Study: A Canadian prospective, multicenter study of the incidence and severity of residual neuromuscular blockade. *Anesth Analg* 2015; 121:366–72
- Saager L, Maiese EM, Bash LD, Meyer TA, Minkowitz H, Groudine S, Philip BK, Tanaka P, Gan TJ, Rodriguez-Blanco Y, Soto R, Heisel O: Incidence, risk factors, and consequences of residual neuromuscular block in the United States: The prospective, observational, multicenter RECITE-US study. *J Clin Anesth* 2019; 55:33–41
- Caldwell JE: Reversal of residual neuromuscular block with neostigmine at one to four hours after a single intubating dose of vecuronium. *Anesth Analg* 1995; 80:1168–74
- Debaene B, Plaud B, Dilly MP, Donati F: Residual paralysis in the PACU after a single intubating dose of nondepolarizing muscle relaxant with an intermediate duration of action. *ANESTHESIOLOGY* 2003; 98:1042–8
- Naguib M, Kopman AF, Ensor JE: Neuromuscular monitoring and postoperative residual curarisation: A meta-analysis. *Br J Anaesth* 2007; 98:302–16
- Plaud B, Debaene B, Donati F, Marty J: Residual paralysis after emergence from anesthesia. *ANESTHESIOLOGY* 2010; 112:1013–22
- Viby-Mogensen J, Jensen NH, Engbaek J, Ording H, Skovgaard LT, Chraemmer-Jørgensen B: Tactile and visual evaluation of the response to train-of-four nerve stimulation. *ANESTHESIOLOGY* 1985; 63:440–3
- Carvalho H, Verdonck M, Cools W, Geerts L, Forget P, Poelaert J: Forty years of neuromuscular monitoring and postoperative residual curarisation: A meta-analysis and evaluation of confidence in network meta-analysis. *Br J Anaesth* 2020; 125:466–82
- Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G, Alderson P, Glasziou P, Falck-Ytter Y, Schünemann HJ: GRADE guidelines: 2. Framing the question and deciding on important outcomes. *J Clin Epidemiol* 2011; 64:395–400

23. Xu C, Ju K, Lin L, Jia P, Kwong JSW, Syed A, Furuya-Kanamori L: Rapid evidence synthesis approach for limits on the search date: How rapid could it be? *Res Synth Methods* 2022; 13:68–76
24. Evidence Partners: DistillerSR. Ottawa, Canada, 2020
25. Yang B, Olsen M, Vali Y, Langendam MW, Takwoingi Y, Hyde CJ, Bossuyt PMM, Leeflang MMG: Study designs for comparative diagnostic test accuracy: A methodological review and classification scheme. *J Clin Epidemiol* 2021; 138:128–38
26. R Core Team: R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria, 2022
27. Balduzzi S, Rücker G, Schwarzer G: How to perform a meta-analysis with R: A practical tutorial. *Evid Based Ment Health* 2019; 22:153–60
28. Rücker G, Krahn U, König J, Efthimiou O, Davies A, Papakonstantinou T, Schwarzer G: netmeta: Network meta-analysis using frequentist methods. R package version 2.5-0. Available at: <https://CRAN.R-project.org/package=netmeta>. Accessed October 10, 2022.
29. Schwarzer G, Carpenter JR, Rücker G: metasens: Statistical methods for sensitivity analysis in meta-analysis. R package version 1.5-0, Available at: <https://CRAN.R-project.org/package=metasens>. Accessed October 10, 2022.
30. Schwarzer G, Carpenter JR, Rücker G: Meta-analysis with R. New York, Springer, 2015
31. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA: Cochrane Bias Methods Group, Cochrane Statistical Methods Group: The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011; 343:d5928
32. Sterne JA, Hernán MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hrobjartsson A, Kirkham J, Juni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JP: ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016; 355:i4919.
33. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MM, Sterne JA, Bossuyt PM, QUADAS-2 Group: A revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011; 155:529–36
34. Busse J, Guyatt G: Tool to assess risk of bias in cohort studies. Available at: <https://www.evidencepartners.com/resources/methodological-resources/tool-to-assess-risk-of-bias-in-cohort-studies-distillersr>. Accessed October 18, 2022.
35. Schünemann H, Brozek J, Guyatt G, Oxman A: GRADE handbook. Available at: <https://gdt.gradepro.org/app/handbook/handbook.html>. Accessed October 10, 2022.
36. Nikolakopoulou A, Higgins JPT, Papakonstantinou T, Chaimani A, Del Giovane C, Egger M, Salanti G: CINeMA: An approach for assessing confidence in the results of a network meta-analysis. *PLoS Med* 2020; 17:e1003082
37. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, Nasser M, Meerpohl J, Post PN, Kunz R, Brozek J, Vist G, Rind D, Akl EA, Schünemann HJ: GRADE guidelines: 14. Going from evidence to recommendations: The significance and presentation of recommendations. *J Clin Epidemiol* 2013; 66:719–25
38. Andrews JC, Schünemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA, Rind D, Montori VM, Brito JP, Norris S, Elbarbary M, Post P, Nasser M, Shukla V, Jaeschke R, Brozek J, Djulbegovic B, Guyatt G: GRADE guidelines: 15. Going from evidence to recommendation—determinants of a recommendation's direction and strength. *J Clin Epidemiol* 2013; 66:726–35
39. Gatke MR, Viby-Mogensen J, Rosenstock C, Jensen FS, Skovgaard LT: Postoperative muscle paralysis after rocuronium: Less residual block when acceleromyography is used. *Acta Anaesthesiol Scand* 2002; 46:207–13
40. Mortensen CR, Berg H, el-Mahdy A, Viby-Mogensen J: Perioperative monitoring of neuromuscular transmission using acceleromyography prevents residual neuromuscular block following pancuronium. *Acta Anaesthesiol Scand* 1995; 39:797–801
41. Wardhana A, Kurniawaty J, Uyun Y: Optimised reversal without train-of-four monitoring *versus* reversal using quantitative train-of-four monitoring: An equivalence study. *Indian J Anaesth* 2019; 63:361–7
42. Alenezi FK, Alnababtah K, Alqahtani MM, Olayan L, Alharbi M: The association between residual neuromuscular blockade (RNMB) and critical respiratory events: A prospective cohort study. *Perioper Med (Lond)* 2021; 10:14
43. Domenech G, Kampel MA, Garcia Guzzo ME, Novas DS, Terrasa SA, Fornari GG: Usefulness of intra-operative neuromuscular blockade monitoring and reversal agents for postoperative residual neuromuscular blockade: A retrospective observational study. *BMC Anesthesiol* 2019; 19:143
44. Todd MM, Hindman BJ, King BJ: The implementation of quantitative electromyographic neuromuscular monitoring in an academic anesthesia department. *Anesth Analg* 2014; 119:323–31
45. Kirmeier E, Eriksson LI, Lewald H, Jonsson Fagerlund M, Hoeft A, Hollmann M, Meistelman C, Hunter JM, Ulm K, Blobner M; POPULAR Contributors: Post-anaesthesia pulmonary complications after use

- of muscle relaxants (POPULAR): A multicentre, prospective observational study. *Lancet Respir Med* 2019; 7:129–40
46. Weigel WA, Williams BL, Hanson NA, Blackmore CC, Johnson RL, Nissen GM, James AB, Strodtbeck WM: Quantitative neuromuscular monitoring in clinical practice: A professional practice change initiative. *ANESTHESIOLOGY* 2022; 136:901–15
 47. Ademba I, Mung'ayi V, Premji Z, Kanya D: A randomized control trial comparing train of four ratio > 0.9 to clinical assessment of return of neuromuscular function before endotracheal extubation on critical respiratory events in adult patients undergoing elective surgery at a tertiary hospital in Nairobi. *Afr Health Sci* 2018; 18:807–16
 48. Goyal S, Kothari N, Chaudhary D, Verma S, Bihani P, Rodha MS: Reversal agents: Do we need to administer with neuromuscular monitoring—An observational study. *Indian J Anaesth* 2018; 62:219–24
 49. Abdulatif M, el-Sanabary M: Blood flow and mivacurium-induced neuromuscular block at the orbicularis oculi and adductor pollicis muscles. *Br J Anaesth* 1997; 79:24–8
