RESEARCH ARTICLE

Postoperative residual curarisation in geriatric patients: a prospective, observational cohort study

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Abstract

Objective: To evaluate the occurrence and potential risk factors of residual curarisation after surgery and the subsequent acute respiratory events in elderly patients.

Method: The prospective, cohort study was conducted at Ankara City Hospital from July to December 2021, and comprised data of geriatric patients undergoing elective surgery under general anaesthesia using moderate-acting nondepolarising muscle relaxants. Postoperative acute respiratory events in the post-anaesthesia care unit were subsequently noted. Data was analysed using SPSS 25.

Results: Of the 185 patients aged >65 years evaluated, 174(94%) were included; 88(50.6%) females and 86(49.4%) males. The incidence of residual curarisation was in 6(3.4%) patients. Postoperative residual curarisation was significantly associated with smooth recovery process ($p<0.05$). The recovery was associated with intraoperative bleeding, total dose of neuromuscular blocker, and the length of time from the last dose of neuromuscular blocker to antagonist administration ($p<0.05$). Postoperative critical respiratory events were more common in patients with postoperative residual curarisation ($p< 0.001$). The length of stay in post-anaesthesia care unit was 1.57 times longer in such patients ($p=0.001$).

Conclusion: Postoperative residual curarisation increased length of hospital stay and respiratory complications.

Key Words: Postoperative residual curarisation, Neuromuscular monitoring, Anaesthesia recovery period, Sugammadex, Postoperative care, Elderly patient.

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Introduction

Population ageing is a multifactorial, irreversible and global phenomenon. In parallel with the increase in average life expectancy in the world, the development of chronic disease care, and surgical applications, the percentage of the elderly population is also increasing. Anaesthesiologists are expected to more frequently encounter anaesthesia management in geriatric patients with more comorbidities in the near future, resulting in higher perioperative morbidity and mortality rates.[1,2]

Neuromuscular blocking drugs (NMBDs) are indispensable components of general anaesthesia (GA) practice.[3] Postoperative residual curarisation (PORC) refers to the prolonged blockade of some nicotinic receptors at the neuromuscular junction. It may cause important clinical consequences by increasing the incidence of adverse respiratory events during the postoperative recovery period in patients administered NMBDs.[4,5]

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Geriatric patients have been identified as a risk group for PORC owing to prolonged recovery from neuromuscular blockade resulting from pharmacokinetic and pharmacodynamic changes. The residual effects of NMBDs may worsen the condition in geriatric patients who might have already had reduced muscle strength and impaired pharyngeal function.[6,7]

Although PORC has been assessed in the geriatric population, further research is required due to the patterns of reversal agent use that vary over time and owing to each country's medical context.[6-8]

The current study was planned to assess the prevalence and risk factors of PORC and associated acute respiratory events (AREs) during the early recovery phase post-surgery in elderly patients.

Patients and Methods

The prospective, observational, cohort study was conducted at Ankara City Hospital from July to December 2021, after approval from the Ankara City Hospital ethics committee (E1-21-1912, ClinicalTrials.gov with ID: NCT05051371).

The sample size was calculated G*Power 3.1.9 [9] with 90% power, effect size g = 0.13 and alpha (α) = 0.05, based on a study that reported incidence of PORC 43% for TOFR <0.9.[5] The calculated sample size was inflated by 10%.

Those included were patients of either gender aged >65 years who were operated under GA using intermediate-acting NMBDs having physical status matching American Society of Anaesthesiologists (ASA) grade [10] I-III. Patients with unexpected major intraoperative and postoperative surgical complications, patients with neuromuscular neurological disorders, body mass index (BMI) >35kg/m^2, patients with a difference of >10% between two train-of-four (TOF) ratio (TOFR) measurements, and patients with a central body temperature <35.5°C measured in the post-anaesthesia care unit (PACU) were excluded. The primary endpoint was the occurrence of PORC in the patients during their PACU stay, and the secondary endpoints included postoperative AREs in PACU.

