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The year in cardiovascular medicine 2021: imaging

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Citation

Bucciarelli-Ducci, C., Ajmone Marsan, N., Carli, M. di, & Nicol, E. (2022). The year in cardiovascular medicine 2021: imaging. *European Heart Journal*, 43(13), 1288-1295. doi:10.1093/eurheartj/ehac033

Version: Publisher's Version
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Note: To cite this publication please use the final published version (if applicable).

The Use of Muscle Relaxants and Reversal Agents in a Setting Without Cost Restrictions: Experience from a Tertiary Academic Hospital in the Netherlands

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Introduction: Muscle relaxants are often given during general anesthesia to facilitate endotracheal intubation. However lingering effects after anesthesia-end may lead to respiratory compromise in the PACU. Strategies to reduce these adverse events include monitoring neuromuscular block, the use of short-acting agents and active pharmacological reversal before extubation. At Leiden University Medical Center (LUMC), a tertiary care academic hospital in the Netherlands, various muscle relaxants and reversal agents are freely available to all clinicians without restrictions. In this setting, we intended to evaluate how patient and surgical characteristics impacted the use of these agents for a variety of non-cardiac surgeries.

Material and Methods: This is a retrospective database study of adult patients that had received elective, non-cardiac surgery and general anesthesia with endotracheal intubation between 2016 and 2020 at LUMC in the Netherlands. Exclusion criteria consisted of patients pharmacologically reversed with both sugammadex and neostigmine during the same procedure, diagnosed with myasthenia gravis, receiving pyridostigmine therapy, or with renal failure (eGFR <30 mL.min.1.73m²).

Results: We retrieved 23,373 patient records of which 9742 were excluded because one or more exclusion criteria were met. The final cohort consisted of 13,631 cases. Rocuronium was the most commonly used muscle relaxant (88.5%); sugammadex was the most commonly used reversal agent (99.9% of those pharmacologically reversed). Of all cases that received rocuronium as muscle relaxant, 76.9% of patients were not reversed, while 23.1% were reversed with sugammadex. The odds of reversal increased with age, BMI, ASA class (1–3) and shorter duration of surgery.

Conclusion: In an unrestricted clinical environment, rocuronium and sugammadex are the preferred agents for muscle relaxation and reversal. Pharmacologic reversal of neuromuscular block was uncommon overall, but more likely in older and obese patients, higher ASA classification and shorter lasting procedures. Sugammadex has largely replaced neostigmine for this purpose.

Keywords: neuromuscular blockade, muscle relaxants, sugammadex

Introduction

Muscle relaxants are routinely used during general anesthesia to facilitate endotracheal intubation and to maintain optimal surgical working conditions.^{1,2} However, the relatively long half-life of (non-depolarizing) muscle relaxants, poses patients at risk for residual neuromuscular block (NMB) after extubation and in the post-operative care unit,^{3,4} which is associated with complications such as atelectasis, pneumonia, pulmonary failure, and reintubation.^{5,6} To prevent residual NMB, clinicians may pharmacologically reverse neuromuscular block just before the end of anesthesia. This was traditionally accomplished with an acetylcholinesterase inhibitor, however sugammadex, a selective amino-steroidal relaxant binding agent,⁷ is gaining popularity due to its ability to reliably reverse both shallow and deep levels of neuromuscular block in a shorter period of time.⁸ In addition, sugammadex is devoid of major side-effects and especially lack cholinergic complications that often accompany

cholinesterase inhibitors. Despite these advantages, financial considerations may limit the unrestricted use of sugammadex in many hospitals, because of the higher cost-base compared to acetylcholinesterase inhibitors.⁹ Although there are indications that sugammadex reduces the incidence of postoperative residual NMB,¹⁰ and possibly lowers the incidence of respiratory complications,^{11,12} effects on these outcomes remain controversial.^{13,14} In addition, many national and international anesthesia associations lack guidelines on perioperative NMB management. As such, there exists a wide variation in practices with regard to NMB management and reversal strategies. The goal of the current study is to leverage inpatient electronic medical records to describe the incidence of NMB and reversal agent utilization and factors impacting the choice of NMB reversal among patients in the inpatient setting, and specifically, identify factors which distinguish patients who are pharmacologically reversed from those who are not actively reversed. To this end, we conducted a retrospective analysis of patient data in a tertiary academic center in the Netherlands where sugammadex has been freely available since 2013. We hypothesize that use of sugammadex is associated with shorter lasting procedures and with patient characteristics related to postoperative complications, such as older age, higher ASA class, and higher BMI.

