

International survey of neuromuscular monitoring in two European countries: a questionnaire study among Hungarian and Romanian anaesthesiologists

Adrienn Pongrácz¹, Réka Nemes¹, Caius Breazu², László Asztalos¹, Ileana Mitre², Edömér Tassonyi¹, Béla Fülesdi¹, Calin Mitre²

¹ Department of Anaesthesiology and Intensive Care University of Debrecen, Hungary

² Department of Anaesthesiology and Intensive Care, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

Abstract

Background: Accumulating evidence indicates that objective neuromuscular monitoring and pharmacological reversal of neuromuscular block reduces the occurrence of residual muscle paralysis in the acute postoperative phase. However, objective neuromuscular monitoring is not a routine habit in anaesthesia. In order to change this situation, we wished to find out, as a first step to improvement, the current use of neuromuscular monitors and the custom of anaesthetists for reversal of neuromuscular block before tracheal extubation.

Methods A ten-point questionnaire was available via the *SurveyMonkey* website and the link was sent to 2202 Hungarian and Romanian anaesthetists by email.

Results: Three hundred and two (13.7%) of the 2202 registered anaesthetists responded. Less than 10% of them regularly use neuromuscular monitors. They underestimated the occurrence of residual block; only 2.2% gave a correct answer. Neuromuscular monitors are available in 74% of hospitals but are scarcely used. One third of anaesthetists rarely or never use reversal; approximately 20% regularly reverse before extubation. The responders typically believe that clinical signs of residual block are reliable. Instead of monitoring, they use the “timing methods” for tracheal extubation such as time elapsed from last dose, the duration of action of relaxant, the number of top-up doses, the cumulative dose, the return of adequate respiratory tidal volume and the ability to sustain a 5 s head lift.

Conclusions: We concluded that neuromuscular monitoring in these two European countries is suboptimal as is the reversal strategy. Given the fact that monitors are available in the hospitals, the mentality should be changed towards evidence based practice.

Keywords: neuromuscular blocking agents; neuromuscular monitoring; residual neuromuscular block; survey

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Introduction

The use of neuromuscular blocking agents (NMBA) is an integral part of modern anaesthetic practice, facilitating tracheal intubation and mechanical res-

piration of the lungs while ensuring appropriate surgical conditions. However, there are possible complications due to muscle paralysis which may persist postoperatively and may cause unwanted effects such as hypoxia, respiratory depression, bronchoaspiration, atelectasis, pneumonia or even death [1-4]. Therefore, adequate management of neuromuscular transmission and block is indispensable to prevent these complications. Worldwide, about 400 million patients receive NMBA for surgery each year [5]. Anaesthesiologists are responsible to ensure complete reversal of the block once the surgery has ended. In defiance of modern anaesthesia care, postoperative residual

Address for correspondence:

Calin Mitre MD, PhD, DEAA
Department of Anaesthesiology
and Intensive Care
Iuliu Hațieganu University
of Medicine and Pharmacy
Str Victor Babeș 8, Cluj-Napoca
Romania
E-mail: cmitre2001@gmail.com

neuromuscular block (PORNB) is still a frequent phenomenon that may occur in 1/5 to 2/3 of patients [6] and causes a critical respiratory event in 0.8 % of them [1]. Therefore, the issue of “safe curarization” based on objective monitoring of neuromuscular transmission and block is of paramount importance.

Several studies have evidenced the lack of reliable bedside clinical tests to disclose postoperative residual muscle paralysis. [7, 8] and therefore, objective neuromuscular monitoring is recommended to reveal PORNB. Pharmacological reversal of neuromuscular blockade (NMB) with neostigmine or sugammadex, without monitoring, does not guarantee the prevention of PORNB [9-11] neither does qualitative monitoring on its own [12] or in combination with neostigmine reversal [6, 13]. Although the combination of sugammadex reversal with qualitative monitoring has resulted in a significant decrease in the frequency of PORNB [14, 15], there is a general agreement that residual muscle paralysis can only be prevented using objective monitoring and pharmacological reversal if necessary [14, 16].

