

Predictive Study of Pharmacological Reversal for Residual Neuromuscular Blockade, Early and Late Postoperative Pulmonary Complications: A Prospective, Observational, Cohort Study

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Research

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Abstract

Background

The primary objective was to assess the incidence of residual neuromuscular blockade and postoperative pulmonary complications according to spontaneous or pharmacological neuromuscular reversal, comparing neostigmine and sugammadex. The secondary objective was to present a prognostic model to predict the probability of having residual neuromuscular blockade depending on patient's comorbidities and intraoperative neuromuscular blocking agents management.

Methods

Single-center, prospective, observational, cohort study including patients undergoing surgical procedures with general anaesthesia divided into four groups: cisatracurium, cisatracurium with neostigmine antagonism, rocuronium, and rocuronium with sugammadex antagonism. A binomial generalized linear model was used to predict the residual neuromuscular blockade analyzing patients demographic data, comorbidities, intraoperative neuromuscular monitoring and pharmacological reversal for each patient group.

Results

A total of 714 patients were analyzed. According to our model, none of the studied comorbidities were a predisposing factor for an increase in residual neuromuscular blockade. However, the use of rocuronium, pharmacological reversal with sugammadex, and, particularly, neuromuscular monitoring during surgery markedly decreased the probability. When using rocuronium, avoidance of neuromuscular monitoring and pharmacological reversal led to an incidence of residual neuromuscular blockade of 41.27%; conversely, the use of neuromuscular monitoring and pharmacological reversal with sugammadex decreased the probability to 2.17%.

Conclusions

In our study, intraoperative neuromuscular monitoring and pharmacological reversal with sugammadex, unlike neostigmine, were the factors that most effectively reduced the risk of residual neuromuscular blockade as well as early postoperative pulmonary complications in PACU (upper airway obstruction and desaturation) and late postoperative pulmonary complications (pneumonia or atelectasis) within 30 days.

Background

More than 400 million people receive neuromuscular blocking agents annually to paralyze skeletal muscle groups, facilitate tracheal intubation, allow for controlled mechanical ventilation and achieve optimum relaxation conditions for surgery [1,2].

The possibility of residual neuromuscular blockade (RNMB) after the use of neuromuscular blocking agents has been known for some time. However, in recent years, there has been an increase in the number of publications

showing its high incidence, its relationship to postoperative pulmonary complications (POPC), and, therefore, to increase potential healthcare costs [3-6]. POPC include upper airway obstruction, oxygen desaturation, bronchoaspiration, pneumonia, atelectasis, and reintubation for severe respiratory failure requiring an unplanned admission to an intensive care unit (ICU) [2,3,5-7].

Numerous studies and multiple international organizations have suggested that every patient receiving non-depolarising neuromuscular blocking drugs should have at least qualitative, and preferably quantitative intraoperative monitoring of the neuromuscular blockade (NMB) and assessment of the pharmacologic antagonism of NMB [8-11]. Nevertheless quantitative measurements of drug-induced NMB and the adequacy of pharmacologic reversal have not been widely utilized by anaesthesia professionals [3-5]. The rates of intraoperative neuromuscular monitoring (NMM) vary according to each center and do not cover the entire surgical patients with general anaesthesia and neuromuscular blocking agents [11-13].

In addition, in recent years, some studies have generated controversy since they contradict most previous studies, concluding that intraoperative monitoring of the NMB and pharmacological reversal do not contribute in any way to the reduction of postoperative RNMB or pulmonary complications [2,14].

The primary objective of this study was to assess the incidence of RNMB and POPC according to spontaneous or pharmacological neuromuscular reversal, comparing neostigmine and sugammadex. The secondary objective was to present a prognostic model to predict the probability of having RNMB depending on the patient's comorbidities and the intraoperative management of the neuromuscular blocking agents.

Methods

Study Design and Setting

A single-center, prospective, observational, cohort study was designed that included patients undergoing elective or emergency surgery at Miguel Servet University Hospital in Zaragoza from January 2016 to December 2019. The reporting of this study conforms to the STROBE statement.

