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ORIGINAL ARTICLE

Demographic Profile and Incidence of Residual Neuromuscular Blockade with the Use of Rocuronium and Sugammadex in Oncological Patients in the Post-Anesthetic Recovery Room

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Abstract

Introduction: Neuromuscular blockers are drugs that provide safety for general anesthesia. However, when there is no spontaneous and complete return of normal neuromuscular function in the postoperative period, residual neuromuscular blockade (RNMB) may occur, which has a significant impact on airway physiology, increasing the risks of respiratory complications, including hypoxemia. Sugammadex is an agent that reverses the neuromuscular blockade caused by rocuronium bromide through its selective encapsulation. However, in certain cases, RNMB may occur due to factors inherent to the reversal agent. Thus, this study aimed to evaluate the incidence of these events in oncological patients in order to provide greater safety after general anesthesia and improve postoperative outcomes in this patient population.

Objective: To evaluate the incidence of RNMB using rocuronium bromide and sugammadex in the postoperative period in oncological patients undergoing general anesthesia at the Amazonas State Center for Oncology Control Foundation (FCECON).

Methods: Prospective, observational study evaluating the incidence of RNMB using the TOF-WATCH T4/T1 sequence in oncological patients undergoing general anesthesia with rocuronium bromide and sugammadex. Demographic data, perioperative variables, and perioperative complications were also recorded.

Results: RNMB was observed in 4.2% of the sample, with complications occurring in 0.8% of patients.

Conclusion: The low incidence of complications associated with RNMB, along with the analysis of anesthetic practices, reflects the effectiveness of the anesthetic protocol used, highlighting the importance of appropriate dosing of the specific rocuronium bromide reversal agent in preventing RNMB. Furthermore, RNMB monitoring in the post-anesthetic recovery room using TOF-T4/T1 was shown to be a safety factor for the anesthesia procedure.

Keywords

General Anesthesia, Oncological Patients, Neuromuscular Blockers, Sugammadex, Post-anesthetic Recovery

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Introduction

Despite the report issued by the Institute of Medicine (IOM) in May 2012, advising the United States Food and Drug Administration (FDA) to undertake much more rigorous, patient-centered efforts to evaluate the safety of drugs throughout their life cycle, in line with the goals of the Anesthesia Patient Safety Foundation [1], studies still show that residual neuromuscular blockade (RNMB) in the post-anesthetic recovery room (PARR) secondary to non-depolarizing relaxants administered intraoperatively is common [2-5], and a serious patient safety concern.

Defined as postoperative muscle paralysis or weakness resulting from incomplete or absent antagonism to non-depolarizing neuromuscular blockers [6], RNMB can result in acute respiratory events (hypoxemia and airway obstruction), difficulty in breathing and swallowing, slurred speech, blurred vision, delays in tracheal extubation [6], prolonged stay in the PARR, and increased risks of postoperative pulmonary complications [7].

Reversal of neuromuscular blockade can be achieved through the use of anticholinesterase agents (ACAs) or specific reversal agent for rocuronium bromide (Sugammadex). However, there is a consensus among experts that patients receiving neuromuscular blockers should undergo neuromuscular monitoring, as their appropriate use in the perioperative period allows for drug titration and confirms complete recovery of neuromuscular blockade (NMB) preceding tracheal extubation [6]. Considered the gold standard [6,7] in addition to suggesting the best timing for tracheal extubation, it is also a safe method for assessing residual NMB as there is objective monitoring of neuromuscular transmission (NMT) through the sequence of four stimuli and accelerometry with monitoring of the adductor pollicis and ulnar nerve stimulation. Thus, the gold standard reflecting acceptable neuromuscular recovery is a TOF T4/T1 ratio greater than or equal to 0.9, before extubation [8].

However, research has shown that RNMB may persist in the early postoperative recovery period, even when neuromuscular blockade is carefully monitored and reversed in the operating room [9-11], with conflicting data even in more recent studies [12].

From August 2017 to July 2018, a prospective, observational study was conducted in our department, the Amazonas State Center for Oncology Control Foundation (FCECON), involving 190 patients, with results consistent with the current literature. In this sample, 59% of patients used atracurium besylate as a muscle relaxant, with reversal achieved using atropine and neostigmine. However, with the standardization of new non-depolarizing neuromuscular blockers, this research aimed to investigate whether reversal of NMB triggered by rocuronium bromide with the use of its selective antidote sugammadex reduced the incidence of RNMB. In the aforementioned study, the investigation concluded that the incidence of RNMB was 35% in oncological patients who received intermediate-acting neuromuscular blockers and were reversed with atropine and neostigmine [13].