Despite the large body of evidence pertaining to PORNB, its importance is still underestimated by many clinicians. A survey in 2010 showed that 19.3 % of the European and 9.4% of the American anaesthesiologists do not use neuromuscular monitors (NMM) routinely [17]. In 2010 only 50% of Italian anaesthesiologists used NMM in daily practice [18]. A 2013 survey from Australia and New Zealand revealed that 60% of practitioners used NMM at least once a month, and 10% never used one [19].

The aim of the present study was to investigate the practice of anaesthesia in Hungary and Romania regarding NMM and the pharmacological reversal of NMB. The background of this common work was the quite similar resident education of the two countries, the similar historical perspective of healthcare systems as well as the fact that these two countries are among the most significant ones “exporting” anaesthetists to Western countries in Europe. We wished to learn the opinion of anaesthetists pertaining to PORNB and neuromuscular monitoring, enabling us to identify erroneous views and focusing the education on their correction.

Methods

In order to obtain the opinion of Hungarian and Romanian anaesthesiologists on the incidence of PORNB, on the necessity of neuromuscular monitoring and on their habits of reversal of neuromuscular block, we edited a ten-point questionnaire in this respect. We collected data on the professional background (expe-

rience) of the participants, on the type of workplace and on the availability of neuromuscular monitors in their institutions. In order to compare our data with those of international surveys we asked similar questions, but also we included new questions specific to regional circumstances. [17, 19] Accordingly, 10 points were listed including yes or no questions (yes – no – no opinion), single and multiple choice questions, and statements that the participants could agree or disagree with.

Before starting the study we asked the local IRB representatives whether an approval would be necessary but it was deemed unnecessary.

The questionnaire was available on the website via *SurveyMonkey* software (<https://www.surveymonkey.com>). The link was forwarded to all members of the Hungarian and Romanian Society of Anaesthesiology and Intensive Care via e-mail. To complete the questionnaire, participants did not need to register; only a click on the link was required. Participants were informed that they only required a few minutes to answer, that the survey was anonymous and repetition of answers was impossible. Written informed consent from the participants was not taken as electronic participation was considered a voluntary participation. However, in the information letter we informed participants about the eventual anonymous use of their data for publication purposes.

The questionnaire was open between June 27, 2016 and January 4, 2017 in Hungary and September 1, 2017 and February 20, 2018 in Romania.

Descriptive statistics were used for data analysis. Two generations of participants were distinguished according to their professional experience: more than 10 years for senior staff, less than 10 years for junior staff including residents. The Chi-square test was used to compare the monitoring and reversal habits of senior and junior staff.

Results

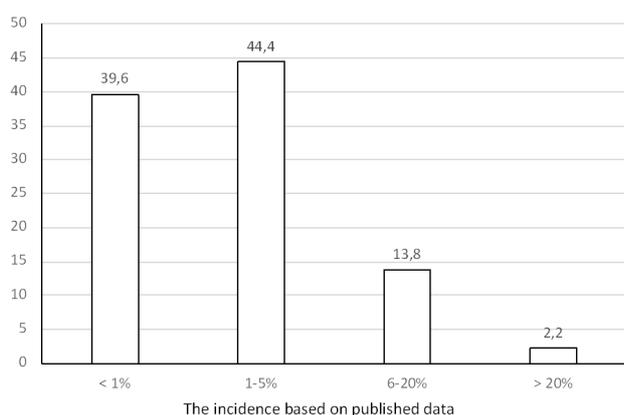
The Hungarian Society of Anaesthesiology and Intensive Care numbers 1328 registered members: 124 participated and completed the questionnaire (9.34 %). The larger proportion (49.2%) of the answers came from senior staff anaesthetists working in city hospitals (41.1%). SRATI (The Romanian Society of Anaesthesiology and Intensive Care) comprises 878 members; among them 423 members were asked to participate and 153 completed the survey (17.4%). The responders were from residents as well as from young specialists (n = 189, 62.5%). In the total cohort, 55% of the answers came from non-academic hospitals and 45% from academic hospitals. (Table 1).

