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Original Article

A retrospective observational study of neuromuscular monitoring practice in 30,430 cases from six Danish hospitals*

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Summary

Timely application of objective neuromuscular monitoring can avoid residual neuromuscular blockade. We assessed the frequency of objective neuromuscular monitoring with acceleromyography and the last recorded train-of-four ratio in a cohort of Danish patients. We extracted data from all patients receiving general anaesthesia from November 2014 to November 2016 at six hospitals in the Zealand Region of Denmark. Acceleromyography was available in all operating rooms and data were recorded automatically. The primary outcome measure was acceleromyography use in patients receiving neuromuscular blocking agents, divided into non-depolarising agents and succinylcholine only. The dataset included 76,743 cases, of which 30,430 received a neuromuscular blocking drug. Non-depolarising drugs were used in 16,525 (54%) and succinylcholine as the sole drug in 13,905 (46%) cases. Acceleromyography was used in 14,463 (88%) patients who received a non-depolarising neuromuscular blocking drug and in 4224 (30%) receiving succinylcholine alone. Acceleromyography use varied between the departments from 58% to 99% for non-depolarising drugs and from 3% to 79% for succinylcholine alone. The median (IQR [range]) of the last recorded train-of-four ratio before tracheal extubation was 0.97 (0.90–1.06 [0.01–2.20]) when non-depolarising drugs were used, and was less than 0.9 in 22% of cases. The OR for oxygen desaturation was higher with the use of succinylcholine [2.51 (95%CI 2.33–2.70) $p < 0.001$] and non-depolarising drugs [2.57 (95%CI 2.32–2.84) $p < 0.001$] as compared with cases where no neuromuscular blockade drug was used. In conclusion, acceleromyography was almost always used in cases where non-depolarising neuromuscular blocking drugs were used, but a train-of-four ratio of 0.9 was not always achieved. Monitoring was used in less than 30% of cases where succinylcholine was the sole drug used.

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Introduction

Many have long advocated the routine use of objective neuromuscular monitoring to avoid residual neuromuscular block from neuromuscular blocking (NMB) drugs [1, 2]. Establishing a train-of-four (TOF) ratio > 0.9 before tracheal extubation in patients receiving non-depolarising NMB drugs minimises the risk of respiratory complications [3, 4]. Neostigmine and sugammadex may be used to facilitate this [5]. Although recommendations for neuromuscular monitoring primarily focus on non-depolarising NMB drugs, the importance of monitoring the effects of succinylcholine have also been demonstrated [6]. However, surveys from several countries show that objective neuromuscular monitoring is used in 32–53% of cases [7–9]. In Denmark, objective neuromuscular monitoring has been available in most operating theatres since the early 2000s and, in a recent survey, 85% of Danish anaesthetists reported use of objective neuromuscular monitoring in at least 75% of procedures involving non-depolarising NMB drugs [10, 11]. However, it is not known how often the equipment is used, and to what degree anaesthetists ensure full recovery of neuromuscular blockade before tracheal extubation.

The aim of our retrospective analysis was to assess: the use of objective neuromuscular monitoring in six Danish anaesthetic departments; the last recorded TOF value before tracheal extubation; the use of NMB drugs and reversal agents; and the association between hypoxaemia after tracheal extubation and use of monitoring by means of electronically recorded anaesthesia data.

Methods

The Danish Patient Safety Authority and the Danish Data Protection Agency approved the study. This retrospective analysis used routinely collected clinical data from six of seven teaching hospitals in the Zealand Region of Denmark. The Danish Committee System on Health Research Ethics waived the requirement for patient consent.

The primary outcome measure was the use of acceleromyography in cases where NMB drugs were used. We divided the primary outcome into cases involving non-depolarising NMB drugs and cases involving succinylcholine only, because the former was mostly used for non-emergency tracheal intubation or surgical muscle relaxation and the latter for rapid sequence tracheal intubation. Secondary outcomes included: the last recorded TOF ratio before tracheal extubation; reversal of neuromuscular block with neostigmine or sugammadex; tracheal intubation without NMB drugs; time from tracheal extubation to discharge from the recovery area; and occurrence of and severity of oxygen desaturation after tracheal extubation.