Methods

The project was approved by the Ethics and Research Committee - CEP of FCECON on November 25, 2021 (opinion number 5,126,972 and CAAE 51217221.8.0000.0004).

This research was characterized by a prospective, observational nature, conducted through TOF-T4/T1 monitoring in the Post-Anesthetic Recovery Room (PARR) in oncological patients undergoing general anesthesia, a technique that makes the group more homogeneous. After surgery, patients were transferred to the Post-Anesthetic Recovery Room (PARR), where neuromuscular function was evaluated using the train-of-four (TOF) sequence of four stimuli at the time of entry into the PARR, along with clinical assessment using vital sign parameters, which served as discharge criteria from the PARR before patient transfer to the inpatient ward.

The sample size was estimated considering the total number of surgeries requiring general anesthesia (Neurosurgery, Mastectomies, Oncological, Head and Neck, and Thoracic surgeries) performed by FCECON in 2021, which totaled 2,016 surgeries, and the incidence of neuromuscular blockade with sugammadex in postoperative patients, found in a study by Yagan, et al. (2015), which was 8%. A margin of error or precision of 5% and a confidence level of 95% were established, resulting in a sample size of 107 patients. The size was estimated considering the statistical parameters of the sample size calculation formula for finite populations, as described by Bussab and Morettin (2016, p. 288).

The neuromuscular monitoring period was from May 2022 to October 2023. Patients undergoing general anesthesia at FCECON who met the inclusion criteria were monitored after surgery while in the PARR using the TOF sequence of four stimuli, and the data were recorded on the data collection form.

Data collection was only performed with prior permission from the patient, who signed an informed consent form (ICF) agreeing to participate in the study.

Patients over 18-years-old undergoing oncological surgeries who received rocuronium bromide for endotracheal intubation and maintenance of general anesthesia with mechanical ventilation. The exclusion criteria for the study included patients diagnosed with neuromuscular dysfunction, those who had neuromuscular function monitored intraoperatively,

patients admitted to the PARR intubated, hypothermic, or receiving any other neuromuscular blocker, those who did not have alterations in potassium, calcium, magnesium levels, or those who refused to participate in the study, as well as patients undergoing anesthetic techniques such as neuraxial blocks, peripheral blocks, and total intravenous anesthesia without administration of muscle relaxants.

The experimental design of the project consisted of 2 phases: The first phase was used to inform patients about the project and obtain informed consent, and the second phase involved monitoring using TOF in patients in the PARR after general anesthesia. Thus, all patients were monitored upon arrival in the PARR with a cardiac monitor, digital pulse oximeter, non-invasive Mean Arterial Pressure (MAP), temperature, peripheral nerve stimulator, and received supplementary oxygen. For neuromuscular function monitoring, the TOF sequence of four stimuli (TOF-WATCH SX-T4/T1 acceleromyography) was used.

Patients were assessed upon arrival at the Post-Anesthesia Care Unit (PACU), with residual neuromuscular blockade considered in those showing a T4/T1 ratio < 0.9. Following the train-of-four (TOF) measurement in the PACU, patients with a T4/T1 ratio between 0.7 and 0.3 would receive 1 mg/kg^{-1} of sugammadex. Patients exhibiting less than two responses (T2) to the TOF sequence would be reintubated. Data from the sample analyzed included: Gender, age, cancer type, time interval between the last administration of neuromuscular blockade and TOF measurement in the PACU, total dose of neuromuscular blockade used, total dose of sugammadex reversal agent, electrolyte values affecting muscle function, use of drugs interfering with neuromuscular blockade, and mean TOF value.

Descriptive and inferential data analysis was performed using IBM Statistics SPP version 21. The results were presented in frequency tables (figures). Possible relationships between variables were verified using Pearson's Chi-square test or the statistical test that best suited the data. A significance level of 5% was adopted for decision-making in statistical tests.