After taking informed consent from the subjects, demographic and clinical data, including age, gender, BMI, ASA status as well as concomitant disease assessed using the Charlson Comorbidity Index (CCI) were recorded.[11] Type and duration of surgery, duration of anaesthesia from induction –to arrival at PACU, type of intermediate-acting NMBDs used, duration of last NMBDs –up to TOFR recording, dose and time of administration of sugammadex and neostigmine (reverse agent administration, TOFR record in PACU) were also recorded. Intraoperative use of anaesthetics, neuromuscular blockers, and reverse agents did not interfere with the procedure, and was at the discretion of the responsible anaesthesia team.

The patient's electrocardiogram (ECG), peripheral oxygen saturation, noninvasive blood pressure (BP), and body temperature (Genius™ 2 IR Tympanic Thermometer Ltd., Gosport, United Kingdom) were routinely monitored immediately upon arrival in PACU. All patients were given supplemental oxygen 2L/min). An accelerometer (TOF-Watch® SX, Organon Inc, Ireland) was used to monitor adductor pollicis neuromuscular function in PACU by an anaesthesiologist blinded to the study. The patient's four fingers were fixed with a plaster and the thumb was relieved. The skin was cleaned with alcohol swab. Two ECG electrodes were placed on the nervus ulnaris trace; one just above the wrist as a negative electrode, and the other a 2-3 cm proximal positive electrode. The acceleration transducer was fixed on the palmar surface of the distal phalanx of the thumb. The thermometer probe was placed in the thenar region of the patient's palm for peripheral temperature. After due calibration, the accelerometer was operated in TOF mode. Two consecutive TOF stimuli of 30-50mA at 15-second intervals were applied, and the motor response of the thumb (adductor pollicis muscle) was measured by TOF counting. The mean of two measurements was recorded. The patients with TOFR <0.9 were considered patients with PORC, and patients with TOFR ≥0.9 were taken as patients without PORC.

To assess AREs, the parameters recorded included upper airway obstruction, hypoxaemia defined as oxygen saturation (SpO^2) <90%, use of accessory muscles, agitation, difficulty swallowing or speaking, and re-intubation. In addition, the Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) score for postoperative pulmonary complications in surgical patients was recorded.[12] In patients with a TOFR <0.90 and SpO2 <90%, 2mg/kg of sugammadex was administered. Patients were discharged to the service when their modified Aldrete score [13] reached 9.

Data was analysed using SPSS 25 and MedCalc 15.8. Data was expressed as frequencies and percentages, mean ± standard deviation (SD), or median with interquartile range (IQR), as appropriate. Data was compared using chi-square test. Kolmogorov-Smirnov test, the skewness-Kurtose and graphical techniques, including histogram, Q-Q plot, stem and leaf and boxplot, were used for checking data normality. The independent samples t-test was applied to evaluate data showing normal distribution. Quantitative data was analysed with Mann-Whitney U test if data did not exhibit normal distribution. A binary logistic regression test was used to determine risk ratios. P<0.05 was considered statistically significant.

Results

Of the 185 patients aged >65 years evaluated, 174(94%) were included (Figure). There were 88(50.6%) females and 86(49.4%) males. Demographic and intraoperative characteristics of all the patients were noted (Table 1).

The incidence of PORC was noted in 6(3.4%) patients. There were 142(81.6%) patients aged 65-74 years, and PORC was detected in 3(2.11%) of them. There were 32(18.4%) patients aged 75-85 years, and PORC was detected in 3(9.38%) of them. The distribution of the type of surgery performed and the duration of anaesthesia were comparable between the PORC and non-PORC patients. Bleeding volume and fluid administered intraoperatively were greater in patients with PORC than in non-PORC patients (p=0.041 and p=0.049 respectively). CCI and ARISCAT scores were higher in patients with TOFR <0.9 than in patients with TOFR ≥0.9 (p=0.028 and p=0.004 respectively).