Materials and Methods

This was a single-center, retrospective observational study using a local electronic database to describe and assess the use of muscle relaxants and reversal agents at the Leiden University Medical Center (LUMC) at Leiden, The Netherlands. In this center, clinicians may freely choose between a variety of muscle relaxants and between neostigmine or sugammadex as reversal agent. Prior to start of the current study, the study protocol was approved by the local research board in June 2020, and by Merck in October 2020. This study was approved by the institutional review board (IRB) of the Departments of Anesthesiology and Intensive Care of the LUMC in June 2020 and the requirement for patient consent was waived as this study involved analysis of preexisting, deidentified data collected for clinical and operational purposes. All patient-related study data was collected in compliance with the Dutch Act on GRDP (General Data Protection Regulation) of 2016. Final data analyses were performed in March 2021 (end of study).

Data Extraction

Data of patients that received anesthesia from April 2016 to December 2020 in LUMC were retrieved from our electronic medical record database (Healthcare Information X-change, HiX, Chipsoft, The Netherlands). Data extraction was performed by CM with the aid of a local database manager. The research team (CM/MB) manually checked and validated the data for inconsistencies and accuracy. Cases were eligible if they had received general anesthesia for any type of elective surgical procedure requiring endotracheal intubation in patients aged 18 years and older. Exclusion criteria consisted of patients pharmacologically reversed with both sugammadex and neostigmine during the same procedure, diagnosed with myasthenia gravis, receiving pyridostigmine therapy, or with renal failure (eGFR <30 mL/min/1.73m²).

From the data, active reversal with sugammadex and spontaneous recovery were identified and compared with each other with respect to (1) patient-related characteristics, including age, gender, height, weight, body mass index (BMI) and American Society of Anesthesiologists (ASA) physical status classification; and (2) anesthesia and surgery related characteristics, including anesthesia type, surgery type, duration of surgery and hospital length of stay.

Procedures without procedure code, diagnostic procedures and procedures with less than 100 cases per specialty were removed. Final analyses focused on rocuronium cases (88.5% of total) and ASA 1 to 4 patients (sixteen ASA 5 patients were excluded).

Statistics

The main endpoint of our study was the utilization of neuromuscular blockade and reversal agent incidence in our hospital and the description of patient and procedure related characteristics. No a priori power analysis was conducted given the retrospective and descriptive study design.

Neuromuscular Monitoring Data and Reversal

In our hospital neuromuscular monitoring is available in every OR. All staff are well trained in the correct use of the monitoring equipment. In the case of a train-of-four (TOF-) ratio below 90% of its baseline value at the end of the surgical procedure, clinicians can either wait for the TOF-ratio to reach the 90% threshold spontaneously, or administer a reversal agent. Unfortunately, the neuromuscular monitoring data is not automatically logged into the electronic medical record database in a standardized manner and we rely on the manual, textual insertion of the data by the employees. After evaluation of the data, it was not suitable to quantitatively analyze for research purposes.

Descriptive statistics were used to analyze the frequency of NMB utilization and reversal agent by patient characteristics (age, gender, height, weight, BMI, ASA class), and procedure type (specialty, anesthesia type, duration of surgery, hospital length of stay). Covariates for reversal strategy were analyzed by stepwise univariate and multivariate logistic regression. All analyses were performed using IBM SPSS (version 25, Armonk NY USA). P-values < 0.05 were considered statistically significant. Data are presented as mean \pm Standard Deviation (SD), min, max unless otherwise stated.

Results

Our search yielded 23,373 cases that were treated with a neuromuscular blocking agent. 7939 cases had to be excluded for various reasons. The final cohort consisted of 13,631 cases. [Figure 1](#) shows a flow chart of the data selection process. Rocuronium was the most commonly used muscle relaxant (88.5%), followed by succinylcholine (10.4%), atracurium (1%) and mivacurium (0.1%), see [Table 1](#). Though pharmacologic reversal was uncommon (approximately 23% of patients), sugammadex was used as reversal agent in 99.9% of these cases; in only 12 cases neostigmine was used as reversal agent (data not shown).

For our primary analysis, we focused on the cases where rocuronium was used as muscle relaxant. In this cohort, the only one case that was reversed with neostigmine was excluded from the analyses. As such, patients in this cohort were either allowed to recover spontaneously or were pharmacologically reversed with sugammadex. For a distribution of active versus spontaneous reversal of rocuronium induced NMB over time, see [Table 2](#). There is a gradual increase of sugammadex use over time, ranging from nearly 19% in 2016 to 26% in 2020.