The Zealand Region of Denmark had implemented the Philips MP70 acceleromyography module (Philips, Amstelplein 2, 1096 BC Amsterdam, Netherlands) in all operating rooms of its seven hospitals. Train-of-four measurements were displayed on the monitoring screen. The module can be calibrated before use, but these data were not recorded in the anaesthesia information management system. The module only calculated the TOF ratio when the fourth TOF response reached a certain threshold value. Therefore, the module may have displayed a TOF count of 4 without a TOF ratio. The TOF ratio was not truncated to 1.0 and thus TOF ratios above this value were seen. No other types of objective neuromuscular monitoring devices were available.

We included records of all patients undergoing general anaesthesia from November 2014 to November 2016 in six hospitals. We limited the analysis of tracheal intubation without NMB drugs to patients aged > 15 y. Patients receiving general anaesthesia on multiple occasions were included with a case for every procedure. All monitoring data were automatically recorded with one entry per minute in the anaesthesia information management system, MetaVision (iMDsoft, Düsseldorf, Germany). Even though the neuromuscular monitoring module may be set to measure a TOF value every 15 s, data were recorded once per minute. Administration of anaesthetic drugs, time of induction of anaesthesia, tracheal intubation and extubation were recorded manually by the anaesthetist. Patients were anaesthetised according to local guidelines and the preferences of the anaesthetists in charge of patient treatment. Data were extracted by one author (DH-P) using MetaVision Query Wizard (iMDsoft) and exported to Excel spreadsheets (Microsoft Corporation, Redmond, WA, USA). We chose to use the highest of the last three TOF ratios recorded, because TOF ratios often fluctuate in clinical practice. For secondary outcomes, we excluded cases with missing data on the specific outcome studied. We limited the analysis of recovery area length of stay to cases < 24 h. We limited analysis of desaturation after tracheal extubation to cases with desaturation within 10 min after tracheal extubation to increase the likelihood that desaturation could be attributed to residual neuromuscular block. We recorded the outcome as the sum of saturation values below 90% and 80%, respectively. For example, two measurements of 88% or one measurement of 86% would both produce a score of 4.

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Continuous variables and ordinal variables are presented as mean (SD) or median (IQR [range]), categorical variables as number (proportion). In the analyses comparing cases with and without acceleromyography, we used Fisher's exact test. In explorative analyses of factors associated with the application of neuromuscular monitoring and desaturation events, we used logistic regression with the following covariates: department; priority, BMI; age; ASA physical status; type of non-depolarising NMB drug; and first dose of rocuronium. We considered a two-tailed p value of < 0.05 to be statistically significant. Analyses were performed using SPSS version 22 and 25 (IBM Corporation, Armonk, NY, USA).

Results

In the 2-year study period, 76,743 general anaesthetics were given to 55,636 patients at the 6 included hospitals (Fig. 1). An NMB drug was administered for 30,430 (40%) of the 76,743 cases (Table 1). The NMB drug administered was a non-depolarising NMB drug (with or without succinylcholine) in 16,525 (54%) and succinylcholine only in 13,905 (46%). Out of the 16,525 cases involving a non-depolarising NMB drug, 4714 (29%) received succinylcholine before the non-depolarising NMB drug.

Acceleromyography was used in 14,463 (88%) of 16,525 cases where a non-depolarising NMB drug was given, and in 4224 (30%) of 13,905 cases where succinylcholine was the sole NMB drug. Acceleromyography was applied before tracheal intubation in 7883 (56.3%) of 14,003 cases where a non-depolarising NMB drug was given, and in 1183 (28.6%) of 4134 cases where succinylcholine was the sole drug. There was large interdepartmental variability in the use of acceleromyography, both for non-depolarising NMB drugs and succinylcholine (Fig. 2). Two departments had the highest rate of use of acceleromyography for non-depolarising and succinylcholine-only cases, while also having the highest proportion of NMB drug use and the lowest proportion of tracheal intubation without NMB drug use.