Results and Discussion

The incidence of postoperative residual neuromuscular blockade (RNMB) is determined by a wide variability of factors with different methods used for evaluation: utilization of T4/T1 ratio values of 0.7, 0.8, or 0.9; use of single or repeated doses or continuous infusion of neuromuscular blockers (NMB); reversal or non-reversal of neuromuscular blockade at the end of anesthesia; age; presence of renal, hepatic, cardiac, or neuromuscular dysfunction; use of drugs that alter the pharmacodynamics and/or pharmacokinetics of NMB; electrolyte imbalances; metabolic or respiratory acidosis; and hypothermia [14].

In this study, 119 surgical patients undergoing general anesthesia were evaluated, of whom 92 (77.3%) were female and 27 (22.7%) were male. The most frequent age ranges of these patients were 35 to 45 (27; 22.7%), 46 to 56 (30; 30.3%), and 57 to 67 (27; 22.7%). The age of the patients ranged from 24 to 80 years, with mean and median ages of 52.9 ± 12.6 and 52 years, respectively (Table 1 and Table 2).

Upon arrival at the Post-Anesthesia Care Unit (PACU) regarding systemic arterial pressure (BP), of the 119 patients, 53 (44.5%) were within normal limits and 44 (37.0%) had elevated blood pressure. As for pulse oxygen saturation (SpO_2), 117 (98.3%) were within normal limits, while 99 (83.2%) had normal temperature (Table 1).

In most patients (49.6%), the surgery time ranged from 2 hours 01 minutes to 4 hours. Overall, it varied between 30 minutes and 6 hours, with mean and median surgery times of 2 hours 19 minutes ± 1 hour 03 minutes and 2 hours 10 minutes, respectively. Electrolyte imbalance, which could influence NMB, was

Table 1: Demographic, clinical, and surgical characteristics of oncological patients undergoing general anesthesia at FCECON.

Characteristics	n (119)	%
Gender		
Female	92	77.3
Male	27	22.7
Age Range		
24 to 34	11	9.2
35 to 45	27	22.7
46 to 56	36	30.3
57 to 67	27	22.7
68 and above	18	15.1
Blood Pressure Classification		
Normal	53	44.5
Borderline	22	18.5
Elevated	44	37.0
$SatO_2$		
95 to 100%	117	98.3
< 95%	2	1.7
Axillary Temperature		
< 36 °C	20	16.8
36° to 36.7 °C	99	83.2
Surgery Time		
< 1h	10	8.4
1 hour 01 minute to 2 hours	47	39.5
2 hours 01 minutes to 4 hours	59	49.6
> 4 hours	3	2.5
Electrolyte Imbalance		
Yes	20	16.8
No	99	83.2

Table 2: Descriptive analysis of the characteristics and quantitative clinical parameters of patients undergoing general anesthesia at FCECON.

Characteristics	n	Descriptive Measures				
		Mean	SD	Min	Median	Max
Age	119	52.9	12.6	24.0	52.0	80.0
SpO_2 (%)	119	98.0	1.3	94.0	98.0	100.0
Axillary Temperature (°C)	116	36.0	0.6	34.0	36.2	36.7
Surgery Time (h)	119	02:19	01:03	00:30	02:10	06:00
Rocuronium Dose (mg)	119	54.1	22.3	30.0	50.0	200.0
Sugammadex Dose (mg)	119	164.3	44.7	50.0	160.0	400.0
TOF Assessment Period (h)	119	01:21	00:40	00:30	01:00	04:00
TOF T4/T1 Ratio Sequence (%)	119	98.4	4.4	69.0	99.0	100.0

Table 3: Highest frequencies by diagnosis location in patients undergoing general anesthesia at FCECON.

Diagnosis Location	n (119)	%
Breast	44	37.0
Thyroid	15	12.6
Uterus (cervix)	9	7.6
Colon	6	5.0
Endometrium	5	4.2
Gastric	5	4.2
Lung	5	4.2
Kidney	5	4.2
Ovary	4	3.4
Other Various Sites	25	21.0

Table 4: Highest frequencies by surgical procedure in patients undergoing general anesthesia at FCECON.

Surgical Procedure	n (119)	%
Mastectomy with or without BLS	19	16.0
HTA + Others	12	10.1
Thyroidectomy	12	10.1
Lumpectomies	10	8.4
Quadrantectomies	6	5.0
Breast Reconstruction	6	5.0
Biopsies	5	4.2
Nephrectomy	5	4.2
Other Various Procedures	44	37.0

present in 20 (16.8%) patients (Table 1 and Table 2).

