

Postoperative residual curarization from intermediate-acting neuromuscular blocking agents delays recovery room discharge[†]

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Key points

- Postoperative residual curarization (PORC) may delay postoperative recovery room (PACU) discharge.
- This observational study measured the effect of PORC on discharge times.
- Length of stay was significantly longer in patients with T4/T1 <0.9 on admission to PACU.
- The authors recommend increased use of neuromuscular monitoring.
- The potential effects of PORC on operating theatre/PACU utilization are discussed.

Background. Postoperative residual curarization (PORC) [train-of-four ratio (T4/T1) <0.9] is associated with increased morbidity and may delay postoperative recovery room (PACU) discharge. We tested the hypothesis that postoperative T4/T1 <0.9 increases PACU length of stay.

Methods. At admission to the PACU, neuromuscular transmission was assessed by acceleromyography (stimulation current: 30 mA) in 246 consecutive patients. The potential consequences of PORC-induced increases in PACU length of stay on PACU throughput were estimated by application of a validated queuing model taking into account the rate of PACU admissions and mean length of stay in the joint system of the PACU plus patients recovering in operation theatre waiting for PACU beds.

Results. PACU length of stay was significantly longer in patients with T4/T1 <0.9 (323 min), compared with patients with adequate recovery of neuromuscular transmission (243 min). Age ($P=0.021$) and diagnosis of T4/T1 <0.9 ($P=0.027$), but not the type of neuromuscular blocking agent, were independently associated with PACU length of stay. The incidence of T4/T1 <0.9 was higher in patients receiving vecuronium. Delayed discharge significantly increases the chances of patients having to wait to enter the PACU. The presence of PORC is estimated to be associated with significant delays in recovery room admission.

Conclusions. PORC is associated with a delayed PACU discharge. The magnitude of the effect is clinically significant. In our system, PORC increases the chances of patients having to wait to enter the PACU.

Keywords: muscle skeletal; neuromuscular block; recovery; relaxation

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Residual effects of neuromuscular blocking agents last well beyond surgery and can have significant clinical consequences.^{1–2} There is evidence that even small degrees of postoperative residual curarization (PORC) increase the incidence of adverse respiratory events in the post-anaesthesia care unit (PACU) and may increase longer-term morbidity as well.^{3–4} On the basis of the best available evidence, current recommendations support a train-of-four (TOF) (T4/T1) ratio of 0.9 or more as an appropriate indication of adequate recovery from neuromuscular transmission block.^{1,5–9}

It is well established that long-acting neuromuscular blocking agents such as pancuronium result in higher levels of PORC than intermediate-acting neuromuscular blocking agents and may delay discharge from the PACU.^{6,10} Although less likely than with long-acting agents, significant PORC does

occur with intermediate neuromuscular blocking agents, even after a single dose (approximately two-fold effective dose 95) given >2 h before arrival to the PACU.^{8,11,12} It is unclear, however, whether or not PORC induced by intermediate-acting neuromuscular blocking agents is associated with an increased PACU length of stay.

As part of a cost-saving effort at our institution, the preferred neuromuscular blocking drug (NMBD) to be used in the operating theatre was changed from cisatracurium to vecuronium. Before this change, cisatracurium was used in 95% of all cases. The proposed change, coupled with scant recent institutional experience with vecuronium, led to heightened awareness about possible residual paralysis, particularly as quantitative neuromuscular transmission monitoring had not been established in our department at this point.

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Accordingly, we tested the primary hypothesis that PORC from the use of an intermediate-acting neuromuscular blocking agent is associated with longer PACU length of stay. We also applied a recently developed queuing model¹³ to evaluate the potential impact of a PORC-associated prolonged PACU discharge time on patient flow from the operating theatre to the PACU.¹⁴

Methods

The study was approved by the Institutional Review Board of the Massachusetts General Hospital, Boston, MA, USA (MGH). We studied 248 patients arriving to the PACU of MGH after receiving NMBDs as part of surgical anaesthesia.

Standard anaesthesia monitoring (ECG, pulse oximetry, end-tidal carbon dioxide concentration, and oscillometric arterial pressure) was used continuously throughout the operating theatre portion of care. All MGH operating theatres and anaesthetizing locations were equipped with basic nerve stimulators (Innervator™, Fisher and Paykel, Healthcare, Inc. Irvine, CA, USA) capable of delivering TOF stimuli and a 5 s tetanic stimulus, and the anaesthesia providers were familiar with their use. Standard recovery room monitoring was performed in PACU.

Patients were excluded if they were <18 yr of age, if they arrived when PACU was on hold (i.e. patients had to wait in the theatre for a bed to be available in PACU); were scheduled to stay in PACU overnight (>12 h); or had received more than one type of neuromuscular blocking agent. Patients were also excluded if they had procedures or a pre-existing condition that did not allow for TOF ratio to be measured accurately by ulnar nerve stimulation.

Measurements

The degree of neuromuscular block was assessed by a single investigator (A.B.) within 10 min of arrival in PACU using acceleromyography of the adductor pollicis muscle (TOF-watch SX; Schering-Plough, Kenilworth, NJ, USA). Surface electrodes (PNS Electrode, NDM, Dayton, OH, USA) were attached to the cleansed skin on the distal forearm over the ulnar nerve with one electrode positioned on the ulnar side of the flexor carpi radialis tendon and the other placed slightly offset (to ensure span over the ulnar nerve) 3 cm proximal. If patients still had well-adherent electrodes from the operating theatre, these were used in lieu of new electrodes. The transducer was attached to the hand adapter,¹⁵ flat side against the thumb, ensuring that the orientation of the electrode was perpendicular with thumb trajectory on stimulation of adductor pollicis. The stimulation current was set to 30 mA,¹⁶ and the TOF-watch SX was then calibrated to set the T1 response to 100% (Calibration 1 mode). The resulting TOF ratios, as measured by the TOF-watch SX from the height of T1 relative to the height of T4, were obtained. We applied two consecutive stimuli to our patients, and if the difference between the two T4/T1 values did not exceed 5%, we used these for analysis. If the difference in the TOF ratio between the two stimuli was

>5%, then we applied additional TOF stimuli until we achieved two subsequent TOF readings that did not differ by >5%.