There was no significant intergroup difference in total vecuronium consumption (p=0.346), but the total amount of rocuronium administered during surgery was higher in patients with PORC (p=0.002).

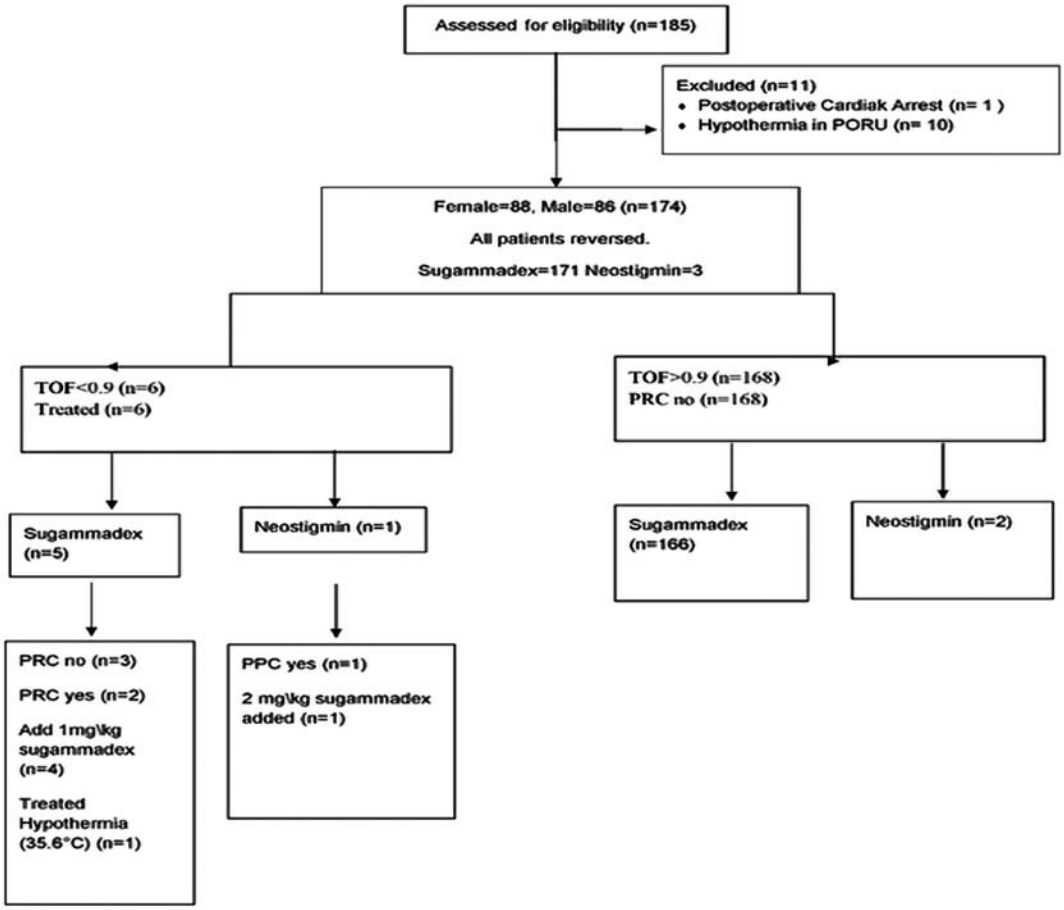

Figure: Study flow-chart.

Table-1: Comparison of demographic and intraoperative characteristics of patients with TORF <90 and TOFR ≥90.