Regarding the anatomical site approached in the 119 patients, it was observed that the most frequent sites, representing 62.2% of the sample, were: Breast (44; 37.0%); Thyroid (15; 12.6%); Uterus (9; 7.6%); and Colon (6; 5.0%) (Table 3).

In relation to the surgical procedures performed on the 119 patients, it was observed that the most frequent surgeries, representing 44.5% of the sample, were: Mastectomy with or without BLS (19; 16.0%); Thyroidectomy (12; 10.1%); and Lumpectomy (10; 8.4%) (Table 4).

Table 5: Characteristics related to dosage of anesthetic agents in oncological patients undergoing general anesthesia at FCECON for surgical procedures.

Characteristics	n (119)	%
Rocuronium Dosage		
30 to 50 mg	91	76.5
60 to 80 mg	21	17.6
> 80 mg	7	5.9
Use of Interfering Drugs		
Yes	0	0.0
No	119	100.0
Sugammadex Dosage		
50 to 110 mg	15	12.6
120 to 160 mg	45	37.8
> 160 mg	59	49.6
TOF Assessment Period in PACU		
30 minutes to 1 hour	61	51.3
1 hour 01 minute to 2 hours	44	37.0
2 hours 01 minutes to 4 hours	14	11.8
Residual Neuromuscular Blockade (RNMB)		
Yes	5	4.2
No	114	95.8
Complications due to RNMB		
Yes (TOF T4/T1 < 0.7)	1	0.8
No	118	99.2

As for the administration of Neuromuscular Blockers, 91 (76.5%) patients received doses between 30 and 50 mg of rocuronium bromide, without the use of interfering drugs in patients, whose most frequent doses of the reverser sugammadex were from 110 to 160 mg (42; 35.3%) and > 160 mg in 25 (21.0%) patients. The most frequent duration of assessment of the degree of neuromuscular blockade (NMB-TOF) in the PACU was 30 minutes to 1 hour, which refers to 61 (51.3%) patients. There was residual NMB in 5 (4.2%) patients and complications in only one (0.8%) patient (Table 5).

It is noteworthy that the total dose of rocuronium bromide administered to patients ranged from 30 to 200

mg, with mean and median doses respectively equal to 54.1 ± 22.3 and 50 mg. Regarding the dose of Sugammadex, it was administered between 50 and 400 mg, with mean and median doses respectively equal to 164.3 ± 44.7 and 160 mg. Regarding the NMB-TOF assessment period, this ranged from 30 minutes to 4 hours, with mean and median times respectively equal to 1 hour 21 minutes and 1 hour. The sequence in NMB-TOF T4/T1 ranged from 69.0 to 100.0%, with mean and median percentages equal to 98.4 ± 4.4 and 99.0% (Table 5).

Patients with the presence of residual neuromuscular blockade (RNMB) (4.2%) were mostly female (80%); in the age range of 46 to 56 years (60%); with normal blood pressure (60%); whose surgery time was between 1 and 2 hours (60%); and whose dosage of neuromuscular blocker (rocuronium bromide) was between 30 and 50 mg (Table 6).

In the analysis of the dosages of rocuronium bromide and sugammadex and their relationship with the

Table 6: Relationship between demographic and clinical characteristics and the presence of residual BNM (BNMr) in evaluated cancer patients.

Characteristics	Residual BNM					*P**
	Yes (n = 5)	%	No (n = 114)	%	n (n = 119)	
Gender						
Female	4	**80.0**	88	**77.2**	92	*0.682*
Male	1	**20.0**	26	**22.8**	27	
Age Range						
24 to 34	0	**0.0**	11	**9.6**	11	*0.353*
35 to 45	0	**0.0**	27	**23.7**	27	
46 to 56	3	**60.0**	33	**28.9**	36	
57 to 67	2	**40.0**	25	**21.9**	27	
68 and above	0	**0.0**	18	**15.8**	18	
PA Classification						
Normal	3	**60.0**	50	**43.9**	53	*0.167*
Borderline	2	**40.0**	20	**17.5**	22	
High	0	**0.0**	44	**38.6**	44	
Surgery Time						
< 1h	2	**40.0**	8	**7.0**	10	*0.008**
1h to 2h	3	**60.0**	44	**38.6**	47	
> 2h	0	**0.0**	62	**54.4**	62	
BNM Dose						
30 to 50 mg	5	**100.0**	86	**75.4**	91	*0.693*
60 to 80 mg	0	**0.0**	21	**18.4**	21	
> 80 mg	0	**0.0**	7	**6.1**	7	
*Significant value for p < 0.05 (5%)						
Pearson's Chi-square test						

Table 7: Relationship between the dosage of NMB and Sugammadex and the presence of residual NMB.