Logistic regression revealed the odds of neuromuscular monitoring use in patients who received a non-depolarising NMB drug was 83% (95%CI 60–108%, $p < 0.001$) higher for emergency procedures as compared with elective procedures. With department six used as the reference, the OR for monitoring use for other departments decreased to as little as 0.006 (95%CI 0.004–0.010, $p < 0.001$). Patient age was found to decrease the odds of monitoring use by 0.5% (95%CI 0.2–0.8%, $p = 0.003$) per year, and ASA physical status 2 grading increased the odds of neuromuscular monitoring use as compared with ASA physical status 1 by 24% (95%CI 9–42%, $p = 0.001$). Patients receiving cisatracurium or mivacurium were 14 (95%CI 9-20, $p < 0.001$) and 2 (95%CI 1.6–2.7, $p < 0.001$) times as likely to receive neuromuscular monitoring, respectively, as compared with those receiving rocuronium.

For cases where a non-depolarising NMB drug was given, the median (IQR [range]) last recorded TOF ratio before tracheal extubation was 0.97 (0.90–1.06 [0.01–2.20]) (Fig. 3). The last recorded TOF ratio was less than 0.9 in 2971 (22%). For individual departments, this proportion varied from 13% to 29%. The last recorded TOF ratio was less than 0.7 in 923 (7%). The median (IQR [range]) time from last recorded TOF ratio to extubation was 12 (6–23 [20–473]) min. Restricting the analysis to cases with extubation time 10 min or less after the last TOF ratio did not affect the proportion of cases with a last recorded TOF ratio < 0.9. The most commonly used non-depolarising NMB drug used was rocuronium. The median (IQR [range]) first dose of rocuronium ranged from 0.31 (0.24–0.41 [0.08–1.14]) to 0.55 (0.47–0.63 [0.06–1.42]) $mg.kg^{-1}$ among departments. The median (IQR [range]) first dose of succinylcholine ranged from 1.11 (0.98–1.28 [0.24–2.38]) to 1.19 (1.06–1.36 [0.14–3.33]) $mg.kg^{-1}$ among departments (Fig. 4).

For 40,819 tracheal intubations, 11,761 (29%) did not receive a NMB drug before tracheal intubation. Of these, 1261 (10.7%) received rocuronium at a median (IQR [range]) time of 12 (3–28 [1–249]) min following tracheal intubation. For individual departments, the proportion of patients that did not receive a NMB drug for tracheal intubation ranged from 8% to 55%, and 71% of all non-NMB drug cases originated from one department (Fig. 2).

Neostigmine was administered to 8570 (52%) of the 16,525 cases where a non-depolarising NMB drug was used. The mean (SD) dose of neostigmine was 32 (10) $mcg.kg^{-1}$. In 86% of cases, the dose administered was 2.5 mg, corresponding to one vial of neostigmine/glycopyrrolate. Another 14% received 1.25 mg, whereas only six received other doses. A total of 476 (7%) patients received more than one dose of neostigmine, and neuromuscular monitoring was applied in all but 11 of these. The total dose in patients receiving multiple doses was 2.5 mg (33%), 3.75 mg (48%) and 5.0 mg (16%). The first dose of neostigmine was administered at TOF count 0–1 in 9%, TOF count 2–4 in 30%, TOF ratio < 0.9 in 55%, and TOF ratio > 0.9 in 6%. Acceleromyography was not used in 573 (7%) of cases that received neostigmine.

Rocuronium-induced neuromuscular block was antagonised with sugammadex in 145 (1.0%) of 13,900 cases. The median (IQR [range]) dose administered was 200