	TOFR <0.9	TOFR ≥0.9	*p-value*
Sex			
Female n (%)	3 (50.0%)	85 (50.6%)	
Male n (%)	3 (50.0%)	83 (49.4%)	1.000[a]
Age (year)	73.5 ± 4.9	70.2 ± 4.7	0.095[b]
Body Weight (kg)	82,8 ± 20.1	75.5 ± 13.5	0.196[b]
BMI (kg/m^2)	30.6 ± 6.6	27.3 ± 4.5	0.090[b]
Body Temperature (C)	35.9 ± 0.3	36.1 ± 0.2	0.229[b]
ASA score			
II	1 (16.7%)	96 (57.1%)	
III	5 (%83,3)	72 (%42,9)	0.044[a]
Type of surgery			
Abdominal	6 (100.0%)	138 (82.1%)	0.592[a]
Non-abdominal	N	30 (17.9%)	
Duration of anaesthesia (min)	261.7 ± 100.9	192.2 ± 109.6	0.128[b]
Bleeding volume (ml)	450(95-1.025)	100(0-300)	0.041[c]
Administered Fluid (ml)	2916.7 ± 1985.4	1869.6 ± 1240.7	0.049[b]

ASA: American Society of Anaesthesiologists, BMI: Body mass index, TOFR: Train-of-four ratio, N: non, a: Chi-square test [n, (%)], b: Independent samples t test (Mean ± standard deviation [SD]), c: Mann-Whitney U Test (Median / interquartile range [IQR]).

There was no significant difference between the groups in the distribution of antagonists used (p>0.05). A significantly lower total sugammadex dose was administered in the PORC group (p<0.05). Neostigmine use was similar between the groups (p>0.05). In patients with PORC, the time from the last NMBD dose to antagonist administration was significantly shorter than in non-PORC patients (p<0.05). The time from antagonist administration to extubation was significantly longer in patients with PORC (p<0.05). The time from antagonist administration to extubation was longer in patients receiving neostigmine than in patients receiving sugammadex (p=0.000). The duration of the PACU stay was longer and AREs in PACU were higher in the patients with PORC compared to the rest (p < 0.05).

Logistic regression showed the length of PACU stay to be significantly different between the groups, and PORC increased the length of stay in PACU 1.57 times (Table 3).

Table-2: Comparison of CCI, ARISCAT score, antagonist drugs administration times and postoperative characteristics of patients with TORF <90 and TOFR ≥90.

	TOFR <0.9 (n=6, %)	TOFR ≥0.9 (n=168, %)	p-value
Antagonist Drugs			
Sugammadex (n, %)	5 (83.3%)	166 (98.8%)	0.100 a
Neostigmin (n, %)	1 (16.7%)	2 (1.2%)	
Sugammadex (mean, mg)	180.0 ± 44.7	203.6 ± 28.9	0,011 b
Neostigmine (mean, mg)	2.0 (2.0 – 2.0)	2.0 (2.0 – 2.0)	1,000 b
Time from antagonist			0.024b
to the extubation (min)	60.0 (35.0 –95.0)	90.0 (75.0 – 123.8)	
Charlson Comorbidity Index (mean)	5.3 ± 1.0	4.1 ± 1.4	0.028b
ARISCAT Score (mean)	43.7 ± 6.1	32.5 ± 15.2	0.004b
Length of PACU stay (mean, min)	55.0 (48,8 – 60.0)	45.0 (45.0 – 45.0)	0.001c
Acut Respiratory Events) in PACU (n,%)	3 (50.0%)	1 (0.6%)	0.000a
Airway Obstruction,+ Breathing +Agitation	1 (%16,7)	N	
Airway Obstruction,+ Breathing+ Difficulty Swallowing	1 (%16,7)	N	
Hypoxaemia+ Abdominal Breathing	N	1 (%0,6)	
Hypoxaemia+ Agitation+ Abdominal Breathing	1 (%16,7)	N	

TOFR: Train-of-four ratio, N: non, PACU: Post-anaesthesia care unit, a: Chi-square test (n, [%]), b: Independent samples t test (Mean ± standard deviation [SD]), c: Mann-Whitney U test (Median / interquartile range [IQR]).

Table-3: Logistic regression analysis of significant parameters.