Ethics

The study was first approved by the Ethical and Research Committee of Miguel Servet University Hospital, Zaragoza, Spain, with registration code 06/2014 (Chairperson J.M. Larrosa Poves) and subsequently it was reauthorized by the Regional Ethics Committee of Aragón (CEICA), with number CAB-SUG-2019-01 (Chairperson M. Gonzalez Hinjos) as requested by regional guidelines. Written informed consent was obtained from all subjects.

Inclusion/Exclusion Criteria

The inclusion criteria were defined as: patients with ASA physical status I to III, age over 18 years, and signed informed consent. Exclusion criteria included patients with ASA physical status IV to V, known neuromuscular disease, diabetes mellitus with diagnosed neuropathy, pregnancy or lactation, known allergy to neuromuscular blocking agents, cardiac surgery, or planned admission to surgical ICU with mechanical ventilation. The patients were selected prior to the surgery having signed the consent form for inclusion in the study.

Patient Population and Anaesthesia

Four patient groups were established according to the neuromuscular blocking agents and its spontaneous or pharmacological reversal, based on current practice: group 1 cisatracurium without pharmacological reversal, group 2 cisatracurium and neostigmine antagonism, group 3 rocuronium without pharmacological reversal, and group 4 rocuronium and sugammadex antagonism.

The recruited patients were those who received neuromuscular blocking agents under general anaesthesia. Neuromuscular blockade was performed according to standard clinical practice with cisatracurium (0.1 - 0.2 mg/kg) or rocuronium (0.6 - 1.2 mg/kg) for anaesthetic induction at the choice of the anaesthesiologist in charge of the patient who was blinded to the patient's inclusion in the study. Similarly, anaesthetic maintenance, intraoperative NMM, repeated doses of the neuromuscular blocking agent, or the need for pharmacological reversal at the end of surgery depended on the clinical criteria of the same anaesthesiologist. If used, patients in the rocuronium group with pharmacological antagonism received sugammadex (2 - 4 mg/kg), and those in the cisatracurium group with antagonism were administered neostigmine (0.03 - 0.05 mg/kg) and atropine (0.02 mg/kg) according to routine clinical practice.

Measurements and Data Handling

Patient demographic data included age, weight, gender, ASA physical status and comorbidities (chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, restrictive lung disease, asthma, acute myocardial infarction, heart failure, high blood pressure, anaemia, chronic renal failure, diabetes mellitus, dyslipidemia, hyperthyroidism, hypothyroidism, chronic liver disease, dementia and fragility).

The type of surgery (general surgery, maxillofacial surgery, otolaryngology, urology, vascular surgery, and others), emergency or elective procedure, quantitative NMM with acceleromyography during surgery and repeated doses of neuromuscular blocking agent were recorded as intraoperative data.

Primary and Secondary Outcomes

The main outcome was the presence of postoperative RNMB, defined as a TOF ratio < 0.9 at admission to the PACU. A single TOF measurement (four stimuli of 0.2 ms in duration at a frequency of 2 Hz) with an intensity of 40 mA using a TOF-Watch-SX® acceleromyography device [Organon, Oss, The Netherlands] calibrated in the operating room prior to the first dose of NMB. It was performed in 100% of the patients at admission to the PACU by the research staff, who was blinded and was not involved in the intraoperative care of the patient.

The secondary outcomes were the POPC, as defined in other studies like ARISCAT [15] or PERISCOPE [16]. Early POPC were considered as at least one of the following respiratory events in the PACU: upper airway obstruction, desaturation below 92%, bronchoaspiration or need for reintubation for severe respiratory failure of the patient. Late POPC were defined as at least one of the following respiratory events in the 30 days following surgery: pneumonia or atelectasis.

For this, the patient's electronic clinical history was consulted, recording any clinical event, laboratory test, radiological study, and primary care or emergency room consultation reports during hospital admission or 30 days after surgery confirming this type of POPC.