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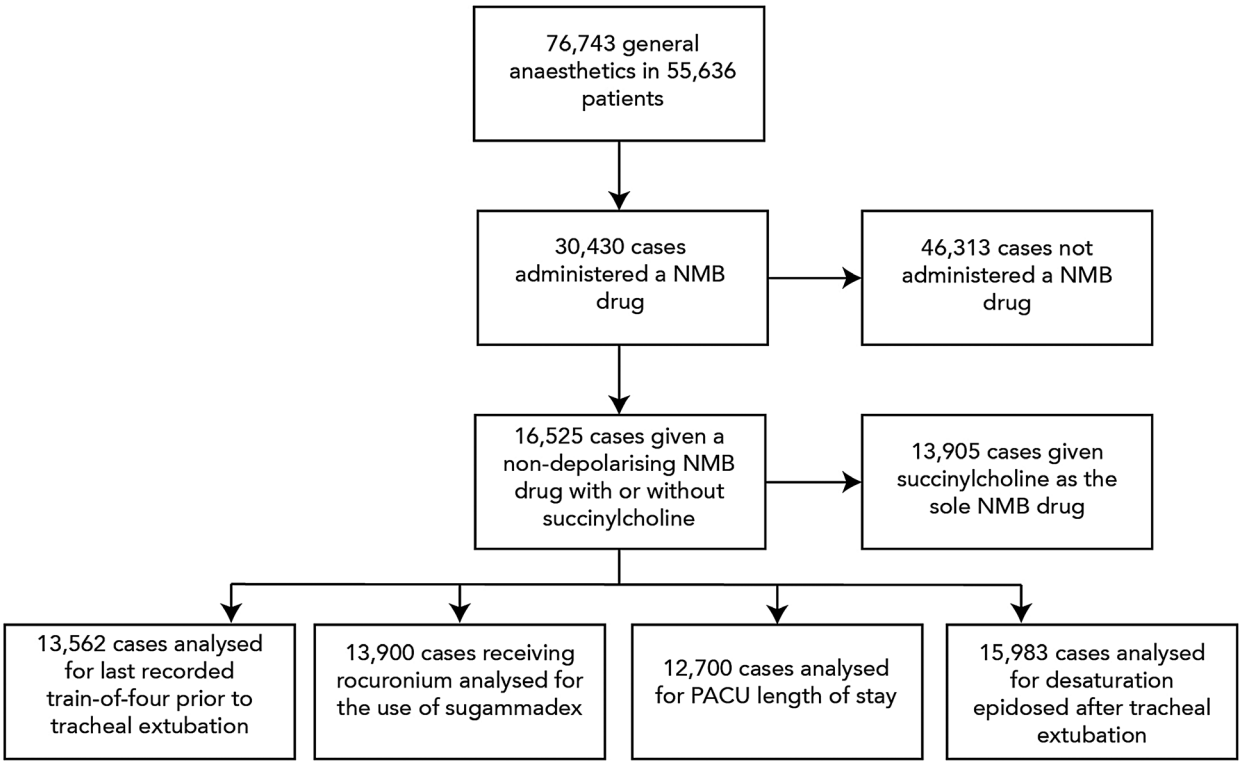

Figure 1 Study flow diagram.

mg (200–350 [100–1000]), or 3.6 (2.2–4.2 [1–16]) mg.kg^{-1}. Sugammadex was administered at a TOF count of 0–1 in 33% of cases, at a TOF count 2 in 47%, and at a TOF ratio > 0.9 in 20%. Post-tetanic count (PTC) data were not available. Six patients who received sugammadex were not monitored with acceleromyography, and received a median (IQR [range]) dose of 2.5 (1.5–3.8 [1–4]) mg.kg^{-1}. In 12,700 cases where a non-depolarising NMB drug was given with a recovery area length of stay of 24 h maximum, the median (IQR [range]) recovery area length of stay was 97 (63–157 [1-1440]) min. In cases without acceleromyography, the median (IQR [range]) recovery area length of stay was 101 (70–153 [1–1302]) min and in cases with acceleromyography, it was 96 (62–158 [1–1440]) min.

For 15,983 cases with available data and where a non-depolarising NMB drug was given, 1753 (11.0%) had at least one documented episode of severe oxygen desaturation below 90% following tracheal extubation. Logistic regression revealed the ORs for desaturation episodes were significantly different between departments, and with department six as the reference, ranged from 0.65 to 1.39. With ASA physical status 1 patients as the reference, the ORs of desaturation episodes were 1.31 (95%CI 1.22–1.41, $p < 0.001$) for ASA physical status 2 patients, 1.38 (95%CI 1.26–1.52, $p < 0.001$) for ASA physical status 3 patients and 1.70 (95%CI 1.35–2.14, $p < 0.001$) for ASA physical status 4 patients. The ORs of desaturation episodes for patients administered succinylcholine or non-depolarising NMB drugs as compared with those who did not receive NMB drugs was 2.51 (95%CI 2.33–2.70, $p < 0.001$) and 2.57 (95% CI 2.32–2.84, $p < 0.001$), respectively but not influenced by the use of acceleromyography [1.05 (95%CI 0.96–1.16) $p = 0.285$]. Extreme oxygen desaturation below 80% in the first 10 min following extubation occurred in 295 (1.8%) cases. Acceleromyography was not applied in 38 (12.9%) of cases with documented desaturations below 80% and in 1942 (12.4%) of 15,688 cases without documented desaturations ($p = 0.800$).