Table 1. Demographics

Registered anaesthetists in the societies		2206	
Participants (responders)	N (%)	302	(13.7%)
Professional background	N		Proportion of participants (%)
Residents	95		21.3
Specialist < 10 years	94		38.2
Specialist > 10 years	109		36.2
Other or skipped question	4		1.3
Affiliation			
University hospital	136		45.0
Regional or large area hospital	89		29.5
City hospital	77		25.5

Frequency and significance of postoperative residual neuromuscular block

Participants clearly underestimated the incidence of PORNB; only 2.2% of the responders corresponded to published data (the incidence in reality is > 20%) (Figure 1).

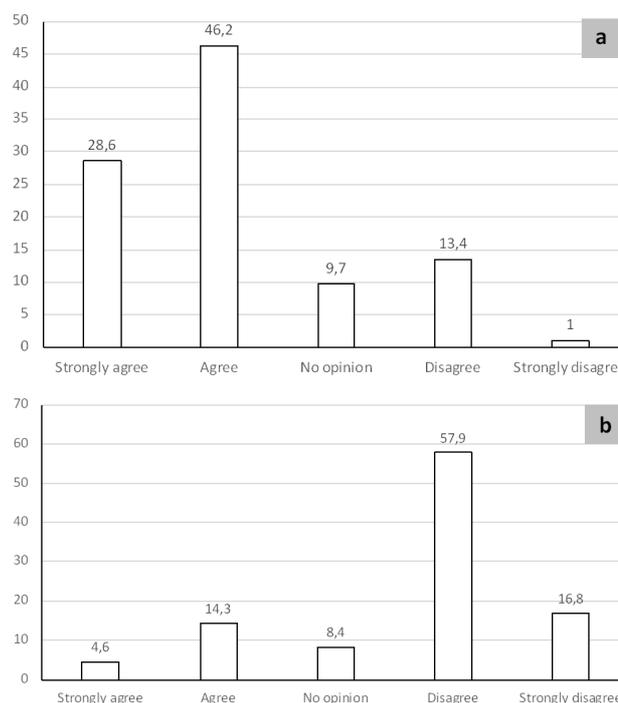
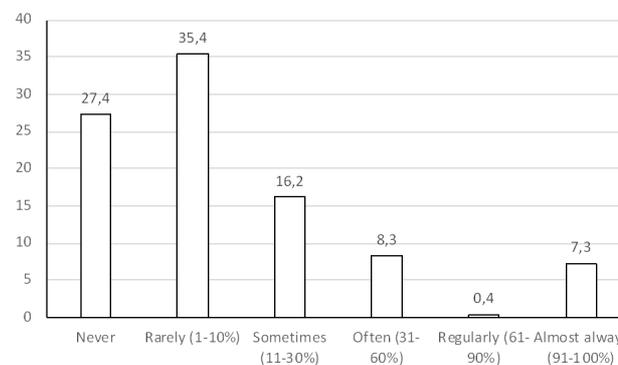

Fig. 1. Estimation of the incidence of PORNB by participants (%)

Twenty-five percent of the participants did not think that PORNB is an important clinical issue, while 74.8% of the participants agreed with the statement that PORNB is an important clinical problem, and should not be considered as a banality (Figure 2).

14.5 percent of participants do not think that latent PORNB presents a risk (Figure 2).

Neuromuscular monitoring habits

Only 7.7% of participants declared the regular use of a neuromuscular monitor during the operations when NMB agents are administered. There was no difference between senior and junior staff anaesthetists. Twenty seven percent of the participants never use NMM; 35% rarely (less than 10% of the cases) (Figure 3).