Sample Size

Assuming an incidence of residual neuromuscular blockade with rocuronium and cisatracurium of 13% [17] and 34,1% [7] respectively, with a significant level of 5% and a 95% of power, a sample size of 103 patients was calculated using the EPIDAT v. 4.1. software. To account for dropouts we included at least 110 patients per group. Patient recruitment was performed through a sequential review of cases in a recruitment period from January 2016 to December 2019.

Statistical Analysis

To perform data analysis, a descriptive analysis was completed using the mean, standard deviation and quartiles to summarize quantitative data according to normal distribution. For qualitative data, frequency and percentages were used. For qualitative variables, a χ^2 test and a Fisher's test were used, and when proportions were compared for different groups, a difference in proportions test was used. A Kruskal-Wallis test and an analysis of variance (ANOVA) test were used to study the relationship of a qualitative variable in a quantitative variable.

To predict RNMB, a Binomial Generalized Linear Model was performed using the demographic data (age, weight, gender, ASA), the comorbidities (chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, restrictive lung disease, asthma, acute myocardial infarction, heart failure, high blood pressure, anaemia, chronic renal failure, diabetes mellitus, dyslipidemia, hyperthyroidism, hypothyroidism, chronic liver disease, dementia and fragility) and the variables of the neuromuscular blockade management (neuromuscular blocking agent, intraoperative NMM, pharmacological reversal) as previously detailed.

For this, the Likelihood-Ratio test was used to select the variables of the Binomial Generalized Linear Model with Logistic Regression (logit link) that were part of the final model. The modeling process was carried out in stages, eliminating in each stage the variables with a lower significance or equivalently with a higher p-value for the Likelihood-Ratio Test.

Differences for which the p-value was < 0.05 were considered significant. The analysis has been developed with R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria). The statistical analysis and the review of the data was developed by Jorge Luis Ojeda Cabrera PhD (Dept. of Statistical Methods of University of Zaragoza).

Results

During the study period, 735 patients were included, 21 of whom were excluded as detailed in Fig 1. STROBE patient flow diagram. Patients were divided into the four groups detailed in the methodology by type of neuromuscular blocking agent and spontaneous or pharmacological reversal (Fig. 1). The groups were homogeneous, and there were no differences between the groups in patient demographic data or comorbidities (Table 1).

Residual Neuromuscular Blockade and Postoperative Pulmonary Complication

We found that 28.3% (n = 202) of all patients had RNMB. According to the four groups, the incidence of RNMB was: group 1 cisatracurium without pharmacological reversal 33.52% (n = 59), group 2 cisatracurium with

neostigmine antagonism 30.35% (n = 34), group 3 rocuronium without pharmacological reversal 35.87% (n = 99), and group 4 rocuronium with sugammadex antagonism 5.33% (n = 8), with $p < 0.001$, χ^2 test (Table 2).

Intraoperative NMM was used in 30.3% (n = 216) of patients, with no statistically significant differences in the four groups ($p = 0.98$, χ^2 test). The percent administration of neuromuscular reversal agents was 36.7% (n = 262) of all patients.

If we analyze the influence of intraoperative NMM and RNMB, patients not monitored intraoperatively had an incidence of RNMB of 35.7% (n = 178), however, when monitored the incidence decreased to 10.2% (n = 22) with $p < 0.001$, χ^2 test (Table 3).

With regard to the respiratory events, a total of 15.27% (n = 109) of all patients had some type of early POPC in the PACU. Of the total patients, 10.92% (n = 78) presented oxygen desaturation and 4.34% (n = 31) presented upper airway obstruction. There were no cases of bronchoaspiration or reintubation for severe respiratory.

On the other hand, the incidence of late POPC at 30 days after surgery was 8.12% (n = 58): 6.44% (n = 46) had atelectasis and 1.68% (n = 12) had pneumonia.

The analysis of the influence of RNMB upon both the early and late POPC shown that all of them had a statistically significant relationship ($p < 0.001$, χ^2 test) and both POPC were decreased when intraoperative NMM was performed (Table 3); early POPC ($p = 0.023$, χ^2 test) and late POPC ($p = 0.011$, χ^2 test).