Discussion

In this retrospective observational study, we found that acceleromyography was used in 88% of cases in six Danish hospitals where a non-depolarising NMB drug was used, and in 30% of cases where succinylcholine was the sole NMB drug. These are among the highest rates reported in routine anaesthesia care. In surveys, self-reported usage rates of neuromuscular monitoring, sometimes even including subjective neuromuscular monitoring, range from 9% to 63%, varying with country, institution and over time [7–9, 12–14]. Quality improvement projects have

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Table 1 Baseline characteristics of 30,430 patients that received a neuromuscular blocking (NMB) drug. Patients that received a non-depolarising drug may or may not have also received succinylcholine. Values are mean (SD) or number (proportion).

	NMB drug n = 16,525	Succinylcholine only n = 13,905
Age; y	56.7 (18.5)	57.3 (21.4)
Sex		
Female	9180 (55.6%)	7721 (55.5%)
Height; cm	170.2 (14.4)	167.3 (20.5)
Weight; kg	78.7 (20.1)	77.4 (23.6)
ASA physical status		
1	4714 (28.5%)	2855 (20.5%)
2	8373 (50.7%)	6353 (45.7%)
3	3261 (19.7%)	4352 (31.3%)
4	157 (1.0%)	303 (2.2%)
5	8 (0.0%)	3 (0.0%)
Unknown	12 (0.1%)	39 (0.3%)
Priority		
Elective	12,229 (74.0%)	7011 (50.4%)
Emergency or urgent	4267 (25.8%)	6843 (49.2%)
Unknown	29 (0.2%)	51 (0.4%)

successfully increased the use of objective neuromuscular monitoring to 95% in an American institution and 60% in a French institution [15, 16]. Although no formal quality improvement project had previously been conducted in the study hospitals, there are possible explanations for the high usage rates.

There has been a strong tradition for neuromuscular monitoring in Denmark following the publication of Viby-Mogensen et al's seminal paper in 1979 in which the authors reported a high incidence of residual neuromuscular block in patients receiving routine care [17]. Since then, and especially in the last decade, the curricula for both Danish anaesthetists and nurse anaesthetists in training have included principles of the management of neuromuscular block. This was reflected in a recent survey of 653 Danish anaesthetists, in which 58% reported always using objective neuromuscular monitoring when administering an NMB drug, while 86% of respondents said they would use it at least 75% of the time [11].

Availability of objective neuromuscular monitoring equipment is an obvious prerequisite for using it. Generally, there is more availability in European as compared with US institutions [9, 18]. That said, although acceleromyography was officially available in all operating rooms in our study, the equipment could have been malfunctioning or the data transfer from the module could have failed, reducing the monitoring rate. Although acceleromyography was nearly always applied when non-depolarising NMB drugs were used, it was only used for 30% of cases where succinylcholine was the sole drug. However, departments five and six seemed to be better at using monitoring for both non-depolarising NMB drug and succinylcholine-only cases (Fig. 2). The reason for this is unknown, but it is worth noting that these two departments had the lowest proportion of tracheal intubations without NMB drugs. Application of neuromuscular monitoring before awakening reduces the risk of a patient with undiagnosed plasma cholinesterase deficiency having accidental awareness during general anaesthesia [6]. Thus, it should be considered best practice to apply neuromuscular monitoring before awakening and extubating the trachea of a patient who has received succinylcholine as the sole drug [19].