 50. Larsen PB, Gatke MR, Fredensborg BB, Berg H, Engbaek J, Viby-Mogensen J: Acceleromyography of the orbicularis oculi muscle II: Comparing the orbicularis oculi and adductor pollicis muscles. *Acta Anaesthesiol Scand* 2002; 46:1131–6
 51. Plaud B, Debaene B, Donati F: The corrugator supercilii, not the orbicularis oculi, reflects rocuronium neuromuscular blockade at the laryngeal adductor muscles. *ANESTHESIOLOGY* 2001; 95:96–101
 52. Suzuki T, Mizutani H, Miyake E, Fukano N, Saeki S, Ogawa S: Infusion requirements and reversibility of rocuronium at the corrugator supercilii and adductor pollicis muscles. *Acta Anaesthesiol Scand* 2009; 53:1336–40
 53. Thudium M, Kornilov E, Raczeck L, Boehm O: Pulmonary function decline in immediate postoperative period is not necessarily related to residual neuromuscular block: An observational study. *Eur J Anaesthesiol* 2020; 37:1008–13
 54. Yamamoto S, Yamamoto Y, Kitajima O, Maeda T, Suzuki T: Reversal of neuromuscular block with sugammadex: A comparison of the corrugator supercilii and adductor pollicis muscles in a randomized dose–response study. *Acta Anaesthesiol Scand* 2015; 59:892–901
 55. Le Merrer M, Frasca D, Dupuis M, Debaene B, Boisson M: A comparison between the flexor hallucis brevis and adductor pollicis muscles in atracurium-induced neuromuscular blockade using acceleromyography: A prospective observational study. *Eur J Anaesthesiol* 2020; 37:38–43
 56. Vega EA, Ibacache ME, Anderson BJ, Holford NH, Nazar CE, Solari S, Allende FA, Cortinez LI: Rocuronium pharmacokinetics and pharmacodynamics in the adductor pollicis and masseter muscles. *Acta Anaesthesiol Scand* 2016; 60:734–46
 57. Thilen SR, Hansen BE, Ramaiah R, Kent CD, Treggiari MM, Bhananker SM: Intraoperative neuromuscular monitoring site and residual paralysis. *ANESTHESIOLOGY* 2012; 117:964–72
 58. Baykara N: High incidence of residual curarization after rocuronium despite administration of neostigmine. *Turk Klinik J Med Sci* 2010; 30:1325–31
 59. Alday E, Munoz M, Planas A, Mata E, Alvarez C: Effects of neuromuscular block reversal with sugammadex *versus* neostigmine on postoperative respiratory outcomes after major abdominal surgery: A randomized-controlled trial. *Can J Anaesth* 2019; 66:1328–37
 60. Boggett S, Chahal R, Griffiths J, Lin J, Wang D, Williams Z, Riedel B, Bowyer A, Royse A, Royse C: A randomised controlled trial comparing deep neuromuscular blockade reversed with sugammadex with moderate neuromuscular block reversed with neostigmine. *Anaesthesia* 2020; 75:1153–63
 61. Brueckmann B, Sasaki N, Grobara P, Li MK, Woo T, de Bie J, Maktabi M, Lee J, Kwo J, Pino R, Sabouri AS, McGovern F, Staehr-Rye AK, Eikermann M: Effects of sugammadex on incidence of postoperative residual neuromuscular blockade: A randomized, controlled study. *Br J Anaesth* 2015; 115:743–51
 62. Khuenl-Brady KS, Wattwil M, Vanacker BE, Lora-Tamayo JI, Rietbergen H, Alvarez-Gomez JA: Sugammadex provides faster reversal of vecuronium-induced neuromuscular blockade compared with neostigmine: A multicenter, randomized, controlled trial. *Anesth Analg* 2010; 110:64–73
 63. Lee YJ, Oh AY, Koo BW, Han JW, Park JH, Hong JP, Seo KS: Postoperative residual neuromuscular blockade after reversal based on a qualitative peripheral nerve stimulator response: A randomised controlled trial. *Eur J Anaesthesiol* 2020; 37:196–202
 64. Nemes R, Fulesdi B, Pongracz A, Asztalos L, Szabo-Maak Z, Lengyel S, Tassonyi E: Impact of reversal strategies on the incidence of postoperative residual paralysis after rocuronium relaxation without neuromuscular monitoring: A partially randomised placebo controlled trial. *Eur J Anaesthesiol* 2017; 34:609–16
 65. Sabo D, Kevin Jones R, Berry J, Sloan T, Chen J-Y: Residual neuromuscular blockade at extubation: A randomized comparison of sugammadex and neostigmine reversal of rocuronium-induced blockade in patients undergoing abdominal surgery. *J Anesth Clin Res* 2011; 2:1000140
 66. Togioka BM, Yanez D, Aziz ME, Higgins JR, Tekkali P, Treggiari MM: Randomised controlled trial of sugammadex or neostigmine for reversal of neuromuscular block on the incidence of pulmonary complications in older adults undergoing prolonged surgery. *Br J Anaesth* 2020; 124:553–61

67. Wu X, Oerding H, Liu J, Vanacker B, Yao S, Dahl V, Xiong L, Claudius C, Yue Y, Huang Y, Abels E, Rietbergen H, Woo T: Rocuronium blockade reversal with sugammadex *vs.* neostigmine: Randomized study in Chinese and Caucasian subjects. *BMC Anesthesiol* 2014; 14:53
68. Schaller SJ, Fink H, Ulm K, Blobner M: Sugammadex and neostigmine dose-finding study for reversal of shallow residual neuromuscular block. *ANESTHESIOLOGY* 2010; 113:1054–60
69. Jones RK, Caldwell JE, Brull SJ, Soto RG: Reversal of profound rocuronium-induced blockade with sugammadex: A randomized comparison with neostigmine. *ANESTHESIOLOGY* 2008; 109:816–24
70. Lemmens HJ, El-Orbany MI, Berry J, Morte JB Jr, Martin G: Reversal of profound vecuronium-induced neuromuscular block under sevoflurane anesthesia: Sugammadex *versus* neostigmine. *BMC Anesthesiol* 2010; 10:15
71. Sacan O, White PF, Tufanogullari B, Klein K: Sugammadex reversal of rocuronium-induced neuromuscular blockade: A comparison with neostigmine-glycopyrrolate and edrophonium-atropine. *Anesth Analg* 2007; 104:569–74
72. Abdulatif M, Lotfy M, Mousa M, Afifi MH, Yassen K: Sugammadex antagonism of rocuronium-induced neuromuscular blockade in patients with liver cirrhosis undergoing liver resection: A randomized controlled study. *Minerva Anesthesiol* 2018; 84:929–37
73. Adamus M, Hrabalek L, Wanek T, Gabrhelik T, Zapletalova J: Intraoperative reversal of neuromuscular block with sugammadex or neostigmine during extreme lateral interbody fusion, a novel technique for spine surgery. *J Anesth* 2011; 25:716–20
74. Blobner M, Eriksson LI, Scholz J, Motsch J, Della Rocca G, Prins ME: Reversal of rocuronium-induced neuromuscular blockade with sugammadex compared with neostigmine during sevoflurane anaesthesia: Results of a randomised, controlled trial. *Eur J Anaesthesiol* 2010; 27:874–81
75. Cheong SH, Ki S, Lee J, Lee JH, Kim MH, Hur D, Cho K, Lim SH, Lee KM, Kim YJ, Lee W: The combination of sugammadex and neostigmine can reduce the dosage of sugammadex during recovery from the moderate neuromuscular blockade. *Korean J Anesthesiol* 2015; 68:547–55
76. Farag E, Rivas E, Bravo M, Hussain S, Argalious M, Khanna S, Seif J, Pu X, Mao G, Bain M, Elgabaly M, Esa WAS, Sessler DI: Sugammadex *versus* neostigmine for reversal of rocuronium neuromuscular block in patients having catheter-based neurointerventional procedures: A randomized trial. *Anesth Analg* 2021; 132:1666–76
77. Flockton EA, Mastronardi P, Hunter JM, Gomar C, Mirakhur RK, Aguilera L, Giunta FG, Meistelman C, Prins ME: Reversal of rocuronium-induced neuromuscular block with sugammadex is faster than reversal of cisatracurium-induced block with neostigmine. *Br J Anaesth* 2008; 100:622–30
78. Gaszynski T, Szweczyk T, Gaszynski W: Randomized comparison of sugammadex and neostigmine for reversal of rocuronium-induced muscle relaxation in morbidly obese undergoing general anaesthesia. *Br J Anaesth* 2012; 108:236–9
79. Geldner G, Niskanen M, Laurila P, Mizikov V, Hubler M, Beck G, Rietbergen H, Nicolayenko E: A randomised controlled trial comparing sugammadex and neostigmine at different depths of neuromuscular blockade in patients undergoing laparoscopic surgery. *Anaesthesia* 2012; 67:991–8