[Table 3](#) displays the baseline characteristics of patients reversed with sugammadex versus spontaneous recovery of rocuronium induced NMB. Among all inpatients administered rocuronium in this period (N=13,631), patients were 55 years old on average, 55% were women, about a third underwent general surgery, with a median of 2 days in hospital stay. Nearly 15% of patients were missing ASA status, and nearly 44% were ASA 2.

In this cohort, 77% were not pharmacologically reversed, while 23% had received at least one dose of sugammadex. The reversal percentage increased with increasing age (19.5% in patients 18–29 years old, to 27.3% in patients of 80+ years old); increasing ASA class from ASA 1 (18.4%) to ASA 3 (30.6%) while patients of ASA class 4 (only 2.1% of the population) had a lower reversal rate (14.8%). Among patients that received inhalational (sevoflurane) anesthesia, 19.3% were reversed, compared to 24.3% of patients that had received total intravenous anesthesia. Procedures that were actively reversed were significantly shorter in duration compared to those which were spontaneously reversed (82 minutes versus 152 minutes respectively, $p < 0.001$). While overall, most procedures were not pharmacologically reversed, there was a wide range in reversal practice by surgery type (as often as 72% pharmacologically reversed among obstetrics, and as few as 3.6% reversed among endocrine procedures).

In the univariate logistic regression analysis, the following covariates yielded a higher probability of active reversal versus spontaneous recovery: older age (patient categories 70–79 and > 80 years were combined yielding a better fit of the logistic regression model), morbidly obese individuals ($BMI > 35 \text{ kg.m}^{-2}$) and patient with underweight ($BMI < 20 \text{ kg.m}^{-2}$), ASA 2 (compared to ASA 1) and ASA 3 (compared to ASA 1 and 2), total intravenous anesthesia (TIVA), eye surgery, and shorter duration of surgery ([Figure 2A](#)). General surgery was used as reference category as it consisted of a large group of procedures (eg, endocrine, gastro-intestinal, trauma and vascular surgery) with an average reversal rate of 28% which was more or less similar to the population mean