The last recorded TOF ratio before tracheal extubation was less than 0.9 for 22% of cases where acceleromyography was used. Many studies reporting the incidence of residual neuromuscular block measured the TOF ratio on arrival in the recovery area [4, 15, 16]. It is possible that if TOF ratios had been recorded on arrival in the recovery area in our study, then they would be higher, although it should still be at least 0.9 before tracheal extubation. Data were only recorded once per minute, even if TOF measurements were performed more frequently. We chose to use the highest of the last three recorded TOF ratios, but the anaesthetist may have observed a TOF ratio above 0.9 between the three measurements. In some cases, the anaesthetist may have removed the monitoring equipment after establishing a steadily increasing TOF ratio before tracheal extubation was expected to be performed, resulting in a final TOF ratio < 0.9. In patients receiving neostigmine, the anaesthetist may have chosen to disconnect the acceleromyograph after administering a reversal drug in the expectation that the TOF ratio would have increased sufficiently. Calibration of the acceleromyograph increases the precision, but calibration data were not recorded. The histogram of last recorded TOF ratios showed close to normal distribution around a mean of 0.97. It is well established that, with acceleromyography, the control TOF ratio before administration of NMB drugs is often higher than 1.0, and sometimes up to 1.5 [20]. In a recent survey, Danish anaesthetists reported that they

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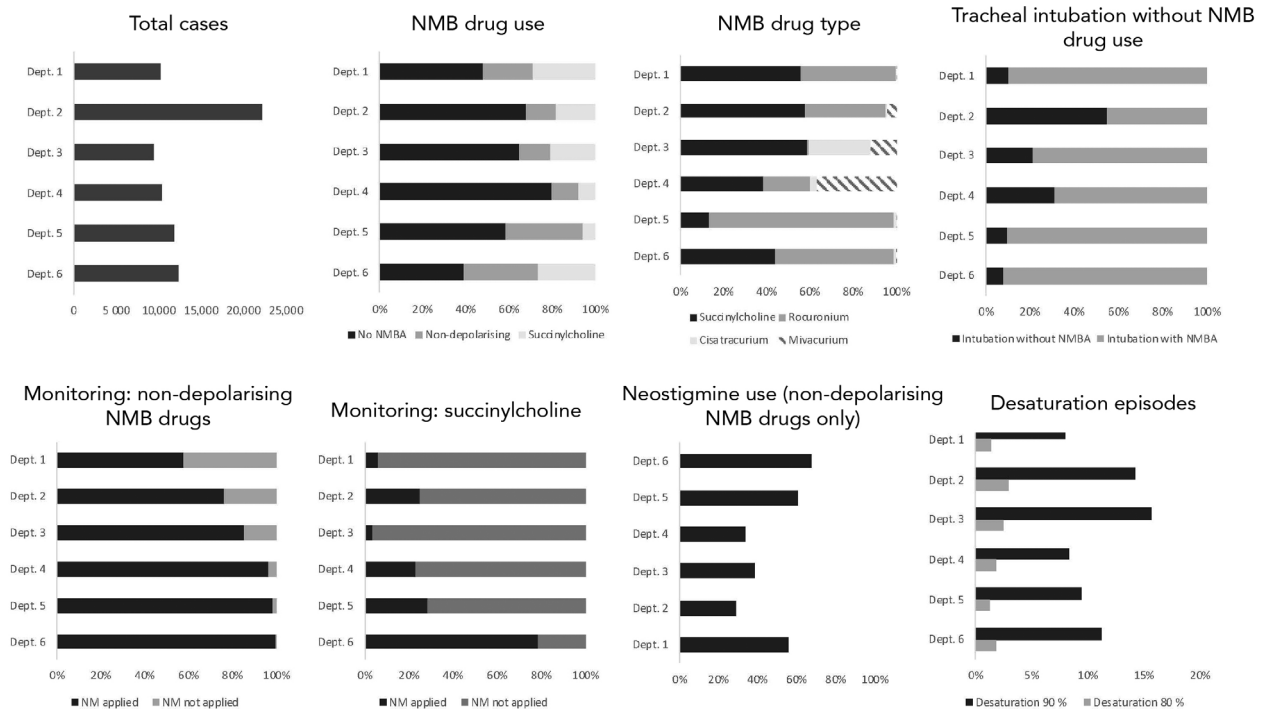

Figure 2 Panel showing main results, including use of neuromuscular blocking (NMB) drugs and neuromuscular monitoring in the six departments.

