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Master thesis | Original study

Perioperative titration habits of rocuronium in the young and elderly patient: A pharmacologic simulation-based survey comparing residents and licensed anesthesiologists

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Abstract

Objective and background: **We explore the association between residents versus licensed anesthesiologist and the intention to adapt rocuronium titration to the patients' age by simulating and comparing the effect-site concentrations of rocuronium (CeROC) and a model derived train of four percentage (TOF%) within and between study groups. The estimation of TOF% by responders is compared with a model derived TOF% and with the intention to use rocuronium antagonists.**
Methods: **A survey in four Belgian hospitals inquired for intended rocuronium dosages of residents and anesthesiologists when managing a laparoscopic procedure in identical ASA1 patients, apart from their age (being respectively 18 versus 80 years). Smart Pilot View® simulator (SPV, Draeger, Lübeck, Germany) calculates the corresponding CeROC and TOF% at several time points and at the end of surgery.**
Results: **87 residents and anesthesiologists responded (= 30% response rate). Compared to licensed anesthesiologists, residents make larger dose adjustments for young versus elderly patients. Residents intubate young patients faster but postpone the intubation in elderly to a similar intubation time as anesthesiologists. Both responder groups estimate TOF% at the end of surgery with wide variation while the model derived TOF% was 100% in all patients. In young patients, respectively 13% and 19% of residents and anesthesiologists do not intend to reverse the rocuronium effect despite expecting a TOF%<90%.**
Conclusions: **Residents intubate young patients (but not elderly) faster compared to anesthesiologists. At induction, both residents and anesthesiologists make age-dependent dose adjustments for rocuronium but make suboptimal reversal decisions when estimating TOF% based on drug administration history only.**

Keywords: **Neuromuscular block, Pharmacodynamics, Drug titration.**

Background and goal of study

Rocuronium is a non-depolarizing neuromuscular blocking agent frequently used to obtain paralysis during anesthesia. It has a fast onset of effect and is reversible both by anticholinergics and sugammadex, which makes it an attractive choice[1].

When using rocuronium in elderly patients, there are some considerations to be made. Pharmacokinetics can be altered as rocuronium is mainly metabolized by the liver and we establish a reduced hepatic blood flow, a decrease in liver mass as well as a reduced intrinsic metabolic capacity of the liver with increasing age, all of which may contribute to a longer duration of the effect of rocuronium. On top of this, studies show

Ethics Committee approval and informed consent: Ethics approval was granted on October 21, 2021, by the Ethics Committee of AZ St. Jan Brugge Oostende AV (Ruddershove 10, 8000 Bruges). The chair of this committee is dr. L. Vanopdenbosch. The study registration number is BUN B04920210000026. Inclusion of participants started on 22/03/2022 and ended on 31/05/2022.

that the onset time of neuromuscular blocking agents is prolonged in elderly patients, thus a longer delay to intubation must be maintained to achieve optimal intubation circumstances. The duration of this interval naturally also depends on the dose of neuromuscular blocking agents given by the anesthesiologist[2].

The recommended dose of rocuronium at induction and during maintenance of anesthesia can be derived from drug manufacturers recommendations or from evidence based clinical protocols. The ED95 of rocuronium is 0.3 mg/kg and to obtain good intubation conditions a dose of 0.6 – 1.2 mg/kg is advised, according to the duration of onset (higher dose for a faster effect)[3].

It remains insufficiently understood whether a decision to adjust the dose of rocuronium in daily clinical practice, is generally determined by these recommendations, or rather by factors such as demographic characteristics of the patient or clinical experience of the anesthetist? In an attempt to improve our understanding of the decision-making process of rocuronium titration, this study explores the association between a clinicians' experience level (being respectively resident or a licensed anesthesiologist) and their respective intention to adapt the dose of rocuronium to a difference in patients' age (respectively 18 versus 80 years of age). The hypothesis is that, having more clinical experience, licensed anesthesiologists adapt the drug dose more accurately according to the patients age compared to residents.