80. Illman HL, Laurila P, Antila H, Meretoja OA, Alahuhta S, Olkkola KT: The duration of residual neuromuscular block after administration of neostigmine or sugammadex at two visible twitches during train-of-four monitoring. *Anesth Analg* 2011; 112:63–8
81. Kurçaloğlu M, Sanhasan BB, Çetinoğlu EC: Comparing the effects of sugammadex and neostigmine on neuromuscular block and bispectral index in recovery from intracranial mass resection operations. *Eastern J Med* 2020; 25:371–7
82. Mekawy N, Fouad Ali EA: Improved recovery profiles in sinonasal surgery sugammadex: Does it have a role? *Egypt J Anaesth* 2019; 28:175–8
83. Suganuma E, Ishikawa T, Kitamura Y, Hayashida T, Matsumura T, Fujie M, Nozaki-Taguchi N, Sato Y, Isono S: Recovery of lower oesophageal barrier function: A pilot study comparing a mixture of atropine and neostigmine and sugammadex: A randomised controlled pilot study. *Eur J Anaesthesiol* 2021; 38:856–64
84. Dong LV, Giang NT, Cuong NM, Dinh NV, Anh VT, Hanh MD, Khanh DT, Thuy LQ, Son LT, Thu ND, Kien NT: Reversal of deep effect of rocuronium by sugammadex or neostigmine after abdominal laparoscopic surgery: A single center experience in Vietnam. *Open Access Macedonian J Med Sci* 2020; 8:295–300
85. Woo T, Kim KS, Shim YH, Kim MK, Yoon SM, Lim YJ, Yang HS, Phiri P, Chon JY: Sugammadex *versus* neostigmine reversal of moderate rocuronium-induced neuromuscular blockade in Korean patients. *Korean J Anesthesiol* 2013; 65:501–7
86. Asztalos L, Szabo-Maak Z, Gajdos A, Nemes R, Pongracz A, Lengyel S, Fulesdi B, Tassonyi E: Reversal of vecuronium-induced neuromuscular blockade with low-dose sugammadex at train-of-four count of four: A randomized controlled trial. *ANESTHESIOLOGY* 2017; 127:441–9
87. He J, He H, Li X, Sun M, Lai Z, Xu B: Required dose of sugammadex or neostigmine for reversal of vecuronium-induced shallow residual neuromuscular block at a train-of-four ratio of 0.3. *Clin Transl Sci* 2022; 15:234–43
88. Pongracz A, Szatmari S, Nemes R, Fulesdi B, Tassonyi E: Reversal of neuromuscular blockade with sugammadex

- at the reappearance of four twitches to train-of-four stimulation. *ANESTHESIOLOGY* 2013; 119:36–42
89. El Sherbeny MA, Elrahman EAA, Kamal RK, Abozena MAM: Efficacy and safety of sugammadex in reversing nmb (rocuronium) in adults. *NY Sci J* 2017; 10:22–9
 90. Kaufhold N, Schaller SJ, Stauble CG, Baumuller E, Ulm K, Blobner M, Fink H: Sugammadex and neostigmine dose-finding study for reversal of residual neuromuscular block at a train-of-four ratio of 0.2 (SUNDRO20). *Br J Anaesth* 2016; 116:233–40
 91. Ruetzler K, Li K, Chhabada S, Maheshwari K, Chahar P, Khanna S, Schmidt MT, Yang D, Turan A, Sessler DI: Sugammadex *versus* neostigmine for reversal of residual neuromuscular blocks after surgery: A retrospective cohort analysis of postoperative side effects. *Anesth Analg* 2022; 134:1043–53
 92. Horrow JC, Li W, Blobner M, Lombard J, Speck M, DeAngelis M, Herring WJ: Actual *versus* ideal body weight dosing of sugammadex in morbidly obese patients offers faster reversal of rocuronium- or vecuronium-induced deep or moderate neuromuscular block: A randomized clinical trial. *BMC Anesthesiol* 2021; 21:62
 93. Kheterpal S, Vaughn MT, Dubovoy TZ, Shah NJ, Bash LD, Colquhoun DA, Shanks AM, Mathis MR, Soto RG, Bardia A, Bartels K, McCormick PJ, Schonberger RB, Saager L: Sugammadex *versus* neostigmine for reversal of neuromuscular blockade and postoperative pulmonary complications (STRONGER): A multi-center matched cohort analysis. *ANESTHESIOLOGY* 2020; 132:1371–81
 94. Orihara M, Takazawa T, Horiuchi T, Sakamoto S, Nagumo K, Tomita Y, Tomioka A, Yoshida N, Yokohama A, Saito S: Comparison of incidence of anaphylaxis between sugammadex and neostigmine: A retrospective multicentre observational study. *Br J Anaesth* 2020; 124:154–63
 95. Herring WJ, Mukai Y, Wang A, Lutkiewicz J, Lombard JF, Lin L, Watkins M, Broussard DM, Blobner M: A randomized trial evaluating the safety profile of sugammadex in high surgical risk ASA physical class 3 or 4 participants. *BMC Anesthesiol* 2021; 21:259
 96. Burbridge MA: Incidence of anaphylaxis to sugammadex in a single-center cohort of 19,821 patients. *Anesth Analg* 2021; 132:93–7
 97. Miyazaki Y, Sunaga H, Kida K, Hobo S, Inoue N, Muto M, Uezono S: Incidence of anaphylaxis associated with sugammadex. *Anesth Analg* 2018; 126:1505–8
 98. Moon TS, Reznik S, Pak T, Jan K, Pruszyński J, Kim A, Smith KM, Lu R, Chen J, Gasanova I, Fox PE, Ogunnaike B: Sugammadex *versus* neostigmine for reversal of rocuronium-induced neuromuscular blockade: A randomized, double-blinded study of thoracic surgical patients evaluating hypoxic episodes in the early postoperative period. *J Clin Anesth* 2020; 64:109804
 99. Niu L, Wang Y, Yao C, Sun Y, Yao S, Lin Y: Efficacy and safety of neuromuscular blockade in overweight patients undergoing nasopharyngeal surgery. *Med Sci Monit* 2020; 26:e926452
 100. Quang TL, Thu HNT, Quoc KN, Thu HN, Van DP, Tien NLB, Thanh VV, Nga VT, Toi CD: Neuromuscular blockade agents reversal with sugammadex compared to neostigmine in the living kidney donors. *Open Access Macedonian J Med Sci* 2019; 7:4420–5
 101. Mraovic B, Timko NJ, Choma TJ: Comparison of recovery after sugammadex or neostigmine reversal of rocuronium in geriatric patients undergoing spine surgery: A randomized controlled trial. *Croat Med J* 2021; 62:606–13
 102. Claroni C, Covotta M, Torregiani G, Marcelli ME, Tuderti G, Simone G, Scotto di Uccio A, Zinilli A, Forastiere E: Recovery from anesthesia after robotic-assisted radical cystectomy: Two different reversals of neuromuscular blockade. *J Clin Med* 2019; 8:1774
 103. Koyuncu O, Turhanoglu S, Ozbakis Akkurt C, Karcioğlu M, Ozkan M, Ozer C, Sessler DI, Turan A: Comparison of sugammadex and conventional reversal on postoperative nausea and vomiting: A randomized, blinded trial. *J Clin Anesth* 2015; 27:51–6
 104. Lee TY, Jeong SY, Jeong JH, Kim JH, Choi SR: Comparison of postoperative pulmonary complications between sugammadex and neostigmine in lung cancer patients undergoing video-assisted thoracoscopic lobectomy: A prospective double-blinded randomized trial. *Anesth Pain Med (Seoul)* 2021; 16:60–7
 105. Ledowski T, Hillyard S, O'Dea B, Archer R, Vilas-Boas F, Kyle B: Introduction of sugammadex as standard reversal agent: Impact on the incidence of residual neuromuscular blockade and postoperative patient outcome. *Indian J Anaesth* 2013; 57:46–51
 106. Li G, Freundlich RE, Gupta RK, Hayhurst CJ, Le CH, Martin BJ, Shotwell MS, Wanderer JP: Postoperative pulmonary complications' association with sugammadex *versus* neostigmine: A retrospective registry analysis. *ANESTHESIOLOGY* 2021; 134:862–73
 107. Cho HY, Kim H, Yoon S, Lee HJ, Kim H, Lee HC, Kim WH, Jang JY: Effect of sugammadex on the recovery of gastrointestinal motility after open pancreaticoduodenectomy: A single-center retrospective study. *Minerva Anestesiol* 2021; 87:1100–8
 108. Cheng KI, Tse J, Li TY: The strategy to use sugammadex to reduce postoperative pulmonary complications after da Vinci surgery: A retrospective study. *J Pers Med* 2022; 12:52
 109. Yu J, Park JY, Lee Y, Hwang JH, Kim YK: Sugammadex *versus* neostigmine on postoperative pulmonary complications after robot-assisted laparoscopic

- prostatectomy: A propensity score-matched analysis. *J Anesth* 2021; 35:262–9
110. Ledowski T, Szabo-Maak Z, Loh PS, Turlach BA, Yang HS, de Boer HD, Asztalos L, Shariffuddin II, Chan L, Fulesdi B: Reversal of residual neuromuscular block with neostigmine or sugammadex and postoperative pulmonary complications: A prospective, randomised, double-blind trial in high-risk older patients. *Br J Anaesth* 2021; 127:316–23