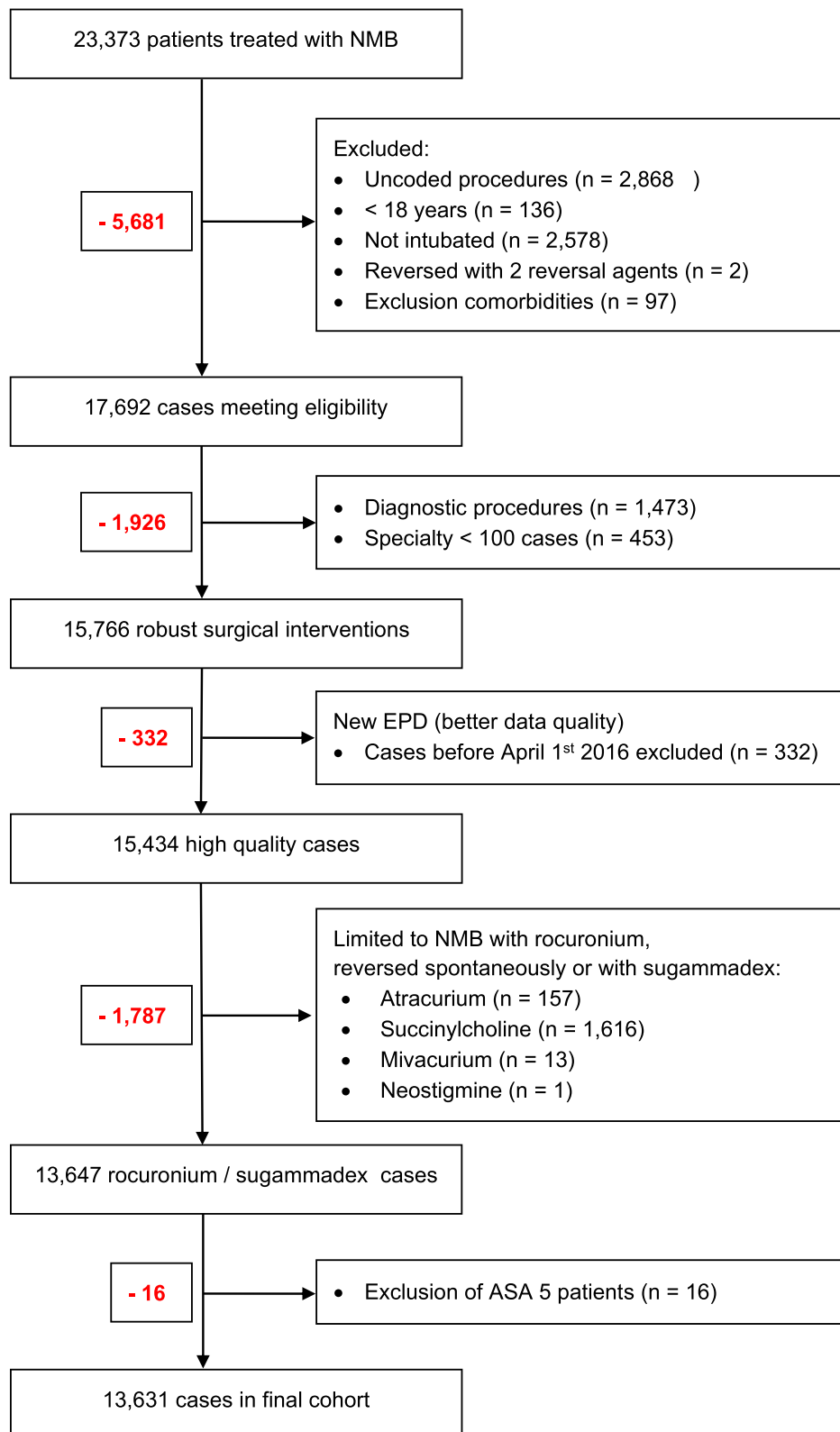


Figure 1 Flowchart of included cases.

Table 1 NMB Utilization Over Time

	Rocuronium	Atracurium	Succinylcholine	Mivacurium	Total
2016	2279 (90.4%)	42 (1.7%)	195 (7.7%)	6 (0.2%)	2522
2017	3226 (88.1%)	40 (1.1%)	395 (10.8%)	2 (0.1%)	3663
2018	3008 (88.8%)	39 (1.2%)	337 (9.9%)	3 (0.1%)	3387
2019	2891 (87.7%)	25 (0.8%)	380 (11.5%)	2 (0.1%)	3298
2020	2343 (88.0%)	11 (0.4%)	309 (11.6%)	0 (0.0%)	2663
Apr 2016 -Dec 2020	13,747 (88.5%)	157 (1.0%)	1616 (10.4%)	13 (0.1%)	15,533

Notes: There are 15,533 administrations in 15,434 patients. 99 Patients received multiple NMB agents, predominantly succinylcholine + rocuronium.

Table 2 Reversal of Rocuronium Induced NMB Over Time

	Sugammadex	Spontaneous Reversal	Total
2016	438 (19.4%)	1817 (80.6%)	2255
2017	629 (19.6%)	2577 (80.4%)	3206
2018	713 (23.9%)	2265 (76.1%)	2978
2019	765 (26.7%)	2105 (73.3%)	2870
2020	606 (26.1%)	1716 (73.9%)	2322
Grand Total	3151 (23.1%)	10,480 (76.9%)	13,631

of 23%. In multivariate regression analysis the effects remained largely unchanged regarding direction and magnitude, except for anesthesia type (TIVA: univariate OR 1.27 versus multivariate OR 0.79, $p=0.007$) and eye surgery (univariate OR 1.31 vs multivariate OR 0.70, $p=0.019$). Other factors such as underweight, ASA class 1 and gynecologic procedures were not independently associated with reversal choices after adjusting for other perioperative characteristics. See [Figure 2B](#) and [Table 4](#) for multivariate logistic regression results.

Discussion

This study presents data on the use of muscle relaxants and reversal agents in patients that received general anesthesia for a variety of non-cardiac surgical procedures that took place between 2016 and 2020 in a tertiary academic hospital in The Netherlands. In our hospital, sugammadex has been freely available since 2013 and choices regarding the use of muscle relaxants or reversal agents are not regulated (ie, are at the full discretion of the attending anesthesiologist). The data show that rocuronium was the preferred choice of muscle relaxant (88.5%) and sugammadex was the preferred reversal agent (99.9%). Of the patients that had received rocuronium, only 23% were actively reversed; the other 77% were allowed to recover spontaneously. Multivariate analysis showed that pharmacologic reversal was positively and independently associated with patients of advanced age (>70 years), ASA class 3 (compared to ASA 1 or 2) and elevated BMI $>35 \text{ kg.m}^{-2}$. In addition, anesthesia- and surgery related characteristics revealed a higher likelihood for reversal for shorter-lasting procedures, for cases that received sevoflurane anesthesia and for general surgery (compared to other types of surgery).