For each of the rocuronium dosing strategies, the expected time-course of the clinical effect of rocuronium can be quantified, using population derived pharmacokinetic pharmacodynamic (PKPD) models. The time course of the effect-site concentrations of rocuronium (CeROC) (using the Wierda PKPD model) is simulated with the corresponding train of four percentages (TOF%) (using the Masui PD model) to compare whether dose adjustments according to age also result in different TOF% effects between populations[4,5]? The hypothesis is that licensed anesthesiologists titrate towards similar model-derived TOF% values in 18- and 80-year-old patients, whereas residents may evoke different TOF% levels between age groups. This could be explained as residents have less clinical experience and they are thus more dependent on theoretical recommendations based solely on one demographic, being the weight of their patient. (cfr. supra)

Despite the availability of clear recommendations, a substantial number of anesthesiologists waive perioperative neuromuscular function monitoring and decide on the need for a rocuronium antagonist at the end of surgery, purely based on the drug administration history[6]. The use of NMBA antagonists, however, should be a well-considered choice since residual paralysis can be an important reason for increased morbidity and mortality, mainly causing respiratory complications. In the elderly patient, having less physiologic reserve, this becomes even more pronounced[2,7]. On the other hand, the systematic use or overuse of antagonists can lead to avoidable side effects[8] as well as increased medical costs[9,10].

In this simulation-based survey we explore whether estimations of TOF% at the end of surgery by each experience group are consistent with a model derived TOF% and how the expected TOF% affects the intention to use rocuronium antagonists.

Methods

This manuscript presents only a subsection of a larger database collected simultaneously with this study. Other results of the study will be published in sequential manuscripts.

The current manuscript only presents study results related to the intended titration of rocuronium, and the adaptation habits according to the age of the patient.

Following institutional ethics committee approval (AZ Sint Jan Brugge, Belgium, BUN B04920210000026. Approved on 21/10/2021) a survey was conducted in four Belgian hospitals to inquire for respective dosing intentions of a population of board-certified anaesthesiologists versus residents. Questionnaires (added in attachment) were distributed on a voluntary basis in the anaesthesia departments of two Belgian university hospitals (respectively of the University of Ghent and Leuven) and two large non-university centres (AZ Sint-Jan Brugge-Oostende AV, Brugge, Belgium and AZ Damiaan Oostende, Oostende Belgium). The survey was designed using the SurveyMonkey platform and conducted over a two months' time frame (March 2022 until May 2022).

Each participant was challenged to provide an anaesthetic plan for four patients, all scheduled for a diagnostic laparoscopy with an expected surgical time of 30 minutes. The procedures have an identical time-course of events, each patient is assumed to be ASA 1 and fasted. The patients are only differentiated by a single demographic characteristic being either age (18 versus 80 years), body mass index (+/-18 versus +/-33) or gender (male/female). Each participant of the survey was asked to reply to only two out of three possible patient-groups to avoid excessive duration of the survey time.

The intended dose and timing of each administered drug was queried for induction (between first administered drug and incision), as well as for maintenance of anaesthesia (between incision and end of surgery). After induction, intubation of the trachea was performed at a timing decided by the participant (expressed in seconds after last drug administration). Incision was always planned exactly 10 minutes after intubation. It is assumed that no arousal or hemodynamic or movement events are detected by the available monitoring throughout the procedure.

The choice of drugs was restricted to a combination of respectively sufentanil, propofol, rocuronium and sevoflurane. IV drugs were administered in bolus but could be repeated if deemed necessary by the participant throughout the case. After intubation, the desired target end-tidal vol% of sevoflurane vapor pressure was queried, assuming that the fresh gas flow was set in open setting, to ensure the fastest onset of effect. We also inquired for intended tapering strategies during maintenance of anaesthesia, in anticipation of the end of surgery. Sevoflurane administration was stopped at the end of surgery (exactly 30 minutes after incision). Participants are urged to provide doses that are compatible to their common clinical habits, rather than to aim for the correct dose, as proposed by the drug manufacturer or academic guidelines. To simplify the questionnaire and since weight was provided in each case, we asked for absolute doses (µg, mg) rather than weight dependent doses.

At the end of surgery, we inquired for the participants' estimation of the train-of-four (TOF) count and/or TOF percentage (TOF%), considering exclusively the history of their rocuronium administration. As such, the choice and availability of neuromuscular blocking agents monitoring were not investigated. The intention to administer an antagonist of the neuromuscular blocking agent in view of the expected residual rocuronium effect was also registered without specifying the type or the dose of the antagonist.

In this article we only discuss the results obtained from the simulated cases differing in age (18 versus 80 years old). Other demographics provided were weight (68 kg in all cases), height (176 cm in all cases) and sex (male or female).

For a complete survey questionnaire, we refer to the appendix of this article.