 111. Carron M, Veronese S, Foletto M, Ori C: Sugammadex allows fast-track bariatric surgery. *Obes Surg* 2013; 23:1558–63
 112. Schepens T, Janssens K, Maes S, Wildemeersch D, Vellinga J, Jorens PG, Saldien V: Respiratory muscle activity after spontaneous, neostigmine- or sugammadex-enhanced recovery of neuromuscular blockade: A double blind prospective randomized controlled trial. *BMC Anesthesiol* 2019; 19:187
 113. Unal DY, Baran I, Mutlu M, Ural G, Akkaya T, Ozlu O: Comparison of sugammadex *versus* neostigmine costs and respiratory complications in patients with obstructive sleep apnoea. *Turk J Anaesthesiol Reanim* 2015; 43:387–95
 114. Loh PS, Miskan MM, Chin YZ, Zaki RA: Staggering the dose of sugammadex lowers risks for severe emergence cough: A randomized control trial. *BMC Anesthesiol* 2017; 17:137
 115. Krause M, McWilliams SK, Bullard KJ, Mayes LM, Jameson LC, Mikulich-Gilbertson SK, Fernandez-Bustamante A, Bartels K: Neostigmine *versus* sugammadex for reversal of neuromuscular blockade and effects on reintubation for respiratory failure or newly initiated noninvasive ventilation: An interrupted time series design. *Anesth Analg* 2020; 131:141–51
 116. Llauradó S, Sabató A, Ferreres E, Camprubí I, Cabrera A: Postoperative respiratory outcomes in laparoscopic bariatric surgery: Comparison of a prospective group of patients whose neuromuscular blockade was reverted with sugammadex and a historical one reverted with neostigmine. *Rev Esp Anesthesiol Reanim* 2014; 61:565–70
 117. Martinez-Ubieto J, Ortega-Lucea S, Pascual-Bellosta A, Arazo-Iglesias I, Gil-Bona J, Jimenez-Bernardo T, Munoz-Rodriguez L: Prospective study of residual neuromuscular block and postoperative respiratory complications in patients reversed with neostigmine *versus* sugammadex. *Minerva Anesthesiol* 2016; 82:735–42
 118. Choi ES, Oh AY, Koo BW, Hwang JW, Han JW, Seo KS, Ahn SH, Jeong WJ: Comparison of reversal with neostigmine of low-dose rocuronium *vs.* reversal with sugammadex of high-dose rocuronium for a short procedure. *Anaesthesia* 2017; 72:1185–90
 119. Baysal Çitil A, Alici Kuş Tuncel Z, Yapıcı N, Kudsioğlu T, Aykaç Z, Kavaklı AS: Reversal of rocuronium induced neuromuscular blockade in lung resection surgery: A comparison of sugammadex and neostigmine. *GKDA Derg* 2019; 25:23–30
 120. Castro DS Jr, Leao P, Borges S, Gomes L, Pacheco M, Figueiredo P: Sugammadex reduces postoperative pain after laparoscopic bariatric surgery: A randomized trial. *Surg Laparosc Endosc Percutan Tech* 2014; 24:420–3
 121. Hakimoglu S, Tuzcu K, Davarci I, Karcioglu M, Ayhan Tuzcu E, Hanci V, Aydin S, Kahraman H, Elbeyli A, Turhanoglu S: Comparison of sugammadex and neostigmine-atropine on intraocular pressure and postoperative effects. *Kaohsiung J Med Sci* 2016; 32:80–5
 122. Leslie K, Chan MTV, Darvall JN, De Silva AP, Braat S, Devlin NJ, Peyton PJ, Radnor J, Lam CKM, Sidiropoulos S, Story DA: Sugammadex, neostigmine and postoperative pulmonary complications: An international randomised feasibility and pilot trial. *Pilot Feasibility Stud* 2021; 7:200
 123. Nelskyla K, Yli-Hankala A, Soikkeli A, Korttila K: Neostigmine with glycopyrrolate does not increase the incidence or severity of postoperative nausea and vomiting in outpatients undergoing gynaecological laparoscopy. *Br J Anaesth* 1998; 81:757–60
 124. Putz L, Dransart C, Jamart J, Marotta ML, Delnooz G, Dubois PE: Operating room discharge after deep neuromuscular block reversed with sugammadex compared with shallow block reversed with neostigmine: A randomized controlled trial. *J Clin Anesth* 2016; 35:107–13
 125. Sen A, Erdivanli B, Tomak Y, Pergel A: Reversal of neuromuscular blockade with sugammadex or neostigmine/atropine: Effect on postoperative gastrointestinal motility. *J Clin Anesth* 2016; 32:208–13
 126. Yagan O, Tas N, Mutlu T, Hanci V: Comparison of the effects of sugammadex and neostigmine on postoperative nausea and vomiting. *Braz J Anesthesiol* 2017; 67:147–52
 127. Zhu B, Sun D, Yang L, Sun Z, Feng Y, Deng C: The effects of neostigmine on postoperative cognitive function and inflammatory factors in elderly patients—A randomized trial. *BMC Geriatr* 2020; 20:387
 128. von Quillfeldt S, Fohre B, Andrees N, Spies CD, Galvagni D, Jousen AM, Wernecke KD, Boemke W: Rocuronium reversed by sugammadex *versus* mivacurium during high-risk eye surgery: An institutional anaesthetic practice evaluation. *J Int Med Res* 2013; 41:1740–51
 129. John J, Perry G, Perry J, Guttenberg V, Asonganyi N, Laheji S, Raza J, Hall RG: Impact of neostigmine and sugammadex on time to leaving the operating room in a community hospital. *Innov Pharm* 2020; 11:3329

130. Kim JH, Lim MS, Choi JW, Kim H, Kwon YS, Lee JJ: Comparison of the effects of sugammadex, neostigmine, and pyridostigmine on postoperative nausea and vomiting: A propensity matched study of five hospitals. *J Clin Med* 2020; 9:1–11
131. Gu X, Gao R, Li P, Jiao D, Song T, Li T, Gu L: Sugammadex enhances recovery after abdominal surgery in cancer patients: A real-world, observational study. *Ann Palliat Med* 2021; 10:12566–74
132. Alkenany HM: Evaluation of cyclodextrin (sugammadex) for reversal of intense neuromuscular block of rocuronium and vecuronium, experimental and clinical studies. *J Egypt Soc Parasitol* 2013; 43:705–14
133. Boeke AJ, de Lange JJ, van Druenen B, Langemeijer JJ: Effect of antagonizing residual neuromuscular block by neostigmine and atropine on postoperative vomiting. *Br J Anaesth* 1994; 72:654–6
134. Hovorka J, Korttila K, Nelskylä K, Soikkeli A, Sarvela J, Paatero H, Halonen P, Yli-Hankala A: Reversal of neuromuscular blockade with neostigmine has no effect on the incidence or severity of postoperative nausea and vomiting. *Anesth Analg* 1997; 85:1359–61
135. Li D, Wang Y, Zhou Y, Yin C: Efficacy and safety of sugammadex doses calculated on the basis of corrected body weight and total body weight for the reversal of deep neuromuscular blockade in morbidly obese patients. *J Int Med Res* 2021; 49:300060520985679
136. Løvstad RZ, Thagaard KS, Berner NS, Raeder JC: Neostigmine 50 microg kg⁻¹ with glycopyrrolate increases postoperative nausea in women after laparoscopic gynaecological surgery. *Acta Anaesthesiol Scand* 2001; 45:495–500
137. McDonagh DL, Benedict PE, Kovac AL, Drover DR, Brister NW, Morte JB, Monk TG: Efficacy, safety, and pharmacokinetics of sugammadex for the reversal of rocuronium-induced neuromuscular blockade in elderly patients. *ANESTHESIOLOGY* 2011; 114:318–29
138. Paech MJ, Kaye R, Baber C, Nathan EA: Recovery characteristics of patients receiving either sugammadex or neostigmine and glycopyrrolate for reversal of neuromuscular block: A randomised controlled trial. *Anaesthesia* 2018; 73:340–7
139. Rahe-Meyer N, Berger C, Wittmann M, Solomon C, Abels EA, Rietbergen H, Reuter DA: Recovery from prolonged deep rocuronium-induced neuromuscular blockade: A randomized comparison of sugammadex reversal with spontaneous recovery. *Anaesthesist* 2015; 64:506–12
140. Tas Tuna A, Palabiyik O, Orhan M, Sonbahar T, Sayhan H, Tomak Y: Does sugammadex administration affect postoperative nausea and vomiting after laparoscopic cholecystectomy: A prospective, double-blind, randomized study. *Surg Laparosc Endosc Percutan Tech* 2017; 27:237–40