In the case of pharmacological reversal and early POPC in the PACU, the incidence differed between groups ($p < 0.001$, χ^2 test); cisatracurium with neostigmine reversal 18.75% (n = 21), rocuronium with sugammadex reversal 4.67% (n = 7). In the same way, the incidences of late POPC differed also between them ($p = 0.038$, χ^2 test); cisatracurium with neostigmine antagonism 8.93% (n = 10), rocuronium with sugammadex antagonism 2.67% (n = 4) (Table 2).

Predictive Model for Residual Neuromuscular Blockade

All those variables with a positive coefficient estimate contributed to increase the incidence, while those with a negative coefficient decreased it (Table 4). None of the demographic data and none of the comorbidities added to the model predisposed to having more RNMB. However, the type of neuromuscular blocking agent used, TOF monitoring during surgery and pharmacological reversal did have a significant effect.

Specifically, as can be seen from the following data (Table 4), the use of rocuronium (-0.44, coefficient estimate) with pharmacological reversal with sugammadex (-0.88, coefficient estimate) and, particularly, NMM during surgery (-1.46, coefficient estimate) significantly reduced the incidence of RNMB.

When using rocuronium, avoidance of intraoperative NMM and neuromuscular blockers antagonism led to an incidence of RNMB of 41.27%; conversely, the use of monitoring and pharmacological reversal decreased the probability to 2.17% (Table 5).

Discussion

This prospective, observational, cohort study was intended to clarify certain questions arising in recent years from several international studies on RNMB. According to the available literature, this article is one of the few analyzing the patient's demographic data, comorbidities and the intraoperative management of the neuromuscular blocking agents in a single predictive model for RNMB, comparing between neostigmine and sugammadex.

We showed that the incidence of RNMB in our study was 28.3%, i.e. approximately 1 out of every 3 patients under balanced general anaesthesia presented this complication. This figure still appears to be high today; however, it did not differ from the data from the most recent studies, where the incidence ranges from 14% to 32% [18-22].

According to our results, RNMB was significantly decreased when monitoring was performed and the NMB was reversed pharmacologically with sugammadex. As seen in several studies, such as Togioka et al. [5] or Fuchs et al. [22], we showed that when an RNMB existed there was an increase in the POPC.

In cases where intraoperative acceleromyography was used, the expected probability of RNMB decreased by a little over 25%. When pharmacological reversal was used with sugammadex, this probability decreased by 17%. But more importantly, when we performed both techniques in the same intervention, the probability decreased by more than 30%.

In this case, the incidence of RNMB in the group with sugammadex was 5.3%, since it could probably be explained by clinical error. The dosing of sugammadex should be based on actual body weight [23-25]. For moderate NMB, defined as 1 to 2 twitches, the dose is 2 mg/kg, but for deep NMB, defined as post tetanic count of 1 to 2, it is up to 4 mg/kg, and if no monitoring is performed, the degree of NMB cannot be known. Many specialists routinely use 200 mcg of sugammadex [12], and this probably often leads to overdosing, but also to underdosing, particularly in patients weighing more than 100 kg [25]. The same occurs during emergency surgery. The dose of rocuronium is usually doubled, i.e. 1.2 mg/kg, when a rapid sequence intubation is used. Specially in these cases, as always, it is critical to use NMM and, if necessary, to use the correct dose of sugammadex per the patient's real weight and degree of blockade [24-27].

With regard to the percentage of intraoperative NMM at our center, we found that in 30.3% of the surgical procedures quantitatively monitor NMB was used; this figure is similar to those of other studies and centers [7,12,13]. As stated by Naguib et al., the percentage of anaesthesiologists who rely solely on clinical signs for extubation remains very high [28]. According to our results, this lack of intraoperative NMM led to an increase in both early and late POPC. However, of them, this statement is only true for desaturation and atelectasis since, in our sample, we have not been able to demonstrate that intraoperative NMM decreased the incidence of postoperative pneumonia and obstruction. In fact, we have distinguished between early complications in the PACU and late pulmonary complications 30 days after surgery, since the pathophysiological mechanism and the involved factors between them are very different [15,16]. The incidence for early POPC was 15.27%, and for late POPC was 8.12%, similar to those reported by Kheterpal et al. or Ledowsky et al. [3,29]

After analyzing the NMM, we should see what happened with neuromuscular reversal and its influence on POPC. The controversy [31-33] lies with some studies, such as Grosse-Sundrup et al. [2] or POPULAR [14], which have reported that reversal, with one reversal agent and another, was not able to decrease these postoperative

complications, and moreover, they questioned the utility of quantitative monitoring “the use of reversal agents or neuromuscular monitoring could not decrease this risk.” [14].