Data handling and simulation

All obtained answers of the Survey Monkey output file are sorted for the primary and secondary outcomes, in Microsoft Excel 16.0 (Microsoft, Redmond, USA) according to patients age and the participants experience level, being either residents or licenced anaesthesiologists. The Smart Pilot View® simulator software (Dräger, Lübeck, Germany) was used to simulate the time course of the rocuronium effect-site concentration (using the PKPD model of Wierda[4]), based on the drug administration history derived from the survey monkey questionnaire. TOF% was calculated according to Masui at induction (maximal values), intubation, incision and at end of surgery[5]. This Masui model predicts the corresponding population average TOF% that correlates with CeROC

Statistical analysis

Our primary outcome parameters are the total dose of administered rocuronium at induction (mg), the delay in time (s) between rocuronium administration and intubation as well as the intention to use a rocuronium antagonist (yes/no) in perspective to the estimated TOF% at the end of surgery. The maximal CeROC reached after induction (as predicted by Smart Pilot View® simulator software (SPV, Draeger, Lübeck, Germany)), CeROC at intubation, incision, and at the end of surgery, the responder's expectation of TOF count (0-4) and TOF% (%) at the end of surgery are secondary outcome parameters.

The population average TOF% that corresponds with the CeROC of Wierda was calculated at all previous time points using Microsoft Excel 16.0 (Microsoft, Redmond, USA) and the PD covariates defined by Masui et al.[5]. Statistical comparisons were made between age groups within each experience level, as well as between experience levels in a single age group. An F-test determined whether the variation between group samples is significantly different or not. Depending on the F test result, an appropriate T-test was used. Statistical significance was set at $P<0.05$. No adaptation for multiple comparisons was performed as no within group comparisons were performed for any parameter.

The model derived TOF% and the responders' estimation of the TOF% at the end of surgery were plotted on graph in categories as defined in Table I. The accuracy of the responders TOF% prediction is quantified by counting the number of categories between the category selected by the responder and the category which contains the model derived TOF%. As such, a positive/negative value indicates several categories above/below the category that contains the model derived TOF%. A value of 0 indicates that the responder selected the same TOF% category as the Masui model. With this quantification, the prediction accuracy between responder groups can be statistically compared.

Table I. — Categoric value in function of estimated or correct model derived TOF percentages.

Train of four	Category
Not applicable (TOF < 4/4)	Category 0
TOF% < 10%	Category 1
TOF% < 50%	Category 2
TOF% 51-70%	Category 3
TOF% 71-90%	Category 4
TOF% > 90%	Category 5

Results

The survey was sent to 289 residents and anesthesiologist working at four Belgian hospitals (two university hospitals (UZ Leuven (Leuven), UZ Gent (Ghent)), two regional hospitals (AZ Sint-Jan Brugge-Oostende AV, (Bruges), AZ Damiaan, (Ostend)). Data was collected from March to May 2022. We received 87 responses (30% response rate), respectively 51 residents and 33 licensed anesthesiologists. Figure 1 shows the inclusion flow chart. In total, 68 questionnaires (38 residents and 30 anesthesiologists) were analyzed. For this paper, we only selected the cases of 18 (N=92) versus 80 years old patients (N=44), both male and female (Table II).

Table III shows all results of the comparisons of primary and secondary endpoints when comparing age groups within each experience level and within age groups but between residents and anesthesiologists. At induction, residents give similar doses of rocuronium (mean (SD)) in young patients compared to licensed anesthesiologists, but residents make larger dose adjustments between 18- and 80-year-old patients (respectively 33.4 (6.5) vs 29.5 (6.3) mg, p=0.023) compared to licensed anesthesiologists (respectively 35 (6.9) vs 33.7 (7.5) mg, p=0.556). The lower induction doses of rocuronium administered in elderly do evoke a significantly lower CeROC during induction and at incision in the residents' group, but not in the licensed anesthesiologists' group. However, despite lower CeROC in elderly, no significant differences could be identified in the corresponding model derived TOF%, neither at induction, intubation, nor incision.

In the resident group, we see a faster intubation in younger patients compared to anesthesiologists (respectively 125 (44) versus 141 (43) seconds), but in elderly patients the intubation delay is similar between residents and anesthesiologists.