In our center, rocuronium was clearly the preferred muscle relaxant in daily practice. Rocuronium has a rapid onset and intermediate duration of action, which makes it suitable for many elective and emergency cases. Nevertheless, large inter-individual variation in duration mandates that clinicians monitor the level of NMB during anesthesia and decide on

Table 3 Distribution of Patient Characteristics in Patients Reversed with Sugammadex versus Spontaneous Recovery of Rocuronium Induced Neuromuscular Block

Patient Characteristics	Sugammadex N 3152	(Row) % 23.1	Spontaneous Reversal N 10,479	(Row) % 76.9	Total N 13,631	(Column) 100%
Age N (%)	3152	23.1	10,479	76.9	13,631	100
Mean (SD), (y)	57.1 (17.5)		54.5 (17.5)		55.2 (17.6)	
Min, Max, (y)	18, 96		18, 101		18, 101	
Age categories (y)	N	%	N	%	N	%
18–29	283	19.5	1170	80.5	1453	10.7
30–39	367	23.4	1199	76.5	1568	11.5
40–49	341	18.5	1502	81.5	1844	13.5
50–59	553	21.7	1997	78.3	2551	18.7
60–69	707	24.1	2230	75.9	2937	21.5
70–79	674	27.4	1786	72.5	2464	18.1
≥ 80	227	27.3	595	71.7	830	6.1
Total	3152	23.1	10,479	76.9	13,631	100
BMI N (%)	2454	23.0	8233	77.0	10,687	100
Mean (SD) (kg.m ⁻²)	26.5 (5.7)		26.2 (5.2)		26.3 (5.3)	
Min, Max (kg.m ⁻²)	14.9–63.5		14.2–64.1		14.2–64.1	
BMI Classes (kg.m⁻²)	N	%	N	%	N	%
< 20	218	26.4	607	73.6	825	6.1
20.0–24.9	894	21.9	3190	78.1	4084	30.0
25.0–29.9	801	21.9	2860	78.1	3661	26.9
30–34.9	332	23.2	1098	76.8	1430	10.5
≥ 35	209	30.4	478	69.6	687	5.0
Unknown	697	23.7	2247	76.3	2944	21.6
Total	3151	23.1	10,480	76.9	13,631	100
Gender	N	%	N	%	N	%
Male	1394	22.7	4741	77.3	6135	45.0
Female	1758	23.5	5738	76.5	7496	55.0
Total	3152	23.1	10,479	76.9	13,631	100
Height N (%)	2938	23.0	9853	77.0	12,791	100
Mean (SD) (m)	1.71 (0.10)		1.73 (0.10)		1.73 (0.10)	
Min, Max (m)	1.10–2.05		1.10–2.08		1.10–2.08	
Weight N (%)	2601	23.0	8689	77.0	11,290	100
Mean (SD), (kg)	78.3 (18.7)		78.1 (17.5)		78.2 (17.8)	

(Continued)

Table 3 (Continued).