Fig. 2. Subjective evaluation of importance of postoperative residual neuromuscular block (PORNB); **a.** residual neuromuscular blockade is an important clinical issue and its significance is underestimated by many anaesthesiologists (%), **b.** residual neuromuscular block that cannot be revealed with clinical tests is not dangerous (%)

Fig. 3. The association of NMBA administration and monitoring of NMB (%)

Availability of neuromuscular monitors

Only 14.6% of hospitals do not possess some kind of NMM. Quantitative monitors prevail and only 25% of anaesthesia workstations are equipped with any kind of NMM (qualitative or quantitative) (Table 2).

Clinical signs of postoperative residual neuromuscular block

Twenty six percent of participants declared no need for NMM and thought that clinical signs are adequate to determine the level of NMB (Figure 4 a). The majority of participants (63.6%) believe in clinical signs of curarization for detection of PORNB and would use monitoring only for high risk patients (Figure 4 b).

Only 48.9% of the participants agreed with the evidence of insufficiency of clinical signs and the need of neuromuscular monitoring in all cases (Figure 4 c).

General opinion on neuromuscular monitors

26.3% of the responders reported the use of NMM complicated; 13.6% thought them unreliable, 44.7% would use them if they were easier to apply and 9.3% would use them if they had the proper knowledge to do so. 65.5% of the responders said that NMM should be made part of daily routine practice.

Reversal of neuromuscular blockade

One third of participants (22.7%) rarely or never use pharmacological reversal at the end of surgery. Another 45.8% often use reversal (Table 3). For timing of tracheal extubation, these participants consider the elapsed time from last NMBA administration (95.9%), the duration of action of administered NMBA (91.9%), the number of top-up doses (76.3%), the cumulative dose of NMBA (68.7%), the return of adequate respiratory tidal volume (82.1%) and ability to sustain a 5 s head lift (76.8%). These “timing methods” are used more often than NM monitors. Regarding the type of NM monitors, anaesthetists prefer quantitative monitoring (65.6%) versus simple nerve stimulators (26.9%).

The majority (83.2%) of the responders over-estimated the efficacy of neostigmine thinking that it acts within 10 min. Only 16.7% thought that more than 10 min is required for full effect.