For all patients, the CeROC at the end of surgery had become subclinical low. As such, the model-derived TOF% at the end of surgery all ranged in the category >90% (Figure 2). Both residents and licensed anesthesiologists underpredict the model derived TOF% with multiple categories (Table III). This underprediction was smaller in the residents group compared to the licensed anesthesiologists' group, both in young patients (respectively: -1.98 (1.47) versus -2.59 (1.89), p=0.086) as for elderly (respectively -2.05 (1.56) versus -2.78 (2.11),

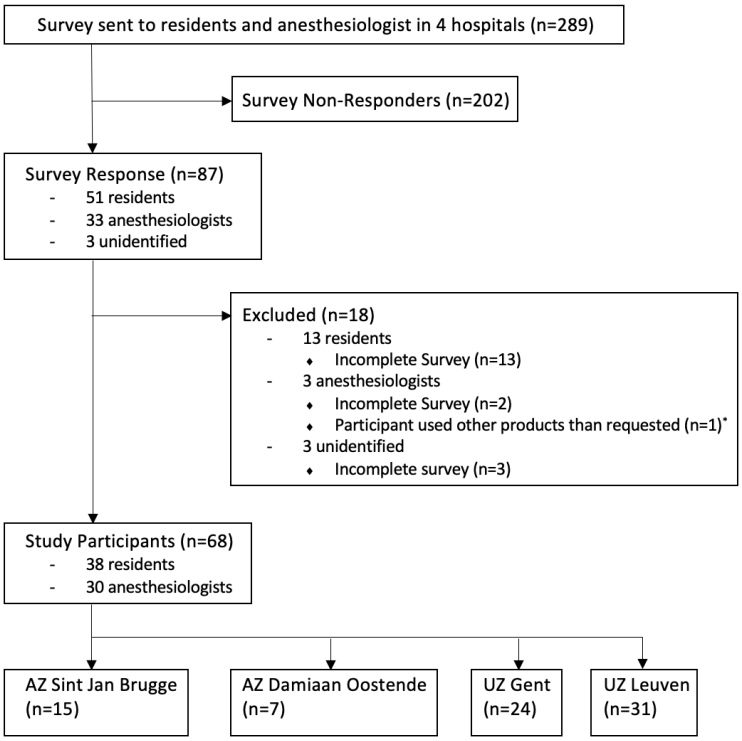

Fig. 1 — Flow chart of survey study responders.
* One responder mentioned the simultaneous use of nitrous oxide when asked for sevoflurane settings, although we specified the answer (EtVol% = …).

Table II. — Number of cases included in data analysis to evaluate titration behavior of residents and anesthesiologists and analyze their intention to adapt the dose of rocuronium according to patients' age.

	Residents	Anesthesiologists	Total
Number of cases included (%)	152 (56)	120 (44)	272
Number of cases with different age (%)	76 (56)	60 (44)	136
Number of cases:			
- 18 years old (%) - 80 years old (%)	55 (60) 21 (48)	37 (40) 23 (52)	92 44