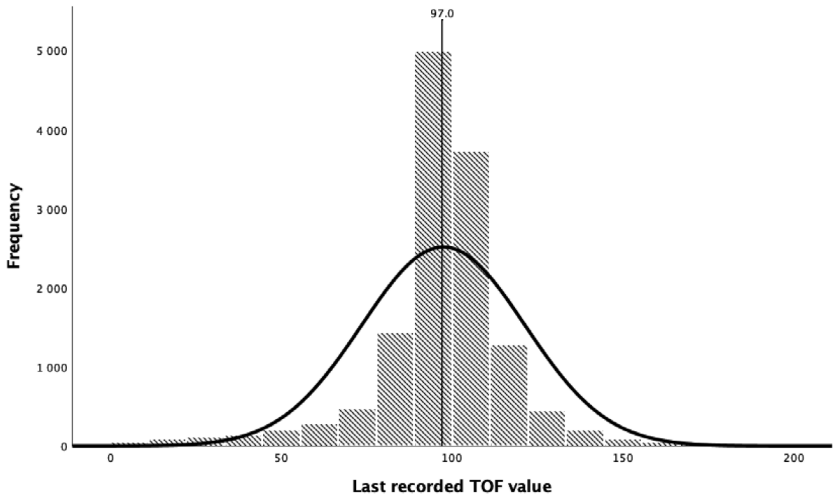

Figure 3 Last recorded TOF values in 13,562 cases. A TOF value of 100 depicts the scenario where no fade is seen and the ratio is 1.0. The vertical line represents the median at 97, while the mean (SD) is 97.4 (24).

experienced fluctuating and unreliable TOF measurements [11]. It has been recommended that TOF ratios obtained using acceleromyography should be normalised to the control TOF ratio [21]. We do not know from our data whether clinicians have adopted this approach. Finally, some anaesthetists may not have been aware that a TOF ratio > 0.9 is recommended to reduce the risk of complications due to residual blockade, as only 71% of respondents in the survey knew this [11]. It is worth noting, however, that the corresponding number in surveys from other countries ranges from 24% to 53% [8, 13, 18].

Succinylcholine was administered to 46% of the patients that received an NMB drug. This is considerably

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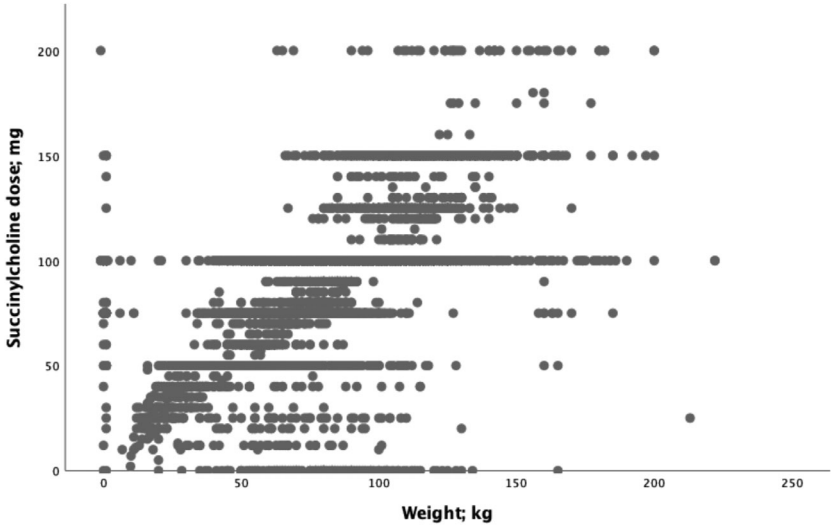

Figure 4 Scatter plot of first dose of succinylcholine against patient weight. The horizontal lines appearing at 50, 100, 150, and 200 mg indicate that succinylcholine is often administered at a 'vial-based dose', as succinylcholine comes in a 50 mg.ml^{-1} 2 ml vial in Denmark.

higher than the 30–32% found in a Danish study using data from the Danish Anaesthesia Database from 2005 to 2007 [22]. Unfortunately, it is not possible from our data to know whether succinylcholine was used only for rapid sequence intubation. There is a suggestion from an interview study with unpublished data that some Danish clinicians who avoid NMB drugs for elective tracheal intubation use a dose of succinylcholine as 'rescue relaxation' when tracheal intubation without NMB drugs proves difficult. Our data shows that 1261 patients seemed to receive rocuronium after tracheal intubation with no preceding NMB drug. In some cases, this may be explained by the clinician simply pressing the 'intubation' button too late, but it could also be explained by a later need of surgical muscle relaxation in cases were tracheal intubation was performed without NMB drugs. In another Danish study, tracheal intubation was performed without NMB drugs in 32% of cases in 2007, close to the 29% in our study [22]. Despite this practice being so common in Denmark for more than a decade, there is no evidence to suggest that the advantages of omission of NMB drugs for tracheal intubation outweighs the increased risk of difficult tracheal intubation [23].