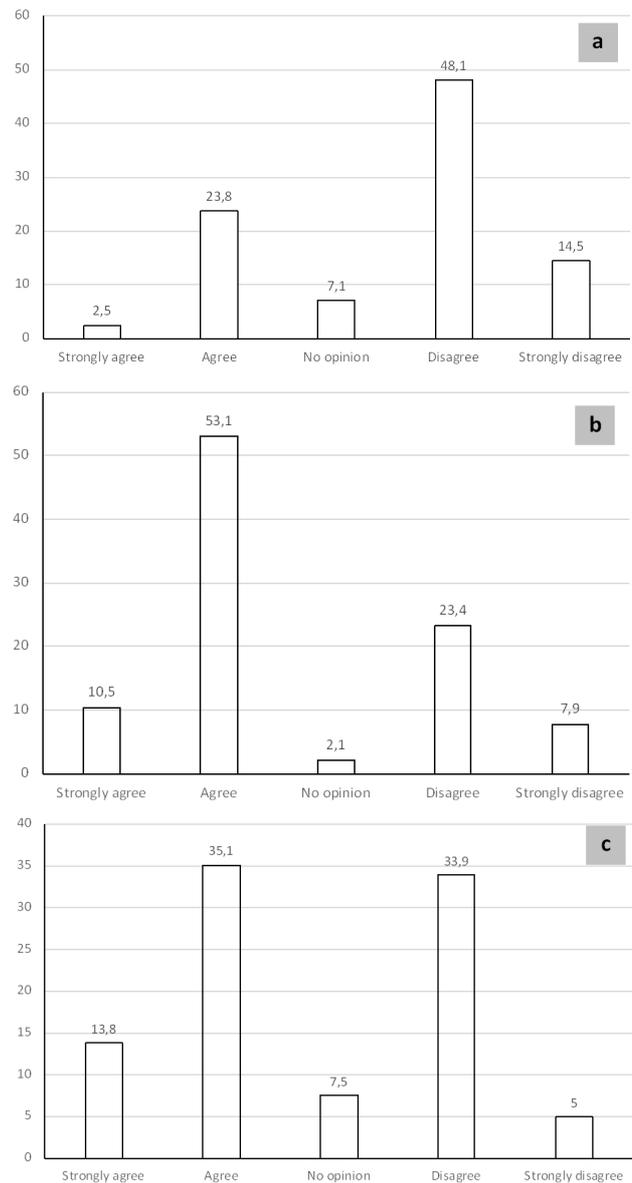


Fig. 4. Responders' opinion about clinical tests and necessity of neuromuscular monitoring; **a.** clinical tests are adequate to determine PORNB, neuromuscular monitors are unnecessary (%), **b.** clinical tests are usually reliable, neuromuscular monitoring is only necessary in high risk patients (%), **c.** clinical tests are inadequate to preclude the presence of PORNB, neuromuscular monitors should be used all times (%)

Table 2. Availability of neuromuscular monitors

Do you have access to any kind (quantitative or qualitative) of neuromuscular monitor in your institute?	Answered 236 N (%)
Qualitative monitor access	88 (37.3)
1 monitor per 1 OR	31
1 monitor per 2 OR	16
1 monitor per 3 OR	41
Quantitative monitor access	175 (74.1)
1 monitor per 1 OR	47
1 monitor per 2 OR	34
1 monitor per 3 OR	94

Table 3. Frequency of pharmacological reversal

When you use non-depolarizing muscular relaxant, how often do you administer reversal agent at the end of operation?	Answered 232 N (%)
Never	7 (3.0)
1-25%	70 (29.7)
26-50%	29 (12.3)
51-75%	28 (11.9)
76-95%	51 (21.6)
Always	47 (19.9)

Discussion

The results of the current study illustrate the suboptimal situation with regard to the safe use of NMBAs. Historically, after the introduction of curare-like agents in clinical practice, mortality rate increased six fold, showing the intrinsic risk associated with their use [20]. Later, due to improvement of anaesthetic techniques and drug quality, the administration of NMBAs did not cause direct mortality, but the risk of respiratory complications persisted. A significant progress was the introduction of the train-of-four (TOF) stimulation pattern by Ali et al. [21] for the measurement of NMB. This method was validated by correlating the evoked muscle responses with the respiratory tidal volume. Since at TOF ratio (T_4/T_1) 0.7 the tidal volume became normal, TOF ratio of 0.7 was defined as the criterion for tracheal extubation. However, at this TOF ratio a considerable residual neuromuscular effect persists at the pharyngeal muscles and also the airway protection is diminished [22]. With other words at TOF ratio 0.7 PORNB persists. At the same time, we demonstrated the deficit in neuromuscular transmission while the respiration was apparently normal [23]. Waud reported the safety margin in neuromuscular transmission [24], showing the limited sensitivity of TOF measurement to detect residual NMB. In spite of the evidence of residual NMB at TOF-ratio 0.7, this value persisted for several generations of anaesthetists until this misleading figure was corrected. Today there is general agreement that TOF ratio (T_4/T_1) 1.0 has to be achieved to exclude clinically relevant residual curarization [25], and this can only be done using objective monitoring, because a TOF ratio = 0.5 cannot be perceived visually or by palpation [26]. However, the concept of TOF-ratio 0.7 as a criterion for tracheal extubation seems to be very difficult to change. Clinicians do not seem to be convinced of the benefit for monitoring versus clinical signs arguing that if residual curarization is not clinically remarked there is no need to deal with. The problem is that TOF-ratio 0.7 cannot be perceived without objective monitoring, thus it is easily deemed as normal recovery. However, normal respiration does not mean normal airway protection,

because the diaphragm, unlike pharyngeal muscles recovers at 0.7 TOF-ratios ensuring normal respiratory tidal volume [27]. Accordingly, when the patient is transferred to the ward, he/she may regurgitate during the transport, the gastric content may get into the lungs because the airway protection is imperfect [22]. More often than not broncho-aspiration happens unnoticed. The first 15 to 30 min after extubation of the trachea is the most critical period for complications that can be prevented with adequate reversal of the block before tracheal extubation.