Patient Characteristics	Sugammadex N 3152	(Row) % 23.1	Spontaneous Reversal N 10,479	(Row) % 76.9	Total N 13,631	(Column) 100%
Min, Max, (kg)	33–180		29–181		29–181	
ASA Class	N	%	N	%	N	%
1	441	18.4	1959	81.6	2400	17.6
2	1350	22.4	4666	77.6	6016	44.1
3	877	30.6	1988	69.4	2865	21.0
4	43	14.8	248	85.2	291	2.1
Unknown	440	21.4	1619	78.6	2059	15.1
Total	3151	23.1	10,480	76.9	13,631	100
Anesthesia type	N	%	N	%	N	%
Volatile	630	19.3	2633	80.7	3263	23.9
TIVA	2410	24.3	7510	75.7	9920	72.8
Unknown	112	25.0	336	75.0	448	3.3
Total	3153	23.1	10,479	76.9	13,631	100
Surgery type	N	%	N	%	N	%
General surgery	1229	28.5	3085	71.5	4314	31.6
ENDOCRINE	17	3.6	458	96.4	475	3.5
GASTROENTEROLOGICAL	369	36.9	630	63.1	999	7.3
GENERAL	634	38.2	1024	61.8	1658	12.2
TRANSPLANTATION	9	34.6	17	65.4	26	0.2
TRAUMA	135	19.5	557	80.5	692	5.1
VASCULAR	65	14.0	399	86.0	464	3.4
Gynecology	244	23.0	815	77.0	1059	7.8
Oral surgery	83	12.0	606	88.0	689	5.1
ENT surgery	717	27.8	1865	72.2	2582	18.9
Neurosurgery	224	10.1	2004	89.9	2228	16.3
Eye surgery	253	35.2	465	64.8	718	5.3
Orthopedics	124	9.2	1218	90.8	1342	9.8
Plastic surgery	73	26.9	198	73.1	271	2.0
Urology	75	30.4	172	69.6	247	1.8
Obstetrics	130	71.8	51	28.2	181	1.3
Total	3152	23.1	10,479	76.9	13,631	100
DoS N (%)	3152	23.1	10,479	76.9	13,631	100

(Continued)

Table 3 (Continued).

Patient Characteristics	Sugammadex N 3152	(Row) % 23.1	Spontaneous Reversal N 10,479	(Row) % 76.9	Total N 13,631	(Column) 100%
Median, IQR (min)	82 (63–112)		152 (108–219)		134 (90–198)	
Min, Max, (min)	15–955		21–1257		15–1257	
DoS Classes (min)	N	%	N	%	N	%
< 60	648	71.2	262	28.8	910	6.7
60–120	1834	37.2	3095	62.8	4929	36.2
120–180	497	13.6	3151	86.4	3648	26.8
> 180	173	4.2	3971	95.8	4144	30.4
Total	3152	23.1	10,479	76.9	13,631	100
LoHS N (%)	3132	23.3	10,329	76.7	13,461	100
Median, IQR (days)	1 (0–7)		2 (1–6)		2 (1–6)	
Min, Max, (days)	0–171		0–171		0–171	
LoHS Classes (days)	N	%	N	%	N	%
0	944	39.7	1435	60.3	2379	17.7
1	654	21.2	2435	78.8	3089	22.9
2–6	747	16.0	3912	84.0	4659	34.6
> 6	787	23.6	2547	76.4	3334	24.8
Total	3132	23.3	10,329	76.7	13,461	100

Abbreviations: BMI, Body Mass Index; ASA, American Society of Anesthesiologists; TIVA, Total Intravenous Anesthesia; ENT, Ear, Nose & Throat; DoS, Duration of Surgery (defined as start incision to closure of skin); LoHS, Length of Hospital Stay (includes PACU and ICU stay).

whether to pharmacologically reverse or not before the endotracheal tube is removed. Should residual NMB exist at this time, ie, the train-of-four (TOF-) ratio is below 90% of its baseline value, clinicians can either wait for the TOF-ratio to reach the 90% threshold spontaneously, or speed up the recovery by administering a reversal agent. The latter may be achieved with an acetylcholinesterase inhibitor, or sugammadex, in case an amino steroidal muscle relaxant such as rocuronium is used. Although both agents speed up the recovery of NMB, sugammadex, by directly encapsulating the muscle relaxant molecules, does this more predictably and effectively, with higher speed and without ceiling effect that limits the use of acetylcholinesterase inhibitors for reversal of deep NMB. Additionally, sugammadex has fewer side effects.¹⁵ However the higher cost-base may limit its use in settings where budgets are restricted. In our center, cost-implications of sugammadex do not restrict its clinical use. Therefore, we wished to study how this situation affects the use of muscle relaxants and reversal agents and what factors impacted these choices. Somewhat surprisingly, we observed in our population that in 77% of cases no reversal agent was used. This contrasts with the previous reports from the USA and Europe, where active reversal was performed in 50 to 80% of cases.^{16,17} In addition, a time related decrease in spontaneous recovery was noted in USA based hospitals since the approval of sugammadex.¹⁶ Intuitively, the absence of reversal would increase the risk for postoperative residual neuromuscular block, especially when neuromuscular monitoring is not used appropriately, although current literature does not support this hypothesis.^{17,18} In our center, neuromuscular monitoring is freely available in every OR, and it is possible that reversal in many of our patients was deemed unnecessary, however we are not informed on the depth of neuromuscular block at extubation as these data are not automatically logged into our electronic health record. Nevertheless, those patients that were actively reversed