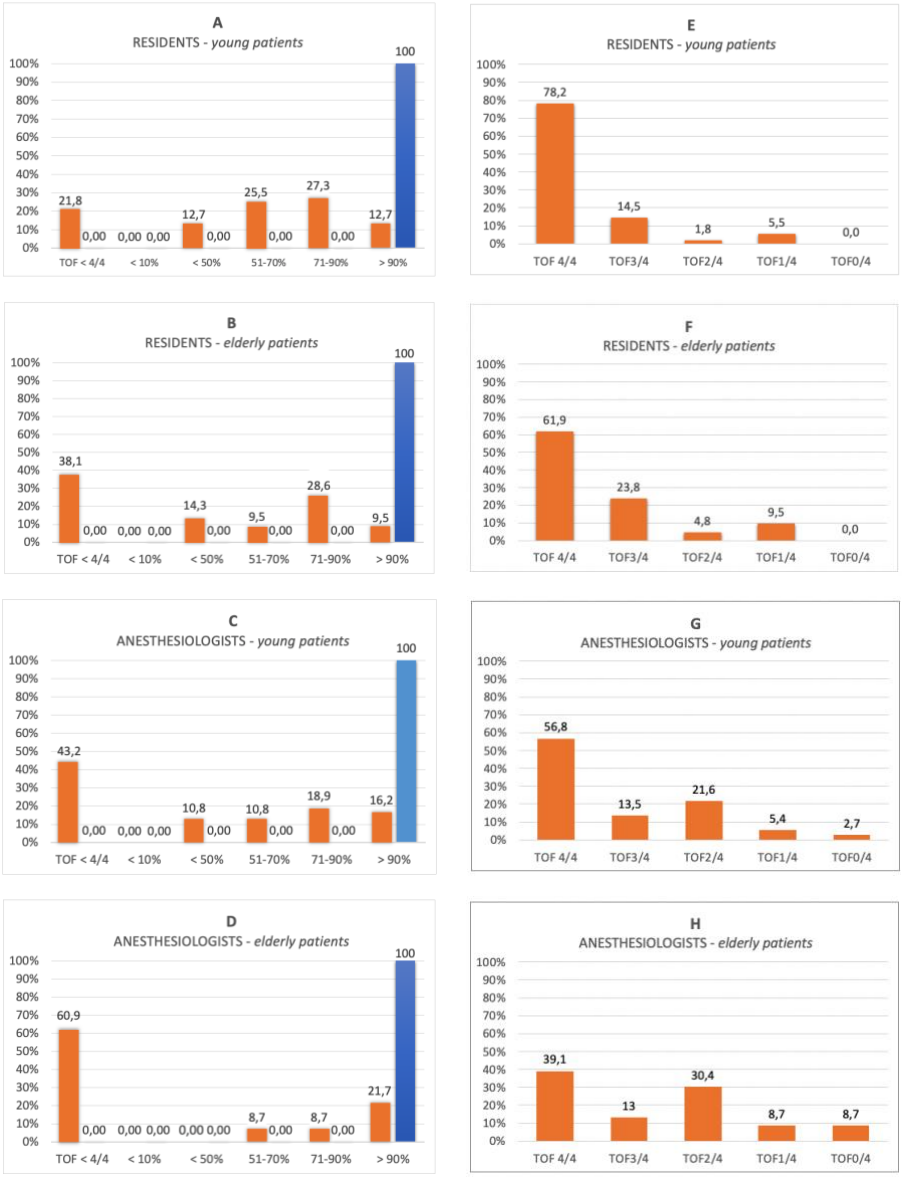

Fig. 2 — Percentage of responded (orange) and model-predicted (blue) TOF% (A,B,C,D) and TOF count (E,F,G,H) at the end of surgery in young (A,C,E,G) and elderly (B,D,F,H) patients by residents (A,B,E,F) and anesthesiologists (C,D,G,H). Based on the demographics of the patient and the dose and timing of drug administration, the Masui model predicts four responses and a TOF% of 100% in all young and elderly patients at the end of surgery, but only a small percentage of residents and anesthesiologist predict this outcome correctly. Using a TOF monitor remains necessary to improve the accuracy of NMBA titration and the decision to antagonize neuromuscular blocking agent effect towards the end of surgery.

Table III. — Induction dose of rocuronium and simulated pharmacokinetic-pharmacodynamic primary endpoints.
Data presented as mean (standard deviation). P < 0,05 is considered statistically significant. # Significant difference between age groups within residents' or anesthesiologists' group. * Significant difference between residents and licensed anesthesiologists within same age group. ROC: rocuronium; CeROC: effect-site concentration of rocuronium (according to Wierda); TOF%: Kenichi model derived Train of Four percentage. $ TOF% categories: 0 = TOF count < 4; 1 = TOF% <10%; 2 = TOF%: 11-50%; 3 = TOF%: 51-70%; 4 = TOF%: 71-90%; 5 = TOF% >90%. ‡ number of categories above (>0) or below (<0) the model derived TOF%). †(0=no, 1=YES).

	ROC dose (induction) (mg)	Max Ce_{ROC} (induction) (µg/ml)	min TOF% (induction) (%)	Ce_{ROC} (intubation) (µg/ml)	DELAY TO INTUBATION (sec)	Ce_{ROC} (incision) (µg/ml)	Ce_{ROC} (end surgery) (µg/ml)	TOF% (end of surgery) (%)	ESTIMATED TOF%-CategorY$ (end of surgery)	Categorical$ Prediction error‡	fraction of responders in favour of using A NMB antagoniST†
Residents											
N=55; case 18 y	33,4 (6,5)#	3,00 (0,56)#	0,38 (0,89)	2,16 (0,65)*	125 (44) *	2,34 (0,47)#	0,74 (0,14)#	102,89 (5,77)	3,02 (1,47)	-1,98 (1,47)	0,76 (0,43)#
N=21; CASE 80 y	29,5 (6,3)#,*	2,65 (0,57)#	1,45 (2,45)	2,01 (0,44)	133 (38)	2,06 (0,47)#	0,66 (0,14)#	104,62 (1,96)	2,95 (1,56)	-2,05 (1,56)	0,95 (0,22)#
Anesthesiologists											
N=37; CASE 18 y	35,0 (6,9)	3,12 (0,61)	0,37 (1,04)	2,44 (0,60)*	141 (43) *	2,40 (0,49)	0,76 (0,15)	102,09 (6,50)	2,41 (1,89)	-2,59 (1,89)	0,68 (0,47)
N=23; CASE 80 y	33,7 (7,46)*	2,95 (0,58)	0,76 (1,77)	2,16 (0,70)	128 (52)	2,29 (0,46)	0,72 (0,14)	103,60 (3,10)	2,22 (2,11)	-2,78 (2,11)	0,87 (0,34)

p=0.203). A significant lower fraction of residents has the intention to use a rocuronium antagonist in young patients compared to elderly. For licensed anesthesiologists a similar trend remained, however not statistically significant in this group (Table III).