The frequency and significance of PORNB cannot be judged without NMM. The incidence of PORNB is quite variable, but, according to recent publications can go as high as 63.5% [6]. In a recent clinical trial that has been performed in a Hungarian university hospital the incidence of PORNB was 22.4% in those patients who did not undergo NMM and only clinical signs were considered at the end of surgery to determine the level of residual NMB [10]. In 12.8% of the cases PORNB was severe (TOFR < 0.7) Nevertheless participants' estimation of 5% of PORNB is a high figure from an anaesthetic perspective, because major complications due to anaesthesia are relatively rare; about 1:1000 [4]. Thus accepting 5% potentially life threatening complication should not be allowed. The NMM habits show that the vast majority of participants do not use a monitor, which suggests that they accept the risk of complications instead of preventing them. Monitoring one patient/10 is highly insufficient and cannot be advised.

In the current study 26% of participants thought that clinical signs reliably show residual curarization. This may be true for severe residual paralyses. However, in less severe cases silent curarization („the zone of blind paralysis”) [28] may exist causing sudden rebound of muscle weakness due to shivering, physical effort, antibiotics or magnesium leading to critical respiratory events. NMM is a safety measure such as CO_2 , O_2 , ECG or temperature monitoring. The answers seem to suggest to us, that education for NMM is insufficient, and the environment is not monitoring friendly. Senior consultants are not more engaged than

junior staff, thus there is no transfer of know-how from generation to generation.

Although equipment for monitoring is available in many hospitals, a TOF module or an equivalent monitoring facility is incorporated in the modern anaesthesia equipment, it is not organized as a system including maintenance, teaching and guidelines for employment. Despite solid evidence showing the need for NMM, participants still believe in clinical observation. Further effort is necessary in education to change this mentality, which is in contrast to all evidence.

Conclusions

Though almost 50 years have passed since the introduction of TOF monitoring with a target ratio of 0.7 for decurarization, it is time to forget this figure and realize that TOF ratio 1.0 should be the target recovery to prevent PORNB. Neuromuscular transmission is a vital function, similar to blood pressure or oxygenation. Thus, NMM should be obligatory, such as pulse oximetry, and should be carried out in each patient who has been given a NMBA. Clinical signs of residual muscle relaxant effect are not reliable and their use cannot be recommended [29-31].

Regarding the habits of participants pertaining to the reversal of NMB, similar confusion was manifested. Firstly, participants were not aware of the time necessary for reversal of NMB with neostigmine, which encodes inadequate extubation of the trachea *per se*. Secondly, without monitoring the necessity of neostigmine reversal cannot be set, neither can the dose. On the one hand neostigmine administration is recommended once 4 responses to TOF stimulation are present; on the other hand it may cause NMB itself if there is no relaxant effect at the postsynaptic acetylcholine receptors [32]. Distinguishing between the two situations requires NMM [31].

Limitations of the study. The main limitation of our study is its small sample size (13.7%), therefore caution is warranted with regard to the generalizing of the results. The nature of the investigation comprises the risk of the inaccuracy of data. On the other hand, it is conceivable that the majority of the participants of the present study were ones who have shown at least some interest to NMM and reversal to complete the survey. Another limitation is the absence of control, i.e. a second round after one week to answer the same questions. This would have greatly improved the quality of information. The study is limited to the use of neostigmine for reversal, questions about sugammadex were not included in the questionnaire.

Interpretation. Objective NMM does not constitute part of routine clinical practice in Hungary and

Romania, and several anaesthesiologists go as far as to suggest that it is even not necessary. Anaesthetists are reluctant to use neostigmine regularly for reversal of the block and prefer spontaneous recovery despite evidence on the benefit of reversal. They would use objective monitoring if it were available, but, while the hospitals possess the devices, there is no organized equipment park, and the costs of the devices are amortized without use. In spite of continuous medical education including NMM, anaesthetists are not motivated for objective NMM and less than 10% of them use it routinely. There is clear evidence that the use of objective neuromuscular monitoring helps to disclose PORNB and thus reduces postoperative complications. Measures have to be taken to make objective NMM obligatory, as a part of routine intra-operative monitoring. The prerequisites of this are training programs, easy-to-use NMM and clear guidelines that are adapted to daily practice.