Rocuronium Dose (NMB)	Residual BNM	Sugammadex Dosage (mg)			Total n	*p**
		50 to 110	120 to 160	> 160		
30 to 50	Yes	1	0	4	5	0.186
	No	12	38	36	86	
60 to 80	Yes	0	0	0	0	
	No	2	6	13	21	
> 80	Yes	0	0	0	0	
	No	0	1	6	7	
Parcial n		**15**	**45**	**59**	**119**	
*Significant value for p < 0.05 (5%)						
Pearson's Chi-square test						

presence of residual neuromuscular blockade (RNMB), the relationship was not significant at a 5% level of significance (p = 0.186) (Table 7).

The study on the incidence of residual neuromuscular blockade (RNMB) with the use of Sugammadex in oncological surgeries, through Train-of-Four (TOF) monitoring assessed via the sequence of four stimuli (SQE), provides a comprehensive analysis of various aspects of perioperative care in these patients. It's not possible to demonstrate satisfactory neuromuscular recovery based solely on clinical parameters, such as maintaining the head elevated for five seconds, exposing the tongue, opening the eyes, deep inspiration, and coughing. It's even discouraged to rely solely on clinical evaluation to avoid RNMB due to the insensitivity of the assessment. Quantitative monitoring of neuromuscular blockade in the adductor pollicis muscle is recommended to confirm a TOF ratio greater than or equal to 0.9 before extubation, accompanied by the use of sugammadex for blockade antagonism [8,15].

In this study, the predominance of female patients, mainly in the age ranges of 46 to 56 years, highlights the relevance of considering demographic variables when evaluating anesthetic responses to neuromuscular blockers and perioperative outcomes. The average surgery time of 2 hours and 19 minutes ± 1 hour and 3 minutes indicates the use of intraoperative additives. These pieces of information are valuable for planning anesthetic management, highlighting the diversity of interventions performed in oncological patients during surgery.

The most frequent anatomical topographies in preoperative diagnosis and the most common surgical procedures, such as Mastectomy, Thyroidectomy, and Mammary Sectorial Resection, highlight specific areas and the diversity of surgeries performed in the treatment of oncological pathologies.

The analysis of the quantity of doses of rocuronium bromide and sugammadex reflects common anesthetic practices in oncological patients, highlighting average doses of 54.1 and 164.3 mg, respectively, of these agents, corroborating the current multicenter study conducted by ESTEVES, et al. (2023) at the Anesthesiology Service of the University Hospital Center of Porto [16]. This information is crucial for optimizing the administration of these drugs.

Considered the gold standard in assessing the degree of neuromuscular blockade, as well as suggesting the best time for intubation and safe extubation, neuromuscular monitoring is also a safe method for assessing residual action through the sequence of four stimuli (TOF-T1/T4) and accelerometry with monitoring of the adductor pollicis muscle with ulnar nerve stimulation. The most reliable methods for assessing neuromuscular blockade are quantitative neuromuscular monitoring methods, such as acceleromyography, because they provide more objective data on neuromuscular transmission and improve the detection of RNMB compared to visual or tactile assessment of TOF response [17-21].

This study found an incidence of RNMB (TOF ratio < 0.9) of 4.2% and RNMB with complications (TOF ratio < 0.7) of 0.8% upon arrival at the Post-Anesthesia Care Unit (PACU), which is numerically lower than the results of similar observational studies reporting an incidence of RNMB between 10.8% and 45.2% and severe RNMB between 3.6% and 28.2% in the same environment [3,22-25]. These discrepancies are possibly due to differences in the variation of total doses of specific neuromuscular blocker reversal agents such as sugammadex and the use of quantitative neuromuscular monitoring, among other factors [26].