Discussion

We found that residents and licensed anesthesiologists give similar doses of rocuronium in young patients, but only residents intend to reduce that dose significantly in elderly. Despite this reduction in dose for the elderly patients of the residents, and the subsequent lower CeROC, this did not evoke a significant difference in the model derived TOF% in any study group, neither at the lowest TOF% value during the induction, nor at the TOF% found at intubation and incision.

This can be explained first due to the consistent low model derived TOF% values ranging between 1 and 10% with limited variability. As such, the probability of finding statistical significance is low. Unfortunately, no contemporary PKPD model links TOF count or post tetanic count measurements to CeROC and therefore, we cannot confirm whether the dose adjustments observed in our survey could result in significantly different TOF count or post tetanic count measurements. Second, the pharmacodynamic model of Masui identifies age as a relevant covariate for EC50, ke0 and the slope of the dose response curve that defines the relationship between effect-site concentration and TOF%. Therefore, a given CeROC will result in lower TOF% values for elderly compared to young patients. As such, it is not surprising that the significant lower CeROC in elderly patients found for the residents does evoke similar TOF% compared to younger patients.

Despite low TOF% values found at intubation, we found that both residents and anesthesiologists titrate rocuronium too low for obtaining safe intubation conditions. A TOF count of 0-1/4 is associated with excellent intubation conditions[11], a TOF count of 2 to 3/4 is associated with acceptable conditions already showing greater risk to moving vocal cords, mild coughing, slight diaphragmatic movements as well as moderate jaw opening[3]. The previous indicates that TOF% should be close to 0 in all patients at the time of intubation.

However, as shown in Table IV, we see that only 73% and 89% of the 18-year-old patients reach TOF% < 5% after rocuronium induction dose given by residents and anesthesiologists respectively. These numbers are slightly better for both groups when we look at the 80 years old patients. This phenomenon is largely explained by the timing of intubation in relation to the administration of

Table IV. — Number of cases (%) representing initial doses of rocuronium and the corresponding TOF% at intubation and during induction (being the time between injection of the first anesthetic and incision) as well as number of cases representing a certain delay to intubation.

	ROC dose < 0,6 mg/kg (induction)	ROC dose = 0,6 mg/kg (induction)	ROC DOSE >= 0,9 mg/ kg (induction)	TOF% < 5% at intubation	TOF% < 5% during induction	Delay to intubation >= 120 sec	DELAY TO INTUBATION >= 180 sec
Residents							
N=55; case 18 y	73%	22%	0%	73%	98%	51%	
N=21; CASE 80 y	86%	14%	0%	67%	81%	62%	5%
Anesthesiologists							
N=37; CASE 18 y	62%	27%	0%	89%	97%	70%	
N=23; CASE 80 y	70%	22%	0%	70%	91%	61%	22%

rocuronium as we observe that a major part of the patients does reach a temporarily TOF% < 5% during the period between drug administration and incision.

When looking at the delay to intubation, anesthesiologists wait significantly longer to intubate the young patient compared to residents. However, this difference is not seen in elderly patients. More important, there is no significant difference in the delay to intubation in relation to age in both groups. However, different studies show that rocuronium behaves different in the elderly patient, shifting from a fast onset to a slower onset neuromuscular blocking agent[2]. A study of Schmarz et al. showed that the onset time in elderly patients (≥ 80 years) shifted to a mean of 190 seconds compared to 123 seconds in younger patients. Looking at our survey, only 5% of the residents and 22% of anesthesiologists maintain a three-minute delay in elderly patients[12].

Another explanation for the insufficient neuromuscular blocking effect at intubation could be the underdosing of rocuronium at induction. A large part of residents as well as anesthesiologists use an induction dose lower than the advised 0.6 mg/kg (table 4) regarding younger patients. Induction doses of 0.3 mg/kg have also been described in literature as sufficient for intubation, however, only when a longer delay to intubation is respected[1].

At incision, residents reach a significantly higher CeROC compared to licensed anesthesiologists, both in young and elderly patients, but this also did not result in a significantly different model derived TOF%.