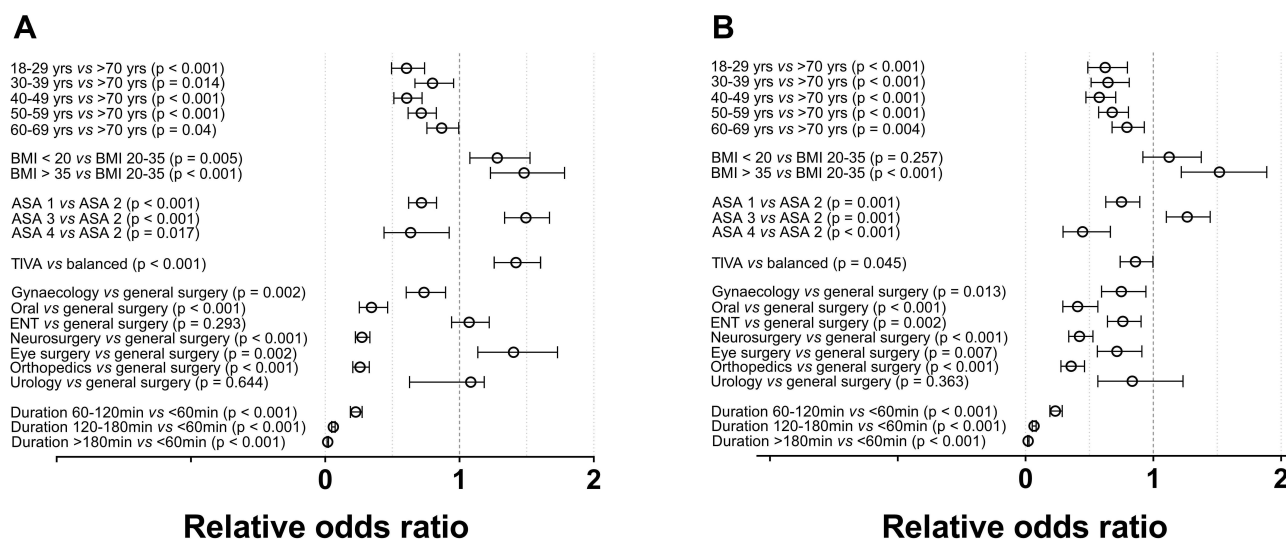


Figure 2 Relative odds ratio of reversal with sugammadex versus spontaneous recovery. **(A)** Univariate analysis. BMI categories 20–35 were combined to show the contrast with multivariate analysis. **(B)** Multivariate analysis. Odds ratios shown are adjusted for all other variables listed. Covariates are relative to age > 70 years, BMI 20–35, ASA = 2, anesthesia = volatile, surgery = general surgery, and duration of surgery < 60 min.

included patients of higher ASA class, BMI and age, which are characteristics that are generally regarded to increase the risk for residual NMB. A similar pattern was observed in recent studies using data from large US healthcare databases.^{16,19,20} This suggests that clinicians are aware of the risk factors for residual NMB and make an individual-based decision on whether to reverse or not based on these, and possibly other, risk factors. Among all factors, awareness of the risk of residual NMB and sufficient knowledge and education on how to prevent this, is probably the most important factor in preventing residual NMB; failure to do so has been demonstrated to negatively impact incidence of residual NMB, even when neuromonitoring and reversal agents are used.¹⁷

Our data also show that, in the setting where sugammadex is freely available, clinicians prefer to use sugammadex over neostigmine as reversal agent. This is broadly consistent with other reports showing that the use of sugammadex in many countries increases with time after regulatory approval for clinical use and hospital access granted.^{19–21} In this respect, our center may have had a head start because approval of sugammadex was granted in 2008 in The Netherlands versus 2015 in the USA. This may in part explain why the use of sugammadex in our center is higher (among those pharmacologically reversed) than what is reported in USA derived data. However, despite early approval of sugammadex in our country and many other European countries, differences between centers within and between EU countries exist. For instance, data from the POPULAR study, which was a European multi-center study, showed that neostigmine was still used in the majority of cases (77.4%).¹⁷ Although time progression since the conclusion of that study may have led to an ongoing gradual decrease in neostigmine use since then, we believe that the time component alone does not fully explain the differences between the POPULAR data and our data. Specifically, in our hospital, a deep neuromuscular block is applied for robotic surgery, retroperitoneal surgery and intravitreal eye surgery. Incidentally, a deep NMB needs reversal with sugammadex at the conclusion of a procedure which may have contributed to higher sugammadex use in our center. Still, most procedures in our center receive a single shot of muscle relaxant at the induction of anesthesia. Therefore, we contend that the choice of the use sugammadex was not primarily based on the depth of block alone, but rather on the merits of sugammadex itself.