141. Williams WH III, Cata JP, Lasala JD, Navai N, Feng L, Gottumukkala V: Effect of reversal of deep neuromuscular block with sugammadex or moderate block by neostigmine on shoulder pain in elderly patients undergoing robotic prostatectomy. *Br J Anaesth* 2020; 124:164–72
142. Yazar E, Yilmaz C, Bilgin H, Karasu D, Bayraktar S, Apaydin Y, Sayan HE: A comparison of the effect of sugammadex on the recovery period and postoperative residual block in young elderly and middle-aged elderly patients. *Balkan Med J* 2016; 33:181–7
143. Badaoui R, Cabaret A, Alami Y, Zogheib E, Popov I, Lorne E, Dupont H: Reversal of neuromuscular blockade by sugammadex in laparoscopic bariatric surgery: In support of dose reduction. *Anaesth Crit Care Pain Med* 2016; 35:25–9
144. Joshi GP, Garg SA, Hailey A, Yu SY: The effects of antagonizing residual neuromuscular blockade by neostigmine and glycopyrrolate on nausea and vomiting after ambulatory surgery. *Anesth Analg* 1999; 89:628–31
145. Kirkegaard H, Heier T, Caldwell JE: Efficacy of tactile-guided reversal from cisatracurium-induced neuromuscular block. *ANESTHESIOLOGY* 2002; 96:45–50
146. Kim KS, Cheong MA, Lee HJ, Lee JM: Tactile assessment for the reversibility of rocuronium-induced neuromuscular blockade during propofol or sevoflurane anesthesia. *Anesth Analg* 2004; 99:1080–5
147. Fuchs-Buder T, Meistelman C, Alla F, Grandjean A, Wuthrich Y, Donati F: Antagonism of low degrees of atracurium-induced neuromuscular blockade: Dose-effect relationship for neostigmine. *ANESTHESIOLOGY* 2010; 112:34–40
148. Fuchs-Buder T, Baumann C, De Guis J, Guerci P, Meistelman C: Low-dose neostigmine to antagonise shallow atracurium neuromuscular block during inhalational anaesthesia: A randomised controlled trial. *Eur J Anaesthesiol* 2013; 30:594–8
149. Naguib M, Brull SJ, Kopman AF, Hunter JM, Fülesdi B, Arkes HR, Elstein A, Todd MM, Johnson KB: Consensus statement on perioperative use of neuromuscular monitoring. *Anesth Analg* 2018; 127:71–80
150. Miller RD, Van Nyhuis LS, Eger Vitez EITS, Way WL: Comparative times to peak effect and durations of action of neostigmine and pyridostigmine. *ANESTHESIOLOGY* 1974; 41:27–33
151. Chambers D, Paulden M, Paton F, Heirs M, Duffy S, Craig D, Hunter J, Wilson J, Sculpher M, Woolacott N: Sugammadex for the reversal of muscle relaxation in general anaesthesia: A systematic review and economic assessment. *Health Technol Assess* 2010; 14:1–211
152. Hurford WE, Welge JA, Eckman MH: Sugammadex versus neostigmine for routine reversal of rocuronium block in adult patients: A cost analysis. *J Clin Anesth* 2020; 67:110027

153. Kopman AF: Sugammadex: A revolutionary approach to neuromuscular antagonism. *ANESTHESIOLOGY* 2006; 104:631–3
154. Decoopman M, Cammu G, Suy K, Heeringa M, Demeyer I: Reversal of pancuronium-induced block by the selective relaxant binding agent sugammadex: 9AP2-1. *Eur J Anaesthesiol* 2007; 24:110
155. Goldhill DR, Carter JA, Suresh D, Whitehead JP, Flynn PJ: Antagonism of atracurium with neostigmine: Effect of dose on speed of recovery. *Anaesthesia* 1991; 46:496–9
156. Preault A, Capron F, Chantreau C, Donati F, Dimet J: Under sevoflurane anaesthesia, a reduced dose of neostigmine can antagonize a shallow neuromuscular block: A double-blind, randomised study. *Anaesth Crit Care Pain Med* 2016; 35:269–73
157. Song IA, Seo KS, Oh AY, No HJ, Hwang JW, Jeon YT, Park SH, Do SH: Timing of reversal with respect to three nerve stimulator end-points from cisatracurium-induced neuromuscular block. *Anaesthesia* 2015; 70:797–802
158. Olesnicki BL, Lindberg A, Marroquin-Harris FB, Ren K: A survey of current management of neuromuscular block and reversal in Australia and New Zealand. *Anaesth Intensive Care* 2021; 49:309–15
159. Naguib M, Kopman AF, Lien CA, Hunter JM, Lopez A, Brull SJ: A survey of current management of neuromuscular block in the United States and Europe. *Anesth Analg* 2010; 111:110–9
160. Kopman AF: Surrogate endpoints and neuromuscular recovery. *ANESTHESIOLOGY* 1997; 87:1029–31
161. Videira RL, Vieira JE: What rules of thumb do clinicians use to decide whether to antagonize nondepolarizing neuromuscular blocking drugs? *Anesth Analg* 2011; 113:1192–6
162. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear T, Vender JS, Gray J, Landry E: Postoperative residual neuromuscular blockade is associated with impaired clinical recovery. *Anesth Analg* 2013; 117:133–41
163. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear TD, Vender JS, Parikh KN, Patel SS, Patel A: Residual neuromuscular block in the elderly: Incidence and clinical implications. *ANESTHESIOLOGY* 2015; 123:1322–36
164. Bronsert MR, Henderson WG, Monk TG, Richman JS, Nguyen JD, Sum-Ping JT, Mangione MP, Higley B, Hammermeister KE: Intermediate-acting nondepolarizing neuromuscular blocking agents and risk of postoperative 30-day morbidity and mortality, and long-term survival. *Anesth Analg* 2017; 124:1476–83
165. Fülesdi B, Brull SJ: Quantitative neuromuscular monitoring: “Love all, trust a few, do wrong to none.” *Anesth Analg* 2022; 135:35–8
166. Eriksson LI: Evidence-based practice and neuromuscular monitoring: It’s time for routine quantitative assessment. *ANESTHESIOLOGY* 2003; 98:1037–9
167. Miller RD, Ward TA: Monitoring and pharmacologic reversal of a nondepolarizing neuromuscular blockade should be routine. *Anesth Analg* 2010; 111:3–5
168. Baillard C, Clec’h C, Catineau J, Salhi F, Gehan G, Cupa M, Samama CM: Postoperative residual neuromuscular block: A survey of management. *Br J Anaesth* 2005; 95:622–6
169. Fruergaard K, Viby-Mogensen J, Berg H, el-Mahdy AM: Tactile evaluation of the response to double burst stimulation decreases, but does not eliminate, the problem of postoperative residual paralysis. *Acta Anaesthesiol Scand* 1998; 42:1168–74
170. Pedersen T, Viby-Mogensen J, Bang U, Olsen NV, Jensen E, Engboek J: Does perioperative tactile evaluation of the train-of-four response influence the frequency of postoperative residual neuromuscular blockade? *ANESTHESIOLOGY* 1990; 73:835–9
171. Ueda N, Muteki T, Tsuda H, Inoue S, Nishina H: Is the diagnosis of significant residual neuromuscular blockade improved by using double-burst nerve stimulation? *Eur J Anaesthesiol* 1991; 8:213–8
172. Shorten GD, Merk H, Sieber T: Perioperative train-of-four monitoring and residual curarization. *Can J Anaesth* 1995; 42:711–5
173. Cammu G, de Baerdemaeker L, den Blauwen N, de Mey JC, Struys M, Mortier E: Postoperative residual curarization with cisatracurium and rocuronium infusions. *Eur J Anaesthesiol* 2002; 19:129–34
174. El-Tahan MR, Regal M: Target-controlled infusion of remifentanyl without muscle relaxants allows acceptable surgical conditions during thoracotomy performed under sevoflurane anesthesia. *J Cardiothorac Vasc Anesth* 2015; 29:1557–66
175. Feltracco P, Tonetti T, Barbieri S, Frigo AC, Ori C: Cisatracurium- and rocuronium-associated residual neuromuscular dysfunction under intraoperative neuromuscular monitoring and postoperative neostigmine reversal: A single-blind randomized trial. *J Clin Anesth* 2016; 35:198–204
176. Koo CH, Chung SH, Kim BG, Min BH, Lee SC, Oh AY, Jeon YT, Ryu JH: Comparison between the effects of deep and moderate neuromuscular blockade during transurethral resection of bladder tumor on endoscopic surgical condition and recovery profile: A prospective, randomized, and controlled trial. *World J Urol* 2019; 37:359–65
177. Kopman AF, Kopman DJ, Ng J, Zank LM: Antagonism of profound cisatracurium and rocuronium block: The role of objective assessment of neuromuscular function. *J Clin Anesth* 2005; 17:30–5
178. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear TD, Deshur MA, Benson J, Newmark RL,

- Mahe CE: Neostigmine administration after spontaneous recovery to a train-of-four ratio of 0.9 to 1.0: A randomized controlled trial of the effect on neuromuscular and clinical recovery. *ANESTHESIOLOGY* 2018; 128:27–37
179. Staals LM, Snoeck MM, Driessen JJ, Flockton EA, Heeringa M, Hunter JM: Multicentre, parallel-group, comparative trial evaluating the efficacy and safety of sugammadex in patients with end-stage renal failure or normal renal function. *Br J Anaesth* 2008; 101:492–7
 180. Stourac P, Adamus M, Seidlova D, Pavlik T, Janku P, Krikava I, Mrozek Z, Prochazka M, Klucka J, Stoudek R, Bartikova I, Kosinova M, Harazim H, Robotkova H, Hejduk K, Hodicka Z, Kirchnerova M, Francakova J, Obare Pyszkova L, Hlozkova J, Sevcik P: Low-dose or high-dose rocuronium reversed with neostigmine or sugammadex for cesarean delivery anesthesia: A randomized controlled noninferiority trial of time to tracheal intubation and extubation. *Anesth Analg* 2016; 122:1536–45
 181. Baysal A, Sagiroglu G, Dogukan M, Ozkaynak I: Half-dose sugammadex after neostigmine *versus* neostigmine as a routine reversal agent: A pilot randomized trial. *J Perianesth Nurs* 2022; 37:326–2
 182. Della Rocca G, Pompei L, Paganis CPDE, Tesoro S, Mendola C, Boninsegni P, Tempia A, Manstretta S, Zamidei L, Gratarola A, Murabito P, Fuggiano L, Di Marco P: Reversal of rocuronium induced neuromuscular block with sugammadex or neostigmine: A large observational study. *Acta Anaesthesiol Scand* 2013; 57:1138–45
 183. Kopman AF, Ng J, Zank LM, Neuman GG, Yee PS: Residual postoperative paralysis. Pancuronium *versus* mivacurium, does it matter? *ANESTHESIOLOGY* 1996; 85:1253–9
 184. Murphy GS, Avram MJ, Greenberg SB, Bilimoria S, Benson J, Maher CE, Teister KJ, Szokol JW: Neuromuscular and clinical recovery in thoracic surgical patients reversed with neostigmine or sugammadex. *Anesth Analg* 2021; 133:435–44
 185. Azizoğlu M, Özdemir L: Quantitative neuromuscular monitoring with train-of-four ratio during elective surgery: A prospective, observational study. *J Patient Saf* 2021; 17:352–7
 186. Batistaki C, Tentes P, Deligiannidi P, Karakosta A, Florou P, Kostopanagiotou G: Residual neuromuscular blockade in a real life clinical setting: Correlation with sugammadex or neostigmine administration. *Minerva Anesthesiol* 2016; 82:550–8
 187. Cammu GV, Smet V, De Jongh K, Vandeput D: A prospective, observational study comparing postoperative residual curarisation and early adverse respiratory events in patients reversed with neostigmine or sugammadex or after apparent spontaneous recovery. *Anaesth Intensive Care* 2012; 40:999–1006
 188. Gonçalves P, Vieira AV, Silva C, Gomez RS: Residual neuromuscular blockade and late neuromuscular blockade at the post-anesthetic recovery unit: Prospective cohort study. *Braz J Anesthesiol* 2021; 71:38–43
 189. Carron M, Baratto F, Zarantonello F, Ori C: Sugammadex for reversal of neuromuscular blockade: A retrospective analysis of clinical outcomes and cost-effectiveness in a single center. *Clinicoecon Outcomes Res* 2016; 8:43–52
 190. White PF, Tufanogullari B, Sacan O, Pavlin EG, Viegas OJ, Minkowitz HS, Hudson ME: The effect of residual neuromuscular blockade on the speed of reversal with sugammadex. *Anesth Analg* 2009; 108:846–51
 191. Peček B, Polh D, Priman T: New way of dosing sugammadex for termination of vecuronium induced neuromuscular block. *Zdravniški Vestnik* 2015; 84:439–46
 192. Norton M, Xara D, Parente D, Barbosa M, Abelha FJ: Residual neuromuscular block as a risk factor for critical respiratory events in the post anesthesia care unit. *Rev Esp Anestesiol Reanim* 2013; 60:190–6
 193. Thilen SR, Ng IC, Cain KC, Treggiari MM, Bhananker SM: Management of rocuronium neuromuscular block using a protocol for qualitative monitoring and reversal with neostigmine. *Br J Anaesth* 2018; 121:367–77
 194. Claudius C, Skovgaard LT, Viby-Mogensen J: Is the performance of acceleromyography improved with preload and normalization? A comparison with mechanomyography. *ANESTHESIOLOGY* 2009; 110:1261–70
 195. Dubois PE, Broka SM, Jamart J, Joucken KL: TOF-tube, a new protection for acceleromyography, compared with the TOF-Guard/TOF-Watch arm board. *Acta Anaesthesiol Belg* 2002; 53:33–8
 196. Dubois PE, Gourdin M, Russell K, Jamart J: Installation of the hand influences acceleromyography measurement: A comparison with mechanomyography during neuromuscular recovery. *Acta Anaesthesiol Belg* 2005; 56:163–6
 197. Eriksson LI, Lennmarken C, Jensen E, Viby-Mogensen J: Twitch tension and train-of-four ratio during prolonged neuromuscular monitoring at different peripheral temperatures. *Acta Anaesthesiol Scand* 1991; 35:247–52
 198. Motamed C, Kirov K, Combes X, Duvaldestin P: Does repetition of post-tetanic count every 3 min during profound relaxation affect accelerographic recovery of atracurium blockade? *Acta Anaesthesiol Scand* 2005; 49:811–4
 199. Pelgrims K, Vanacker B: Comparative study of the TOF-ratio measured by the ParaGraph *versus* the

- TOF-Guard, with and without thumb repositioning. *Acta Anaesthesiol Belg* 2001; 52:297–300
200. Phillips S, Stewart PA, Freeland N, Heller G: Comparison of evoked electromyography in three muscles of the hand during recovery from non-depolarising neuromuscular blockade. *Anaesth Intensive Care* 2012; 40:690–6
 201. Sugi Y, Nitahara K, Katori K, Kusumoto G, Shigematsu K, Higa K: Acceleromyography at the flexor hallucis brevis muscle underestimates residual neuromuscular blockade. *Open Anesthesiol J* 2013; 7:26–9
 202. Schreiber JU, Mucha E, Fuchs-Buder T: Acceleromyography to assess neuromuscular recovery: Is calibration before measurement mandatory? *Acta Anaesthesiol Scand* 2011; 55:328–31
 203. Capron F, Alla F, Hottier C, Meistelman C, Fuchs-Buder T: Can acceleromyography detect low levels of residual paralysis? A probability approach to detect a mechanomyographic train-of-four ratio of 0.9. *ANESTHESIOLOGY* 2004; 100:1119–24
 204. Kopman AF, Chin W, Cyriac J: Acceleromyography *vs.* electromyography: An ipsilateral comparison of the indirectly evoked neuromuscular response to train-of-four stimulation. *Acta Anaesthesiol Scand* 2005; 49:316–22
 205. Mazzinari G, Errando CL, Diaz-Cambronero O, Martin-Flores M: Influence of tetanic stimulation on the staircase phenomenon and the acceleromyographic time-course of neuromuscular block: A randomized controlled trial. *J Clin Monit Comput* 2019; 33:325–32
 206. Abdulatif M, Mowafi H, al-Ghamdi A, el-Sanabary M: Dose-response relationships for neostigmine antagonism of rocuronium-induced neuromuscular block in children and adults. *Br J Anaesth* 1996; 77:710–5
 207. Abola RE, Romeiser J, Rizwan S, Lung B, Gupta R, Bennett-Guerrero E: A randomized-controlled trial of sugammadex *versus* neostigmine: Impact on early postoperative strength. *Can J Anaesth* 2020; 67:959–69
 208. Abu Yazed MM, Ahmed SA: Deep *versus* moderate neuromuscular block in laparoscopic bariatric surgeries: Effect on surgical conditions and pulmonary complications. *Egypt J Anaesth* 2019; 35:57–64
 209. Adamus M, Belohlavek R, Koutna J, Vujcikova M, Janaskova E: Cisatracurium *vs.* rocuronium: A prospective, comparative, randomized study in adult patients under total intravenous anaesthesia. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2006; 150:333–8
 210. Alsaed A, Bamehriz F, Eldin S, Alzahrani T, Alharbi A, Eldawlatly A: Sugammadex *versus* two doses of neostigmine for reversal of rocuronium in gastric sleeve surgery. *Saudi J Anaesth* 2017; 11:309–11