Neostigmine was administered to half of all patients where a non-depolarising NMB drug was given, at a mean dose of 32 μg.kg^{-1}, but predominantly in doses of a full or half vial, regardless of patient weight. The proportion of patients that received a reversal drug was considerably lower than in an American study where 86% received neostigmine, where only subjective neuromuscular monitoring was available [24]. The use of objective neuromuscular monitoring in our study enabled anaesthetists to omit reversal in cases with spontaneous recovery to a TOF ratio > 0.9. Objective neuromuscular monitoring also allowed titration of neostigmine with repeated doses. This probably explains the widespread use of a rather small standard dose of one or a half vial of neostigmine. This is in contrast to when only subjective neuromuscular monitoring is available, where it is reasonable to use a weight-based dosing standard, as was also the case in the American study [24]. In 6% of cases with neostigmine, reversal was administered at a TOF ratio > 0.9. This finding could have been caused be imprecise manual registration of the time of reversal, or by the anaesthetist suspecting residual neuromuscular block despite a recorded TOF ratio > 0.9. Finally, if the control TOF value was > 1.0, the anaesthetist may have chosen to administer reversal despite a TOF ratio > 0.9.

Our finding that arterial oxygen desaturation below 90% after tracheal extubation occurred in 29% of patients may seem higher than expected. In a Brazilian observational study with 415 patients, oxygen desaturation below 90% occurred in 4% of cases, and a low TOF ratio was associated with oxygen desaturation [18]. Although our data reflect a clinical reality, it is important to consider that, due to the way we defined desaturation, a single false measurement below 90%, for example, by displacement of the monitoring probe, would have caused the patient to be categorised with desaturation. Although it would have been valuable in

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assessing the severity of oxygen desaturation, tracheal re-intubation and other airway interventions were not available from our data. Logistic regression showed that although the use of neuromuscular monitoring was not associated with a decrease in the risk of desaturation, the use of NMB drugs did. This is in agreement with other studies, [25] and should serve as a spur for careful clinical postoperative monitoring.

Our study is one of the largest investigations of the use of neuromuscular monitoring in clinical practice yet it has limitations. Although data on use or non-use of neuromuscular monitoring were recorded automatically, and therefore of high validity, the TOF measurements were not as meticulously recorded as they could be in a prospective, controlled trial. This implies that anaesthetists may have varying experience and proficiency with neuromuscular monitoring, and data were only recorded once per minute, even if TOF measurements were performed more often [26]. Due to the way we defined desaturation, a single false measurement of 80% could not be discerned from 5 min of desaturation to 88% (both resulting in a desaturation score of 10). Furthermore, some data were recorded manually by anaesthetists which may have been imprecise. Unfortunately, data on major critical respiratory events, such as need for re-intubation and pulmonary aspiration, were not available. Missing values may have affected the results, and it is likely that manually entered data were less precisely entered – or not at all – in cases of severe arterial oxygen desaturation. Future studies could combine data from the anaesthesia information management system with controlled measurements of residual neuromuscular block and registration of adverse respiratory events.

In summary, this retrospective database study, which utilised routinely collected clinical data from six departments, found that acceleromyography was applied for 88% of cases where a non-depolarising NMB drug was used, but only for 30% of cases where succinylcholine was the sole NMB drug. We conclude that it is possible to obtain consistent use of objective neuromuscular monitoring when non-depolarising NMB drugs are used, and that objective neuromuscular monitoring may guide the dosing of neostigmine and establish when reversal is not necessary. There remains a need to convince anaesthetists that depolarising neuromuscular blockade following succinylcholine should be monitored routinely.

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