Our study has several limitations. First, clinical variables that were not available in our dataset (such as categorized patient medical history, history of coded previous surgeries, neuromonitoring data, etc.) may have had an undetermined impact on the decision to reverse or not reverse a patient. These may include details of the perioperative care (eg, dosing information of medication and fluids), provider bias, surgeon preference, patient anthropometric data (eg, habitus or smoking status) and previous patient clinical events. When looking at associations we must interpret the current findings

Table 4 Characteristics of Multivariate Logistical Regression Analysis

Age Category (y)	OR	95% CI Lower	95% CI Upper	p-value
18–29	0.623	0.487	0.797	<0.001
30–39	0.645	0.513	0.811	<0.001
40–49	0.577	0.472	0.705	<0.001
50–59	0.678	0.572	0.805	<0.001
60–69	0.793	0.677	0.929	0.004
70–	1.000	Reference		
BMI	OR	95% CI Lower	95% CI Upper	p-value
Underweight (< 20 kg.m ⁻²)	1.124	0.918	1.375	0.257
Normal – obese (20–34.9 kg.m ⁻²)	1.000	Reference		
Morbidly obese (≥ 35 kg.m ⁻²)	1.517	1.219	1.888	<0.001
ASA Class	OR	95% CI Lower	95% CI Upper	p-value
1	0.749	0.628	0.894	0.001
2	1.000	Reference		
3	1.262	1.102	1.445	0.001
4	0.441	0.293	0.664	<0.001
Anesthesia Type	OR	95% CI Lower	95% CI Upper	p-value
TIVA	0.860	0.741	0.997	0.045
Volatile	1.000	Reference		
Specialty	OR	95% CI Lower	95% CI Upper	p-value
General Surgery	1.000	Reference		
Gynecology	0.749	0.595	0.942	0.013
Oral surgery	0.407	0.292	0.566	<0.001
ENT surgery	0.761	0.641	0.904	0.002
Neurosurgery	0.422	0.338	0.527	<0.001
Eye surgery	0.715	0.562	0.910	0.007
Orthopedics	0.357	0.277	0.461	<0.001
Urology	0.835	0.566	1.232	0.363
DoS (min)	OR	95% CI Lower	95% CI Upper	p-value
<60	1.000	Reference		
60–120	0.233	0.190	0.287	<0.001
120–180	0.066	0.052	0.083	<0.001
>180	0.020	0.016	0.027	<0.001

Abbreviations: BMI, Body Mass Index; ASA, American Society of Anesthesiologists; TIVA, Total Intravenous Anesthesia; ENT, Ear, Nose & Throat; DoS, Duration of Surgery (defined as start incision to closure of skin).

with caution considering unmeasured confounding and the potential impact these variables may have had on observed effects.

Conclusion

In conclusion, this study assessed the use of neuromuscular blocking agents and reversal strategy during anesthesia in a tertiary academic hospital in the Netherlands with unrestricted access to sugammadex. Of the patients that had received rocuronium, only 23% were actively reversed overall, with sugammadex as the preferred reversal agent (99.9% of reversals). The decision to actively reverse NMB with sugammadex in our cohort depended on patient age, BMI, ASA state, type of anesthesia and type and duration of surgery.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was funded by Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc, Kenilworth, NJ. The sponsors collaborated with the investigators in the design of the study, and preparation of the manuscript. Sponsors had no access to patient level data and took no part in data analysis.

Disclosure

Lori D Bash is a full-time employee of Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Inc, Kenilworth, NJ, USA which manufactures and distributes sugammadex, and may own stock and/or hold stock options in Merck & Co., Inc., Kenilworth, NJ. Marieke Niesters reports grants from Grunenthal, outside the submitted work. Albert Dahan reports grants and/or personal fees from MSD, MEDTRONIC, Trevena, Grunenthal, Medasense, AMO Pharma, ZonMW, and FDA, outside the submitted work. Dr Martijn Boon reports grants from MSD, during the conduct of the study. The authors report no other conflicts of interest in this work.

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