Risk Factors	B	OR	95 % CI	Wald	P-value
ARISCAT Score	-0.046	0.955	0.84 – 1.09	0.452	0.502
Time from NMBA to the antagonist (min) -	0.004	0.996	0.95 – 1.04	0.032	0.857
Length of PACU stay (min)	0.448	1.565	1.10 – 2.23	6.205	0.013*
Total rocuronium dose (mg)	0.028	1.028	0.99 – 1.06	2.489	0.115
CCI	1,120	3.064	0.67 – 14.04	2.077	0.149

*: Binary Logistic Regression Test, Nagelkerke R2 = 0.626, Hosmer and Lemeshow Test = 0.322, CCI: Charlson Comorbidity Index, NMBD: Neuromuscular blocking drug, PACU: Post-anaesthesia care unit, B: Regression coefficient, OR: Odds ratio, CI: Confidence interval, Wald: test statistics * $p < 0.05$ significantly different with logistic regression analysis.

Discussion

In the present study, the prevalence of PORC in geriatric patients was 3.4%. Although it was 2.11% in patients aged 65-74 years, and 9.38% in patients aged 75-85 years. Sugammadex effectively reversed neuromuscular blockade in 98.3% of the geriatric patients, with a PORC incidence of only 3.4%, which was lower than in earlier findings.[3,13,14]

In the current study, PORC was associated with higher ASA physical risk score and CCI values, greater intraoperative bleeding, higher dose of NMBDs, higher ARISCAT risk score, and shorter duration of antagonist agent administration after the last dose of NMBDs.

The length of stay in PACU was 1.57 times longer in patients with PORC, and the incidence of PORC was high in patients with high ARISCAT risk score and high risk of postoperative AREs.

A wide range of incidences of PORC has been reported in several studies. Carvalho et al. performed a meta-analysis of data from 1979 to 2019 to analyse the correlation between neuromuscular monitoring (NMM) and PORC. The meta-analysis comprised 109 study arms and 12,664 patients in 53 studies. It summarised the outcomes of NMBDs with intermediate effect, described by TOFR <0.9 and PORC, as 11.9% with quantitative NMM, 31.1% with qualitative NMM and 33.8% with no NMM follow-up. The type of anaesthesia did not significantly affect the incidence of PORC. In addition, lower PORC rates were associated with sugammadex use.[3] Carvalho et al. indicated that quantitative NMM was more appropriate than follow-up with subjective NMM to reduce PORC, defined by TOFR <0.9.[3] Aytac et al. reported that the prevalence of PORC in an observational study was 43% for TOFR <0.9 and 15% for TOFR <0.7. They also reported a TOFR <0,9 in 46.3% of patients with reversal agent neostigmine. The mean age and ASA score in patients who developed PORC were higher, and the time between early extubation, anaesthesia, last NMBD administration, and TOFR assessment after NMB antagonism was shorter.[5] The reason for the lower incidence of PORC in the current study was the use of sugammadex at a rate of 98.3% and neostigmine at a rate of 1.7% [15].

In 2015, Fortier et al. reported in their multicentre, prospective, observational study that the PORC rate upon arrival in the recovery room was 56.5%. The incidence of PORC was positively correlated with higher rocuronium doses per minute during surgery. Despite the use of qualitative NMM and neostigmine, the study emphasised that residual paralysis was common during tracheal extubation and PACU presentation.[16] In the current study, patients who received higher total doses of rocuronium had a greater incidence of PORC.

Raval et al. systematically screened 1,438 observational studies on the epidemiology and outcomes of PORC, and included 58 studies with a total of 25,277 patients. The review reported conflicting definitions of PORC in studies,

including quantitative and qualitative measures of PORC detection. The most common definition of PORC in these studies was TOFR <0.9 in 29 studies and TOFR <0.7 in 16 studies, measured at PACU entry. The incidence of PORC on arrival to PACU ranged 0-90.5% (median 30%).It was found in 0-16% of patients reversed with sugammadex, 3.5-90.5% of patients reversed with neostigmine, and 15-89% of patients who recovered spontaneously without antagonist medication.[17]