In our study, we found that pharmacological reversal with sugammadex was associated with a lower risk of suffering early POPC in the PACU. When rocuronium and sugammadex were used instead of cisatracurium and neostigmine, the incidence of desaturation decreased by approximately 12% and, in the case of upper airway obstruction, by up to 2%.

With regard to late POPC and pharmacological reversal, we also showed that sugammadex was able to reduce them. In fact, reversal with neostigmine did not appear to decrease, but to subtly increase, the incidence of these complications, which paradoxically aligned with the conclusions of recent studies [2,22,34-36]. Thus, when rocuronium was used with sugammadex, instead of cisatracurium and neostigmine, these complications decreased by up to 7%.

One of our limitations was that detection of late respiratory complications, of both pneumonia and atelectasis, was based on clinical and laboratory criteria, and it may underestimate the complication rate. We reviewed the clinical history of the patient, without performing systematic X-ray in all cases, since the patients can develop well-tolerated clinical postoperative atelectasis, which would imply unnecessary radiological exposure to all study patients. Perhaps a more effective and improved method for future research would be systematic examination with pulmonary ultrasound. It currently provides similar results to chest CT and chest X-ray for the evaluation of pneumonia and atelectasis [37].

In addition, our results were based on clinical management under real-life conditions. We have not analyzed other factors, such as mechanical ventilation parameters, recruitment maneuvers, multimodal anaesthesia techniques, opioid doses, fluid therapy, duration of surgery and others that are known to contribute to increasing these complications and are probably factors that need to be assessed in subsequent studies and reviews [38,39].

Conclusion

Thus, based on the results of our study, it may be concluded that RNMB derived from the use of neuromuscular blocking agents was associated with higher risk of having both early and late POPC.

Intraoperative NMM was one of the factors that most effectively reduced the risk of all these postoperative complications and, furthermore, pharmacological reversal of NMB with sugammadex, unlike neostigmine, was associated to lower risk of RNMB and postoperative desaturation in the PACU and atelectasis during hospitalization.

Abbreviations

RNMB, Residual Neuromuscular Blockade; POPC, Postoperative Pulmonary Complications; NMM, Neuromuscular Monitoring; NMB, Neuromuscular Blockade; PACU, Post-anaesthesia Care Unit; TOF, Train of Four;

Declarations

Ethics approval and consent to participate: The study was first approved by the Ethical and Research Committee of Miguel Servet University Hospital, Zaragoza, Spain, with registration code 06/2014 (Chairperson J.M. Larrosa Poves) and subsequently it was reauthorized by the Regional Ethics Committee of Aragón (CEICA), with number CAB-SUG-2019-01 (Chairperson M. Gonzalez Hinjos) as requested by regional guidelines. Written informed consent was obtained from all subjects.

Consent for publication: Not applicable

Availability of data and materials: The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interest: There is no conflict of interest on the part of any author.

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Authors' contributions: Cristian Aragón-Benedí: Methodology, Formal Analysis, Investigation, Writing-Original draft preparation; Ana Pascual-Bellosta: Conceptualization, Methodology, Investigation, Writing- Reviewing and Editing, Supervision; Sonia Ortega-Lucea: Conceptualization, Methodology, Investigation, Writing- Reviewing and Editing, Project administration; Sara Visiedo-Sanchez: Investigation, Visualization, Validation; Javier Martinez-Ubieto: Conceptualization, Methodology, Investigation, Writing-Reviewing and Editing, Supervision. All authors read and approved the final version of the manuscript.

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Tables

Table 1 - Homogeneity and Comparison of Demographic Data and Comorbidities Between Groups.