We assume that both residents and anesthesiologists achieve immobility at intubation (and incision) rather using the effects of sufentanil and propofol as a compensation for the relative (under)dosing of rocuronium found in our study. The latter is confirmed in our analysis of the remaining data of the survey's database, where we focus on titration habits of residents and anesthesiologists for propofol, sufentanil and sevoflurane. (Not shown here, results published in subsequent manuscript).

A large fraction of patients remains at a model derived TOF% >5% throughout maintenance of anesthesia as almost no repeated rocuronium doses were administered, neither by residents, nor by licensed anesthesiologists. We assume that this may be evoked by the absence of appropriate NMBA effect monitoring in our study, but it also may reflect the unreliability of estimating elimination time of rocuronium, based solely on the knowledge of the rocuronium administration history. This is also reflected in the systematic under-prediction of the model derived TOF% at the end of surgery by both residents and licensed anesthesiologists. We assume that in absence of appropriate monitoring of the neuro-muscular blocking agent or without bed-side advisory information on the time course of CeROC, the clinical goal to avoid residual neuro-muscular blocking effects at the end of surgery is deemed more important by residents and licensed anesthesiologists compared to the goal of targeting a moderate deep (TOF count 1/4) or a deep neuromuscular block (PTC 0-5) throughout surgery. This is remarkable since it has been demonstrated that a deep neuromuscular block in laparoscopic procedures may be associated with better surgical conditions, lower intraperitoneal pressure, and less postoperative pain[13].

The model-calculated TOF% at the end of surgery predicts a complete reversal of neuromuscular blocking effect (TOF% >90%). On average, the respondents estimate the TOF% at the end of surgery ranging two to three categories lower than the category identified by the model predicted TOF%. Figure 2 shows that only 12.7% and 16.2% of respectively residents and anesthesiologists correctly estimate TOF% in young patients. For elderly this is respectively 9.5% and 21,7%.

Figure 3 shows the relationship between the intention to use a NMBA antagonist and the responders' estimated TOF% at the end of surgery.

In some cases, an antagonist was administered despite a correct estimation of TOF% >90%. This could be explained by the lack of adequate neuromuscular blocking monitoring. However, we must note that the overuse of antagonists can lead to avoidable side effects such as anaphylaxis (sugammadex, neostigmine), bronchoconstriction (neostigmine), bradycardia (neostigmine), blurred vision (neostigmine) and even muscle weakness when used after complete neuromuscular blockade reversal (neostigmine)[8] as well as unnecessary medical costs (mainly due to an excessive use of sugammadex)[9].

At the other hand, some responders intended not to use antagonists despite assuming a TOF% of less than 90% (Figure 3). The latter observation was exclusively observed in younger patients and occurred more in the licensed anesthesiologist group. We assume that this observation may be related to the absence of individual TOF% monitoring in our study. Some respondents might consider to use rocuronium antagonists only after confirming residual NMBA effects with appropriate monitoring. Alternatively, the negative effects of a TOF% <90% at the end of surgery might be underestimated in young patients by some responders. The latter is indirectly suggested by the observation that all elderly patients did receive NMB antagonization, independent of the responder's estimation of TOF%. This suggests that the risk for negative consequences of a TOF% < 90% is deemed more serious in elderly, compared to young patients.

This study was also initiated to identify gaps in knowledge and performance for anesthetic drug titration in common practice, such that educational improvement steps can be focused on the gaps better. Our findings suggest the potential educational value of additional technology (such as NMBA effect monitoring or a bed-side simulation of CeROC and TOF%) to improve the maintenance of a moderate to deep block during surgery while simultaneously avoiding residual NMBA effects and to improve the appropriate use of NMBA antagonists, at the end of surgery. We deliberately used identical PKPD models for calculating CeROC, as used in Smart Pilot View®, a commercially available advisory screen (Draeger, Lübeck, Germany) that calculates drug specific effect-site concentrations and interaction effects at the bedside of the patient, using the drug administration history as an input. The relationship between CeROC and TOF% is age dependent and not common knowledge for many anesthesiologists.