 211. Baurain MJ, Dernovoi BS, d'Hollander AA, Hennart DA: Comparison of neostigmine-induced recovery with spontaneous recovery from mivacurium-induced neuromuscular block. *Br J Anaesth* 1994; 73:791–4
 212. Bevan JC, Collins L, Fowler C, Kahwaji R, Rosen HD, Smith MF, de Scheepers LD, Stephenson CA, Bevan DR: Early and late reversal of rocuronium and vecuronium with neostigmine in adults and children. *Anesth Analg* 1999; 89:333–9
 213. Brull SJ, Ehrenwerth J, Connelly NR, Silverman DG: Assessment of residual curarization using low-current stimulation. *Can J Anaesth* 1991; 38:164–8
 214. Carroll MT, Mirakhor RK, Lowry D, Glover P, Kerr CJ: A comparison of the neuromuscular blocking effects and reversibility of cisatracurium and atracurium. *Anaesthesia* 1998; 53:744–8
 215. Carron M, Iepariello G, A DEC, Lambertini C, Linassi F, Navalesi P: Corrected *versus* total body weight for dosage of sugammadex in morbidly obese patients. A randomized, double-blind, controlled trial. *Minerva Anesthesiol* 2021; 87:371–3
 216. Jones S, Platt S: Trainee confidence with rocuronium for rapid sequence induction. *Anaesthesia* 2015; 70:77
 217. Czarnetzki C, Tassonyi E, Lysakowski C, Elia N, Tramer MR: Efficacy of sugammadex for the reversal of moderate and deep rocuronium-induced neuromuscular block in patients pretreated with intravenous magnesium: A randomized controlled trial. *ANESTHESIOLOGY* 2014; 121:59–67
 218. Dahl V, Pendeville PE, Hollmann MW, Heier T, Abels EA, Blobner M: Safety and efficacy of sugammadex for the reversal of rocuronium-induced neuromuscular blockade in cardiac patients undergoing noncardiac surgery. *Eur J Anaesthesiol* 2009; 26:874–84
 219. de Boer HD, Driessen JJ, Marcus MA, Kerkkamp H, Heeringa M, Klimek M: Reversal of rocuronium-induced (1.2 mg/kg) profound neuromuscular block by sugammadex: A multicenter, dose-finding and safety study. *ANESTHESIOLOGY* 2007; 107:239–44
 220. Deana C, Barbariol F, D'Inca S, Pompei L, Rocca GD: Sugammadex *versus* neostigmine after rocuronium continuous infusion in patients undergoing liver transplantation. *BMC Anesthesiol* 2020; 20:70
 221. Deng J, Balouch M, Albrink M, Camporesi EM: Sugammadex reduces PACU recovery time after abdominal surgery compared with neostigmine. *South Med J* 2021; 114:644–8
 222. Duranteau O, Fernandez W, Tuna T, Engelman E, Van Obbergh L, Tabolcea I: Earlier and lower dose administration of sugammadex: A randomised placebo-controlled trial. *Eur J Anaesthesiol* 2021; 38:865–71
 223. Evron S, Abelansky Y, Ezri T, Izakson A: Respiratory events with sugammadex *vs.* neostigmine following laparoscopic sleeve gastrectomy: A prospective pilot study assessing neuromuscular reversal strategies. *Rom J Anaesth Intensive Care* 2017; 24:111–4

224. Fuchs-Buder T, Ziegenfuss T, Lysakowski K, Tassonyi E: Antagonism of vecuronium-induced neuromuscular block in patients pretreated with magnesium sulphate: Dose-effect relationship of neostigmine. *Br J Anaesth* 1999; 82:61–5
225. Germano Filho PA, Cavalcanti IL, Barrucand L, Vercosa N: Effect of magnesium sulphate on sugammadex reversal time for neuromuscular blockade: A randomised controlled study. *Anaesthesia* 2015; 70:956–61
226. Gunes ME, Dural AC, Akarsu C, Guzey D, Sahbaz NA, Tulubas EK, Bulut S, Donmez T: Effect of intraoperative neuromonitoring on efficacy and safety using sugammadex in thyroid surgery: Randomized clinical trial. *Ann Surg Treat Res* 2019; 97:282–90
227. Han J, Oh AY, Jeon YT, Koo BW, Kim BY, Kim D, Hwang I: Quality of recovery after laparoscopic cholecystectomy following neuromuscular blockade reversal with neostigmine or sugammadex: A prospective, randomized, controlled trial. *J Clin Med* 2021; 10:938
228. Hayes A, Breslin D, Reid J, Mirakhur RK: Comparison of recovery following rapacuronium, with and without neostigmine, and succinylcholine. *Anaesthesia* 2000; 55:859–63
229. Hayes AH, Mirakhur RK, Breslin DS, Reid JE, McCourt KC: Postoperative residual block after intermediate-acting neuromuscular blocking drugs. *Anaesthesia* 2001; 56:312–8
230. Kao YJ, Le ND: The reversal of profound mivacurium-induced neuromuscular blockade. *Can J Anaesth* 1996; 43:1128–33
231. Karwacki Z, Niewiadomski S, Rzaska M: The use of sugammadex for the reversal of vecuronium-induced neuromuscular block following intracranial surgery. *Anaesthesiol Intensive Ther* 2015; 47:297–302
232. Khan SJ, Sareen R: Comparison of residual neuromuscular blockade between two intermediate acting nondepolarizing neuromuscular blocking agents—rocuronium and vecuronium. *Indian J Anaesth* 2006; 50:115–7
233. Kim KS, OhYN, Kim TY, Oh SY, SinYH: Relationship between first-twitch depression and train-of-four ratio during sugammadex reversal of rocuronium-induced neuromuscular blockade. *Korean J Anesthesiol* 2016; 69:239–43
234. Kim NY, Koh JC, Lee KY, Kim SS, Hong JH, Nam HJ, Bai SJ: Influence of reversal of neuromuscular blockade with sugammadex or neostigmine on postoperative quality of recovery following a single bolus dose of rocuronium: A prospective, randomized, double-blinded, controlled study. *J Clin Anesth* 2019; 57:97–102
235. Koo BW, Oh AY, Ryu JH, Lee YJ, Han JW, Nam SW, Park DJ, Seo KS: Effects of deep neuromuscular blockade on the stress response during laparoscopic gastrectomy randomized controlled trials. *Sci Rep* 2019; 9:12411
236. Kumar GV, Nair AP, Murthy HS, Jalaja KR, Ramachandra K, Parameshwara G: Residual neuromuscular blockade affects postoperative pulmonary function. *ANESTHESIOLOGY* 2012; 117:1234–44
237. Lederer W, Reiner T, Khuenl-Brady KS: Neostigmine injected 5 minutes after low-dose rocuronium accelerates the recovery of neuromuscular function. *J Clin Anesth* 2010; 22:420–4
238. Lien CA, Belmont MR, Wray Roth DL, Okamoto M, Abalos A, Savarese JJ: Pharmacodynamics and the plasma concentration of mivacurium during spontaneous recovery and neostigmine-facilitated recovery. *ANESTHESIOLOGY* 1999; 91:119–26
239. Maddineni VR, Mirakhur RK, McCoy EP: Recovery of mivacurium block with or without anticholinesterases following administration by continuous infusion. *Anaesthesia* 1994; 49:946–8
240. Martini CH, Boon M, Bevers RF, Aarts LP, Dahan A: Evaluation of surgical conditions during laparoscopic surgery in patients with moderate vs deep neuromuscular block. *Br J Anaesth* 2014; 112:498–505
241. Maybauer DM, Geldner G, Blobner M, Puhlinger F, Hofmockel R, Rex C, Wulf HF, Eberhart L, Arndt C, Eikermann M: Incidence and duration of residual paralysis at the end of surgery after multiple administrations of cisatracurium and rocuronium. *Anaesthesia* 2007; 62:12–7
242. McCourt KC, Mirakhur RK, Kerr CM: Dosage of neostigmine for reversal of rocuronium block from two levels of spontaneous recovery. *Anaesthesia* 1999; 54:651–5
243. McCourt KC, Mirakhur RK, Lowry DW, Carroll MT, Sparr HJ: Spontaneous or neostigmine-induced recovery after maintenance of neuromuscular block with Org 9487 (rapacuronium) or rocuronium following an initial dose of Org 9487. *Br J Anaesth* 1999; 82:755–6
244. Omar AM: Effect of systemic lidocaine infusion on train-of-four ratios during recovery from general anesthesia. *Egypt J Anaesth* 2019; 28:281–6
245. Ornek DH, Tezcan AH, Terzi HO, Yildiz BD: Dosage of sugammadex in morbidly obese patients. *Ann Clin Anal Med* 2020; 11:S52–6
246. Plaud B, Meretoja O, Hofmockel R, Raft J, Stoddart PA, van Kuijk JH, Hermens Y, Mirakhur RK: Reversal of rocuronium-induced neuromuscular blockade with sugammadex in pediatric and adult surgical patients. *ANESTHESIOLOGY* 2009; 110:284–94