	Cisatracurium - No Reversal Group		Cisatracurium + Neostigmine Group		Rocuronium - No Reversal Group		Rocuronium + Sugammadex Group		P- value
	n = 176		n = 112		n = 276		n = 150		
Quantitative variables (n)	Mean	SD	Mean	SD	Mean	SD	Mean	SD	ANOVA
Age; years (714)	59.8	17.3	60.8	16.7	60.7	16.3	59.4	15.5	0.81
Weight; kg (714)	70.2	11.9	72.6	12.5	72.1	13.2	75.4	16.8	0.11
ASA Score (714)	2.10	0.69	2.16	0.71	2.11	0.67	2.14	0.66	0.89
Qualitative variables (n)	Percent % (n)		Percent % (n)		Percent % (n)		Percent % (n)		χ ² test
Male (474)	23.2 % (110)		16.2 % (77)		40.1 % (190)		20.4 % (97)		0.49
Female (240)	27.5 % (66)		14.5 % (35)		35.8 % (86)		22.1 % (53)		
COPD (85)	21.1 % (18)		16.4 % (14)		49.4 % (42)		12.9 % (11)		0.09
OSAS (32)	40.6 % (13)		3.10 % (1)		34.3 % (11)		21.8 % (7)		0.07
Restrictive Lung Disease (8)	12.5 % (1)		25.0 % (2)		25.0 % (2)		37.5 % (3)		0.49
Asthma (14)	35.7 % (5)		0.00 % (0)		42.8 % (6)		21.4 % (3)		0.38
AMI (67)	22.3 % (15)		23.8 % (16)		35.8 % (24)		17.9 % (12)		0.28
Heart Failure (20)	20.0 % (4)		15.0 % (3)		40.0 % (8)		25.0 % (5)		0.94
High Blood Pressure (329)	26.4 % (87)		17.6 % (58)		37.9 % (125)		17.9 % (59)		0.16
Anaemia (62)	30.6 % (19)		17.7 % (11)		35.4 % (22)		16.1 % (10)		0.54
Chronic Renal Failure (40)	37.5 % (15)		17.5 % (7)		27.5 % (11)		17.5 % (7)		0.20
DM (131)	23.6 % (31)		21.3 % (28)		36.6 % (48)		18.3 % (24)		0.25
Dyslipidemia (165)	24.2 % (40)		18.7 % (31)		37.5 % (62)		19.3 % (62)		0.64
Hyperthyroidism (4)	0.00 % (0)		25.0 % (1)		50.0 % (2)		25.0 % (1)		0.71
Hypothyroidism (2)	27.2 % (6)		13.6 % (3)		45.4 % (10)		13.6 % (3)		0.80
Chronic Liver Disease (20)	35.0 % (7)		20.0 % (4)		20.0 % (4)		25.0 % (5)		0.36
Dementia (2)	0.00 % (0)		0.00 % (0)		0.00 % (0)		100 % (2)		0.05
Fragility (114)	20.1 % (23)		17.5 % (20)		43.8 % (50)		18.4 % (21)		0.42

Basic descriptives and tests for the demographic and comorbidity variables for each group. As can be seen, there was no significant relationship between the demographic and comorbidity variables and each group. Absolute (N) and relative (%) frequencies along with independence tests (χ^2) for the qualitative variables, and mean and standard deviation (SD) along with comparing means tests (analysis of variance [ANOVA]) for the quantitative variables. *Significance defined as p-value < 0.05. ASA, American Society of Anesthesiologists score; COPD, Chronic Obstructive Pulmonary Disease; OSAS, Obstructive Sleep Apnea Syndrome; AMI, Acute Myocardial Infarction; DM, Diabetes Mellitus.

Table 2 - Incidence of Residual Neuromuscular Blockade, Early and Late Postoperative Pulmonary Complications between Groups.