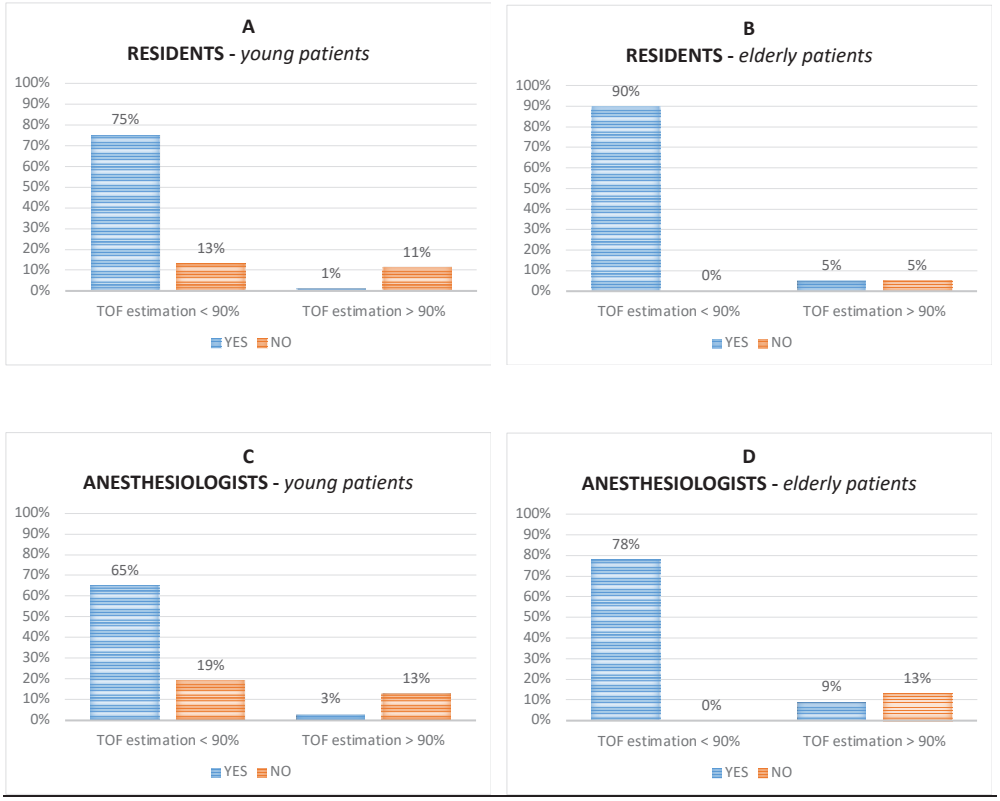

Fig. 3 — Percentage of participants who have the intention to antagonize the neuromuscular blocker effect based on their TOF% estimations at the end of surgery. Comparing residents (A, B) and anesthesiologists (C, D) in young (A, C) and elderly (B,D) patients. Note the intention of some residents and anesthesiologists to antagonize the neuromuscular blocking agent effect despite the estimated TOF ratio of > 90% in young and elderly patients. More important, note an important part of residents and anesthesiologists not giving an antagonist despite an estimated TOF% < 90% in young patients.

Therefore, we suggest that the educational value of such technology could be improved for titration of rocuronium by adding a model-derived TOF% to the advisory screen as a guide for a better control over the time course of rocuronium effect. However, such technology should only be used as complimentary information as it cannot replace objective monitoring (Train-of-four), which remains essential when neuromuscular blocking agents are used.

Our study has limitations as it is derived from a survey only, including the use of hypothetical cases of ASA 1 patients and assuming no perioperative disturbances in hemodynamic or respiratory effects throughout surgery. The decision to adjust a dose in clinical practice might be affected by clinical observations and individually monitored measures. Therefore, this study should be seen as a quantification of dosing intentions rather than a reflection of real clinical dosing behavior. We also did not perform an a priori power analysis as adequate assumptions on the magnitude of expected differences are hypothetical and we could not know the response rate of the survey in advance. Due to the low response rate (30%), and due to the limited number of hospitals included in this study, questions can be raised on the external validity of our findings. The low response rate did not allow us to make an analysis of interhospital differences also.

Finally, effect-site concentrations of rocuronium were obtained using the model of Wierda. Recent findings have shown that simulated TOF% ratios based on the PK/PD models of Wierda and Masui do not always accurately predict intraoperative train-of four ratios and that they tend to overestimate the TOF ratio[14].

Despite these limitations, this explorative study provides insight in the drug titration decision process of residents and licensed anesthesiologists.

Conclusion

Residents reduce their intended rocuronium dose at induction significantly in elderly compared to young patients. This is not seen with licensed anesthesiologists. Both groups fail to adjust their delay to intubation in elderly patients, causing insufficient neuromuscular blockade at intubation. Additionally, 13% of residents as well as 19% of licensed anesthesiologists decide not to use a NMBA antagonist following their TOF% < 90% estimation in young patients. Our study results suggest that using bedside predictions of CeROC and TOF% as an addition to objective NMBA effect monitors has potential educational value as a tool to optimize the rocuronium titration skills of residents and licensed anesthesiologists.

Declaration of interest: None declared..

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