247. Puhlinger FK, Rex C, Sielenkamper AW, Claudius C, Larsen PB, Prins ME, Eikermann M, Khuenl-Brady KS: Reversal of profound, high-dose rocuronium-induced neuromuscular blockade by sugammadex at two

- different time points: An international, multicenter, randomized, dose-finding, safety assessor-blinded, phase II trial. *ANESTHESIOLOGY* 2008; 109:188–97
248. Puhlinger FK, Gordon M, Demeyer I, Sparr HJ, Ingimarsson J, Klarin B, van Duijnhoven W, Heeringa M: Sugammadex rapidly reverses moderate rocuronium- or vecuronium-induced neuromuscular block during sevoflurane anaesthesia: A dose-response relationship. *Br J Anaesth* 2010; 105:610–9
 249. Sorgenfrei IF, Norrild K, Larsen PB, Stensballe J, Ostergaard D, Prins ME, Viby-Mogensen J: Reversal of rocuronium-induced neuromuscular block by the selective relaxant binding agent sugammadex: A dose-finding and safety study. *ANESTHESIOLOGY* 2006; 104:667–74
 250. Sparr HJ, Vermeyen KM, Beaufort AM, Rietbergen H, Proost JH, Saldien V, Velik-Salchner C, Wierda JM: Early reversal of profound rocuronium-induced neuromuscular blockade by sugammadex in a randomized multicenter study: Efficacy, safety, and pharmacokinetics. *ANESTHESIOLOGY* 2007; 106:935–43
 251. Suy K, Morias K, Cammu G, Hans P, van Duijnhoven WG, Heeringa M, Demeyer I: Effective reversal of moderate rocuronium- or vecuronium-induced neuromuscular block with sugammadex, a selective relaxant binding agent. *ANESTHESIOLOGY* 2007; 106:283–8
 252. Suzuki T, Mizutani H, Ishikawa K, Miyake E, Saeki S, Ogawa S: Epidurally administered mepivacaine delays recovery of train-of-four ratio from vecuronium-induced neuromuscular block. *Br J Anaesth* 2007; 99:721–5
 253. Tassonyi E, Pongracz A, Nemes R, Asztalos L, Lengyel S, Fulesdi B: Reversal of pipecuronium-induced moderate neuromuscular block with sugammadex in the presence of a sevoflurane anesthetic: A randomized trial. *Anesth Analg* 2015; 121:373–80
 254. Trevien V, Lienhart A, Just B, Chandon M, Baras E, Camatte S: Effect of neostigmine at different levels of mivacurium-induced neuromuscular blockade. *Acta Anaesthesiol Scand Suppl* 1995; 106:66–9
 255. Bissinger U, Schimek F, Lenz G: Postoperative residual paralysis and respiratory status: A comparative study of pancuronium and vecuronium. *Physiol Res* 2000; 49:455–62
 256. Johnson M, Khan OA, McGlone ER, Roman AA, Qureshi JS, Kayal A: Sugammadex is associated with better respiratory recovery than neostigmine following reversal of anaesthesia-associated neuromuscular blockade in the morbidly obese patients following elective laparoscopic surgery. *Laparosc Endosc Robot Surg* 2018; 1:33–6
 257. Muramatsu T, Isono S, Ishikawa T, Nozaki-Taguchi N, Okazaki J, Kitamura Y, Murakami N, Sato Y: Differences of recovery from rocuronium-induced deep paralysis in response to small doses of sugammadex between elderly and nonelderly patients. *ANESTHESIOLOGY* 2018; 129:901–11
 258. Sanfilippo M, Alessandri F, Wefki Abdelgawwad Shousha AA, Sabba A, Cutolo A: Sugammadex and ideal body weight in bariatric surgery. *Anesthesiol Res Pract* 2013; 2013:389782
 259. Arslantas R, Cevik BE: Retrospective investigation of grafted kidney function after reversal of neuromuscular blockade using neostigmine or sugammadex. *Transplant Proc* 2019; 51:2265–7
 260. Baillard C, Gehan G, Reboul-Marty J, Larmignat P, Samama CM, Cupa M: Residual curarization in the recovery room after vecuronium. *Br J Anaesth* 2000; 84:394–5
 261. Cho HC, Lee JH, Lee SC, Park SY, Rim JC, Choi SR: Use of sugammadex in lung cancer patients undergoing video-assisted thoracoscopic lobectomy. *Korean J Anesthesiol* 2017; 70:420–5
 262. De Robertis E, Zito Marinosci G, Romano GM, Piazza O, Iannuzzi M, Cirillo F, De Simone S, Servillo G: The use of sugammadex for bariatric surgery: Analysis of recovery time from neuromuscular blockade and possible economic impact. *Clinicoecon Outcomes Res* 2016; 8:317–22
 263. de Souza CM, Tardelli MA, Tedesco H, Garcia NN, Caparros MP, Alvarez-Gomez JA, de Oliveira IS Jr: Efficacy and safety of sugammadex in the reversal of deep neuromuscular blockade induced by rocuronium in patients with end-stage renal disease: A comparative prospective clinical trial. *Eur J Anaesthesiol* 2015; 32:681–6
 264. Errando CL, Garutti I, Mazzinari G, Diaz-Cambronero O, Bebawy JF, Grupo Espanol de Estudio del Bloqueo Neuromuscular: Residual neuromuscular blockade in the postanesthesia care unit: Observational cross-sectional study of a multicenter cohort. *Minerva Anesthesiol* 2016; 82:1267–77
 265. Fawcett WJ, Dash A, Francis GA, Liban JB, Cashman JN: Recovery from neuromuscular blockade: Residual curarisation following atracurium or vecuronium by bolus dosing or infusions. *Acta Anaesthesiol Scand* 1995; 39:288–93
 266. Fujita A, Ishibe N, Yoshihara T, Ohashi J, Makino H, Ikeda M, Setoguchi H: Rapid reversal of neuromuscular blockade by sugammadex after continuous infusion of rocuronium in patients with liver dysfunction undergoing hepatic surgery. *Acta Anaesthesiol Taiwan* 2014; 52:54–8
 267. Kaan N, Kocaturk O, Kurt I, Cicek H: The incidence of residual neuromuscular blockade associated with single dose of intermediate-acting neuromuscular blocking drugs. *Middle East J Anaesthesiol* 2012; 21:535–41
 268. Kadoi Y, Nishida A, Saito S: Recovery time after sugammadex reversal of rocuronium-induced muscle relaxation for electroconvulsive therapy is

- independent of cardiac output in both young and elderly patients. *J ECT* 2013; 29:33–6
269. Kocaturk O, Kaan N, Kayacan N, Ertugrul F: The incidence of postoperative residual curarization following the use of intermediate-acting muscle relaxants and related factors. *Middle East J Anaesthesiol* 2014; 22:583–90
 270. Kotake Y, Ochiai R, Suzuki T, Ogawa S, Takagi S, Ozaki M, Nakatsuka I, Takeda J: Reversal with sugammadex in the absence of monitoring did not preclude residual neuromuscular block. *Anesth Analg* 2013; 117:345–51
 271. Motamed C, Bourgain JL: Comparison of the time to extubation and length of stay in the PACU after sugammadex and neostigmine use in two types of surgery: A monocentric retrospective analysis. *J Clin Med* 2021; 10:1–9
 272. Murphy GS, Szokol JW, Marymont JH, Franklin M, Avram MJ, Vender JS: Residual paralysis at the time of tracheal extubation. *Anesth Analg* 2005; 100:1840–5
 273. Oh CS, Rhee KY, Yoon TG, Woo NS, Hong SW, Kim SH: Postoperative delirium in elderly patients undergoing hip fracture surgery in the sugammadex era: A retrospective study. *Biomed Res Int* 2016; 2016:1054597
 274. Pietraszewski P, Gaszynski T: Residual neuromuscular block in elderly patients after surgical procedures under general anaesthesia with rocuronium. *Anaesthesiol Intensive Ther* 2013; 45:77–81
 275. Serrano AB, Díaz-Cambronero O, Melchor-Ripollés J, Abad-Gurumeta A, Ramirez-Rodriguez JM, Martínez-Ubieto J, Sánchez-Merchante M, Rodriguez R, Jordá L, Gil-Trujillo S, Cabellos-Olivares M, Bordonaba-Bosque D, Aldecoa C: Neuromuscular blockade management and postoperative outcomes in enhanced recovery colorectal surgery: Secondary analysis of POWER trial. *Minerva Anesthesiol* 2021; 87:13–25
 276. Suzuki T, Masaki G, Ogawa S: Neostigmine-induced reversal of vecuronium in normal weight, overweight and obese female patients. *Br J Anaesth* 2006; 97:160–3
 277. Yip PC, Hannam JA, Cameron AJ, Campbell D: Incidence of residual neuromuscular blockade in a post-anaesthetic care unit. *Anaesth Intensive Care* 2010; 38:91–5