	Cisatracurium - No Reversal Group n = 176	Cisatracurium + Neostigmine Group n = 112	Rocuronium - No Reversal Group n = 276	Rocuronium + Sugammadex Group n = 150	P- value
Qualitative variables	Percent % (n)	Percent % (n)	Percent % (n)	Percent % (n)	χ^2 test
RNMB	33.5 % (59)	30.3 % (34)	35.8 % (99)	5.33 % (8)	< 0.001*
Early POPC	26.7 % (47)	18.7 % (21)	12.3 % (34)	4.67 % (7)	< 0.001*
Late POPC	7.39 % (13)	8.93 % (10)	9.78 % (27)	2.67 % (4)	0.038*

Absolute (N) and relative (%) frequencies for each group along with independence tests (χ^2) *Significance defined as p-value < 0.05. RNMB, Residual Neuromuscular Blockade; POPC, Postoperative Pulmonary Complications.

Table 3 - Incidence of Residual Neuromuscular Blockade and Postoperative Pulmonary Complications if exists both Intraoperative Neuromuscular Monitoring and Pharmacological Reversal.

	No Intraoperative NMM	Intraoperative NMM	P-value	No Pharmacological Reversal	Pharmacological Reversal	P-value
Qualitative variables	Percent % (n)	Percent % (n)	χ^2 test	Percent % (n)	Percent % (n)	χ^2 test
RNMB	35.7 % (178)	10.2 % (22)	< 0.001*	35.0 % (158)	16.0 % (42)	< 0.001*
Early POPC	17.2 % (86)	10.6 % (23)	0.023*	17.9 % (81)	10.7 % (28)	0.009*
Hypoxaemia	12.2 % (61)	7.87 % (17)	0.084	12.8 % (58)	7.63 % (20)	0.031*
Airway obstruction	5.02 % (25)	2.78 % (6)	0.176	5.09 % (23)	3.03 % (8)	0.198
Late POPC	9.24 % (46)	3.70 % (8)	0.011*	8.85 % (40)	5.34 % (14)	0.087
Pneumonia	2.01 % (10)	0.92 % (2)	0.301	1.99 % (9)	1.15 % (3)	0.396
Atelectasis	7.63 % (38)	3.70 % (8)	0.049*	7.30 % (33)	4.96 % (13)	0.219

Absolute (N) and relative (%) frequencies for each group along with independence tests (χ^2) *Significance defined as p-value < 0.05. RNMB, Residual Neuromuscular Blockade; POPC, Postoperative Pulmonary Complications; NMM, Neuromuscular Monitoring.

Table 4 - Variables and Coefficients of the Generalized Linear Model with Likelihood-Ratio Test to Predict Residual Neuromuscular Blockade.

	Estimate	Std. Error	Z value	Pr (> z)
(Intercept)	-0.08	0.15	-0.56	0.57
Rocuronium	-0.44	0.17	-2.50	0.010*
Intraoperative NMM	-1.46	0.24	-5.91	< 0.001*
Sugammadex	-0.88	0.20	-4.33	< 0.001*

Significant coefficients of the Generalized Linear Model along with the standard error (Std. Error), the corresponding Z value and p-values [Pr (>|z|)]. The sign of the coefficients of each variables indicates the direction of the influence in the residual neuromuscular blockade. In our case, all the coefficients were negative, so they were factors that reduced the probability of the residual neuromuscular blockade; *Significance defined as p-value < 0.05.

NMM, Neuromuscular Monitoring.

Table 5 - Probability of Residual Neuromuscular Blockade according to the Neuromuscular Blocking Agent, Neuromuscular Monitoring and Pharmacological Reversal according to the Generalized Linear Model.

NMB agent	Intraoperative NMM	Pharmacological Reversal	Probability RNMB
Cisatracurium	No	No	40.5 %
Rocuronium	No	No	41.2 %
Cisatracurium	Yes	No	14.2 %
Rocuronium	Yes	No	14.6 %
Cisatracurium	No	Neostigmine	39.5 %
Rocuronium	No	Sugammadex	8.33 %
Cisatracurium	Yes	Neostigmine	13.7 %
Rocuronium	Yes	Sugammadex	2.17 %

NMB, Neuromuscular Blockade; NMM, Neuromuscular Monitoring; RNMB, Residual Neuromuscular Blockade.