In this sample, the characteristic that influenced the occurrence of RNMB was surgery time (p = 0.008), considering the significance level of 1% and 5%, according to Pearson's Chi-square test (Table 6), which corroborates similar results from other studies, where RNMB was not associated with age or dose of neuromuscular blocker and antagonist use, showing only a relationship with the duration of the surgical procedure [27,28].

The incidence of RNMB in 4.2% of patients, even when using a specific reversal agent, demonstrates the need for a more sensitive evaluation of NMJ reversal with neuromuscular monitoring equipment. Although quantitative monitoring is recommended by current guidelines [8,17,26] these numbers compare favorably with others from similar studies reporting a very low frequency of quantitative neuromuscular monitoring of patients in the PACU [13,14,22-24]. Additionally, the occurrence of complications in only 0.8% is positive, indicating efficient management in most cases when using such methods of NMJ monitoring associated with the specific neuromuscular blocker reversal agent.

The variation in the time needed for neuromuscular blockade assessment in the PACU, between 30 minutes to 1 hour, provides insights into postoperative monitoring practices. The TOF-T4/T1 sequence ranging between 69.0% and 100.0% (0.69-1), with a mean and median of 98%, suggests good reversal of neuromuscular blockade with the specific antidote sugammadex in oncological surgeries. However, there is a variable of the time interval between extubation and TOF measurement in the PACU that may differ among patients, and this may have influenced the incidence of RNMB, particularly regarding Sugammadex reversal, because 2 or 3 minutes can make a substantial difference in the TOF ratio [16].

Comparing to neostigmine, which cannot rapidly reverse deep neuromuscular blockade, sugammadex has a distinct mechanism of action, with very rapid onset of action, and most importantly, causes fewer

side effects [29]. Such benefits are particularly relevant in cancer patients undergoing surgical treatment due to the high rate of comorbidities [30].

The administration of sugammadex at specific doses, 110 to 160 mg in most cases (35.3%), is a key point in understanding the reversal efficacy in patients with altered pharmacokinetic profile due to their underlying oncological disease. The low incidence of RNMB (4.2%) may indicate an overall effectiveness of sugammadex in preventing this event in oncological patients, although this study did not find a statistically significant difference, since current guidelines dictate the recommendation of sugammadex instead of neostigmine in deep, moderate, and superficial intensities of neuromuscular blockade induced by rocuronium or vecuronium associated with the use of the adductor pollicis muscle for neuromuscular monitoring, to avoid RNMB [8,15].

However, it is interesting to note that RNMB occurred even in patients reversed with Sugammadex, confirming what was suggested earlier by other authors that this agent is not always 100% effective in preventing RNMB [23,31,32], probably because of insufficient dose administration for the depth of neuromuscular blockade at the time of reversal and the duration of the surgical procedure [16,27,28].

Ultimately, this prospective observational study, conducted at this hospital, revealed a remarkable advancement in RNMB management by employing rocuronium and sugammadex as anesthetic agents. The RNMB index, recorded at 4.2%, significantly contrasts with the results obtained in the previous study [13], conducted at this same hospital, where the use of atracurium besylate and neostigmine resulted in a significant index of 35%. This disparity highlights the effectiveness of new non-depolarizing muscle relaxants, showing that the choice of modern anesthetic agents, such as rocuronium, combined with specific reversers, such as sugammadex, represents a superior approach. The use of rocuronium and sugammadex not only demonstrated a remarkable reduction in RNMB but also emphasizes the clinical importance of adopting contemporary anesthetic strategies to optimize patient safety and promote more effective postoperative recovery. These results reinforce the recommendation to prioritize muscle relaxants with specific reversers, highlighting the positive evolution in anesthetic practice and emphasizing the need to act according to current clinical guidelines [8,14,15,33].

Conclusion

The results of the present study suggest that quantitative monitoring of neuromuscular blockade (NMB) with the adductor policies muscle to confirm a Train-of-Four (TOF) ratio greater than or equal to 0.9 and the use of sugammadex are associated with a decrease in the incidence of residual neuromuscular blockade (RNMB) in the Post-Anesthesia Care Unit (PACU). These findings have the potential to influence clinical protocols and guide improvements in strategies for safer and more effective perioperative care in oncological patients undergoing surgical procedures.

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