Conflict of interest

Nothing to declare

References

- Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. *Anesth Analg* 2008; 107: 130-137. doi: 10.1213/ane.0b013e31816d1268
- Berg H, Roed J, Viby-Mogensen J, Mortensen CR, Engbaek J, Skovgaard LT, et al. Residual neuromuscular block is a risk factor for postoperative pulmonary complications. A prospective, randomised, and blinded study of postoperative pulmonary complications after atracurium, vecuronium and pancuronium. *Acta Anaesthesiol Scand* 1997; 41: 1095-1103. doi: 10.1111/j.1399-6576.1997.tb04851.x
- 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. doi: 10.4103/0019-5049.108562
- Arbous MS, Meursing AE, van Kleef JW, de Lange JJ, Spoomans HH, Touw P, et al. Impact of anesthesia management characteristics on severe morbidity and mortality. *Anesthesiology* 2005; 102: 257-268
- Grosse-Sundrup M, Henneman JP, Sandberg WS, Bateman BT, Uribe JV, Nguyen NT, et al. Intermediate acting non-depolarizing neuromuscular blocking agents and risk of postoperative respiratory complications: prospective propensity score matched cohort study. *BMJ* 2012; 345: e6329. doi: 10.1136/bmj.e6329
- Fortier LP, McKeen D, Turner K, de Médicis É, Warriner B, Jones PM, et al. The RECITE Study: A Canadian Prospective, Multicenter Study of the Incidence and Severity of Residual Neuromuscular Blockade. *Anesth Analg* 2015; 121: 366-372. doi: 10.1213/ANE.0000000000000757
- 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: 765-771. doi: 10.1097/00000542-199704000-00005
8. Cammu G, De Witte J, De Veylder J, Byttebier G, Vandeput D, Foubert L, et al. Postoperative residual paralysis in outpatients versus inpatients. *Anesth Analg* 2006; 102: 426-429. doi: 10.1213/01.ane.0000195543.61123.1f
 9. Kotake Y, Ochiai R, Suzuki T, Ogawa S, Takagi S, Ozaki M, et al. Reversal with sugammadex in the absence of monitoring did not preclude residual neuromuscular block. *Anesth Analg* 2013; 117: 345-351. doi: 10.1213/ANE.0b013e3182999672
 10. Nemes R, Fülesdi B, Pongrácz A, Asztalos L, Szabó-Maák Z, Lengyel S, et al. 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: 609-616. doi: 10.1097/EJA.0000000000000585
 11. Sasaki N, Meyer MJ, Malviya SA, Stanislaus AB, MacDonald T, Doran ME, et al. Effects of neostigmine reversal of nondepolarizing neuromuscular blocking agents on postoperative respiratory outcomes: a prospective study. *Anesthesiology* 2014; 121: 959-968. doi: 10.1097/ALN.0000000000000440
 12. Naguib M, Kopman AF, Ensor JE. Neuromuscular monitoring and postoperative residual curarisation: a meta-analysis. *Br J Anaesth* 2007; 98: 302-316. doi: 10.1093/bja/ael386
 13. 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. doi: 10.1177/0310057X1204000611
 14. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS, et al. Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. *Anesthesiology* 2008; 109: 389-398. doi: 10.1097/ALN.0b013e318182af3b
 15. Brueckmann B, Sasaki N, Grobara P, Li MK, Woo T, de Bie J, et al. Effects of sugammadex on incidence of postoperative residual neuromuscular blockade: a randomized, controlled study. *Br J Anaesth* 2015; 115: 743-751. doi: 10.1093/bja/aev104
 16. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Marymont JH, Vender JS, et al. Intraoperative acceleromyography monitoring reduces symptoms of muscle weakness and improves quality of recovery in the early postoperative period. *Anesthesiology* 2011; 115: 946-954. doi: 10.1097/ALN.0b013e3182342840