Figures

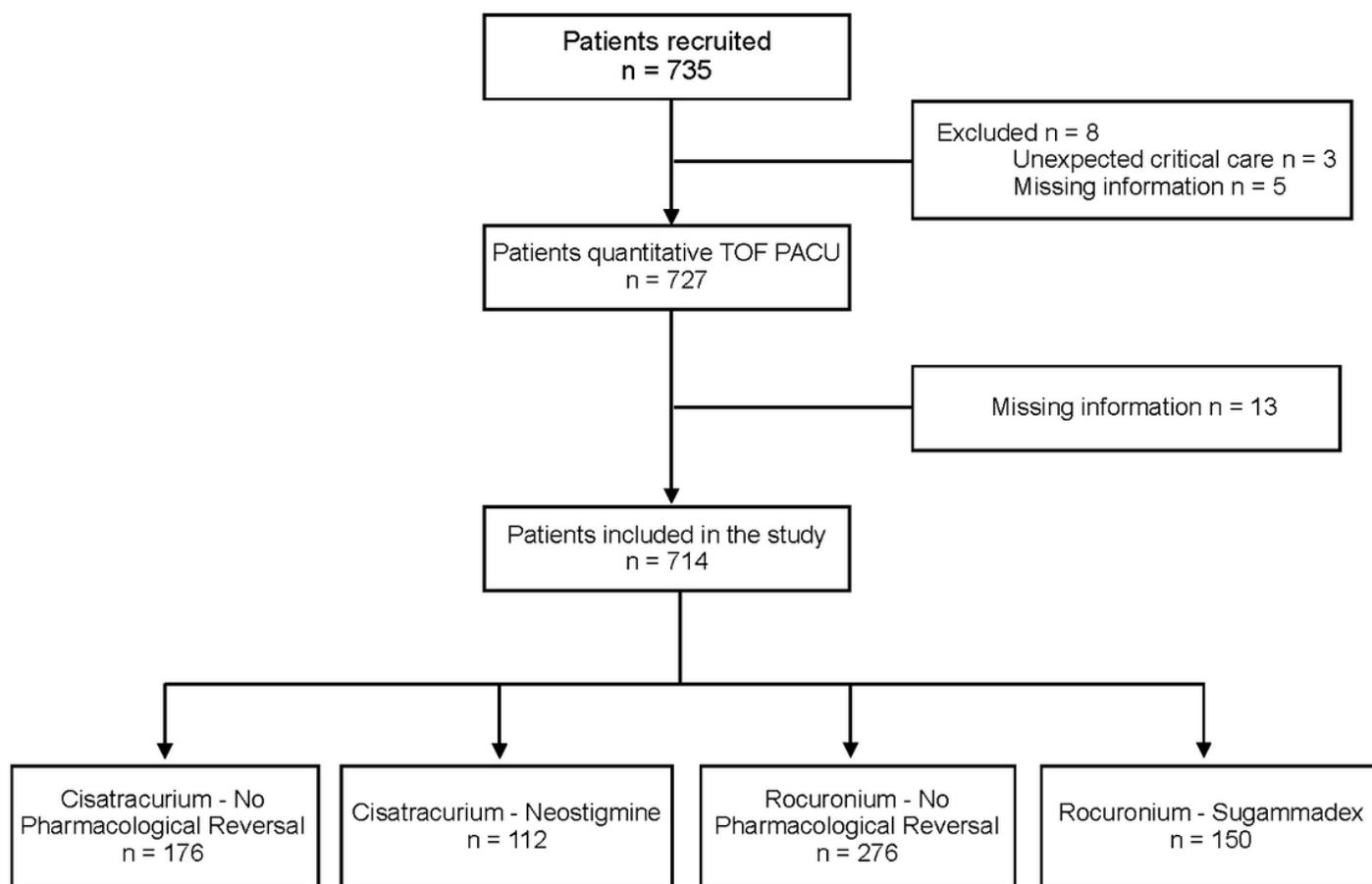


Figure 1

STROBE Patient Flow Diagram. TOF, Train of Four; PACU, Post-Anaesthesia Care Unit.