Differences between the reported PORC values may result from significant differences in the methodology and protocols of the studies. Suzuki et al. showed that the elimination time of neuromuscular blockade was slightly prolonged in older patients due to the prolonged circulation time of sugammadex.[18] Murphy et al. found that the effects of NMBD were prolonged in the elderly population, while the duration of action of neostigmine was prolonged, which could shift the balance in favour of NMBD, and the risk of PORC increased in this population.[6] Pietraszewski et al. reported that PORC was more common in older (44%) than in young patients (20%).[19] Togioka et al. reported that the prevalence of PORC in patients aged 70 years and older who underwent surgery lasting at least 3 hours was 10% in the sugammadex group and 49% in the neostigmine group in their randomised controlled trial (RCT). They showed that moderate blockade with TOF count 2, reversed with sugammadex, reduced PORC by 40% and was associated with a 10% lower 30-day hospital readmission rate.[20] The current study found that PORC developed in 2.92% of 171 patients using sugammadex, and in 33.33% of 3 patients using neostigmine. When the subjects were divided according to certain age groups, PORC detected in 142 patients aged 65-74 years was 2.11%, and PORC detected in 32 patients aged 75-85 years was 9.38%.

Batıstaki et al. prospectively examined 520 patients and reported a PORC frequency of 10.8%. In that study, rocuronium (90.4%), cis-atracurium (9.2 %), and succinylcholine (0.4%) were administered as NMBDs. They attributed the incidence of PORC, which was lower than what has been generally reported, to the use of reverse agents (neostigmine 40.9%, sugammadex 59.1%) in 99.6% of patients, female gender and comorbidities.[21] In the current study, there was no significant difference between the groups in terms of gender. However, the patients who developed PORC were associated with higher ASA physical risk scores and CCI values.

Hristoska et al. in a meta-analysis of 41 RCTs reported that in patients receiving rocuronium, sugammadex 2mg/kg reversed blockade from the second twitch (T2) to a TOFR >0.9 in 1.96 minutes. On the other hand, 0.05mg/kg neostigmine was shown to reverse blockade from T2 to TOFR >0.9 in 12.87 minutes.[22] Carron et al. reported that in patients aged >65 years, the recovery time from neuromuscular blockade with rocuronium was prolonged by an average of 1-2 minutes after the administration of sugammadex compared to younger patients.[23] Yazar et al. examined the effects of sugammadex on age-related reversal time and PORC, and reported that the reversal time with sugammadex was longer in patients aged 75 years than in patients aged 65-74 years.[24] In the current study, TOFR was only measured in the PACU after extubation. The media extubation time was 2 (IQR: 1-3) minutes with sugammadex, and 5 (IQR: 3-5) minutes with neostigmine.

To date, the association between the ARISCAT risk score, used to predict the risk of postoperative pulmonary complications, and the incidence of PORC has not been evaluated. The current study found a higher incidence of PORC in patients with higher ARISCAT risk scores.

The current study has several limitations. First, it is a single-centre, observational, cohort study, so standardisation of anaesthesia could not be performed. Second, the TOFR could not be measured before extubation. Third, the correct antagonist dose could not be determined. Fourth, there was a relatively low use of neostigmine compared with sugammadex due to not being in the hospital pharmacy at the time of the study. Fifth, there was inability to accurately determine the use and doses of drugs that would affect perioperative neuromuscular function. Sixth, the study was limited to the operating room and postoperative recovery room.

Conclusion

The elderly patients were found to be at a high risk for PORC and associated AREs. The altered pharmacokinetics of NMBDs in elderly patients may result in a prolonged duration of action and delayed recovery from neuromuscular blockade compared to younger patients.

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Author's Contributions

ES, BGA: Design, acquisition, analysis interpretation of data for the work, drafting, revising it critically for important intellectual content, agreement to be accountable for all aspects of the work.

AP: Design, acquisition, analysis interpretation of data for the work, drafting, revising it critically for important intellectual content, final approval, agreement to be accountable for all aspects of the work.