 17. 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: 110-119. doi: 10.1213/ANE.0b013e3181c07428
 18. Della Rocca G, Iannuccelli F, Pompei L, Pietropaoli P, Reale C, Di Marco P. Neuromuscular block in Italy: a survey of current management. *Minerva Anesthesiol* 2012; 78: 767-773
 19. Phillips S, Stewart PA, Bilgin AB. A survey of the management of neuromuscular blockade monitoring in Australia and New Zealand. *Anaesth Intensive Care* 2013; 41: 374-379. doi: 10.1177/0310057X1304100316
 20. Beecher HK, Todd DP. A study of the deaths associated with anesthesia and surgery: based on a study of 599,548 anesthetics in ten institutions 1948-1952, inclusive. *Ann Surg* 1954; 140: 2-35. doi: 10.1097/00000658-195407000-00001
 21. Ali HH, Kitz RJ. Evaluation of recovery from nondepolarizing neuromuscular block, using a digital neuromuscular transmission analyzer: preliminary report. *Anesth Analg* 1973; 52: 740-745
 22. Sundman E, Witt H, Olsson R, Ekberg O, Kuylenstierna R, Eriksson LI. The incidence and mechanisms of pharyngeal and upper esophageal dysfunction in partially paralyzed humans. Pharyngeal videoradiography and simultaneous manometry after atracurium. *Anesthesiology* 2000; 92: 977-984.
 23. Tassonyi E. A new concept in the measurement of neuromuscular transmission and block. *Anaesthesist* 1975; 24: 374-377
 24. Waud BE, Waud DR. The relation between tetanic fade and receptor occlusion in the presence of competitive neuromuscular block. *Anesthesiology* 1971; 35: 456-464
 25. 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: 1119-1124. doi: 10.1097/00000542-200405000-00013
 26. Viby-Mogensen J, Jensen NH, Engbaek J, Ørding H, Skovgaard LT, Chraemmer-Jørgensen B. Tactile and visual evaluation of the response to train-of-four nerve stimulation. *Anesthesiology* 1985; 63: 440-443. doi: 10.1097/00000542-198510000-00015
 27. Eikermann M, Groeben H, Hüsing J, Peters J. Accelerometry of adductor pollicis muscle predicts recovery of respiratory function from neuromuscular blockade. *Anesthesiology* 2003; 98: 1333-1337. doi: 10.1097/00000542-200306000-00006
 28. Plaud B, Debaene B, Donati F, Marty J. Residual paralysis after emergence from anesthesia. *Anesthesiology* 2010; 112: 1013-1022. doi: 10.1097/ALN.0b013e3181cded07
 29. Checketts MR, Alladi R, Ferguson K, Gemmell L, Handy JM, Klein AA, et al. Recommendations for standards of monitoring during anaesthesia and recovery 2015: Association of Anaesthetists of Great Britain and Ireland. *Anaesthesia* 2016; 71: 85-93. doi: 10.1111/anae.13316
 30. Brull SJ, Kopman AF. Current Status of Neuromuscular Reversal and Monitoring: Challenges and Opportunities. *Anesthesiology* 2017; 126: 173-190. doi: 10.1097/ALN.0000000000001409
 31. Naguib M, Brull SJ, Kopman AF, Hunter JM, Fülesdi B, Arkes HR, et al. Consensus Statement on Perioperative Use of Neuromuscular Monitoring. *Anesth Analg* 2018; 127: 71-80. doi: 10.1213/ANE.0000000000002670
 32. Herbstreit F, Zigran D, Ochterbeck C, Peters J, Eikermann M. Neostigmine/glycopyrrolate administered after recovery from neuromuscular block increases upper airway collapsibility by decreasing genioglossus muscle activity in response to negative pharyngeal pressure. *Anesthesiology* 2010; 113: 1280-1288. doi: 10.1097/ALN.0b013e3181f70f3d