Patients' temperature, peripheral oxygen saturation, and O₂ supplementation (litre min⁻¹) were recorded on admission. The information collected for each patient included: age, gender, renal function (creatinine, haemodialysis dependence), history of liver failure, and ASA physical status classification score. Surgery-related data assessment included: type of surgery, duration of the procedure, opioid (compound), neuromuscular blocking agent (compound, total dose, and time from last dose to PACU arrival), neostigmine dose, and anaesthetic agent(s). These data were obtained from the electronic medical record.

PACU discharge times were recorded by PACU nurses not involved in this study. The time to PACU discharge readiness was defined as the time from arrival in the PACU to the time deemed medically appropriate for patients to leave the PACU, and the actual PACU length of stay was defined as the time from arrival until actual departure from the PACU.

The potential consequences of PORC-induced increases in PACU length of stay on PACU throughput were estimated by application of a validated queuing model. Basic queuing models consist of the following components. There is a stream of jobs (PACU bed requests) arriving to the system in a random fashion, one after the other. The randomness in the job arrivals is modelled through a probability distribution of the time that elapses between the arrivals of two consecutive jobs. This creates an arrival process that is *a priori* unpredictable. Each of the PACU bed requests (patients) arriving needs to be completed but the time taken is also random and follows its own probability distribution that varies with the time of day. In our institution, PACU bed requests are served on a first-in-first-out basis. On receipt, a PACU bed request may have to wait in the queue until there is a bed available, and all the earlier bed requests are served. As the arrival and service times are unpredictable, it is unpredictable exactly how long a given job will have to wait until it will be served.

Our model took into account the rate of PACU admissions requests per hour, and the (arithmetic) mean length of stay in PACU and also patients recovering in theatre waiting for a PACU bed. Under the conditions studied, the steady-state distribution of the number of patients in the system follows a Poisson distribution,¹³ indicating that model assumptions are met.

Statistical analysis

Normally distributed data are reported as a mean with standard deviation (SD) and other continuous data are reported as median (inter-quartile range). Data were analysed using SPSS software (V 12.0., SPSS Inc., Chicago, IL, USA).

The main outcome variable was PACU length of stay. We tested the primary hypothesis that PACU length of stay is longer in patients with PORC (T4/T1 <0.9 at PACU arrival) compared with patients with adequate recovery of

neuromuscular transmission. The Mann–Whitney *U*-test was used to test for statistical significance, as appropriate.

Our power analysis (power: 80%, α error=0.05) was based on the data of Murphy and colleagues,⁴ who observed a 30% incidence of PORC, and on the data of Ballantyne and Chang,¹⁷ who previously assessed PACU discharge times in our institution.

We expected a ~25% incidence of PORC, and we calculated that 50 patients with and 200 patients without PORC would provide a >80% power to detect a 10% difference in PACU length of stay with an *SD* of 20%.

The potential impact of prolonged PACU discharge times on patient flow was explored using a queuing model of the PACU and its upstream dependencies as reported previously.¹³ We evaluated the association between the dependent variable PACU length of stay and a set of predetermined independent variables by using backward stepwise multiple regression analysis. We included the following as independent variables: PORC, neuromuscular blocking agent (cisatracurium and vecuronium), gender, age, creatinine, ASA risk score, neostigmine dose given for reversal, body temperature at the time of PACU arrival and duration of anaesthesia, and the use of volatile anaesthetic.

Results

We included a total of 248 patients in this prospective, observer-blinded, observational study (Table 1). We could not obtain reliable measurements of the TOF ratio in two patients, so we report data from 246 patients.

Descriptive analysis of T4/T1 in patients with and without PORC showed that the 10th percentile of the T4/T1 ratios in patients with and without PORC was 0.65 and 0.9, respectively (Fig. 1).

Patients with and without PORC did not differ significantly in terms of gender, creatinine concentration, duration of the case, and ASA physical status classification. The incidence of PORC was higher in those who had received vecuronium [total dose: 10.4 (*SD* 4.4) mg] compared with cisatracurium [11.4 (4.4) mg, *P*=0.032]. The temperature tended to be lower in patients with PORC [36.3 (0.4) vs 36.5 (0.4)°C, *P*=0.055], and time from last administration to be shorter [110 (70) vs 114 (60) min, *P*=0.08], but these were not statistically significant. Neuromuscular blocking agents were reversed with neostigmine in 78% of the cases, and a mean dose of 2.5 (1.2) mg was given.

The incidence of PORC was 22%. The PACU length of stay was significantly longer in patients with PORC [323 (299) min], compared with patients with adequate recovery of neuromuscular transmission [243 (185) min, *P*=0.026; Fig. 2]. Multiple regression analysis revealed that only age (*P*=0.021) and PORC (*P*=0.036) were independently associated with PACU length of stay (*P*=0.004). The neuromuscular blocking agent (cisatracurium or vecuronium) did not explain additional variance of PACU length of stay after controlling for PORC (T4/T1 <0.9; dichotomous criterion) in the multivariate model.

Table 1 Physical characteristics. NS, not significant; Vec, vecuronium; Cis, cisatracurium. Data are given as mean (range) or mean (*SD*) unless otherwise indicated

	Postoperative residual curarization	No postoperative residual curarization	<i>P</i> -value
<i>n</i>	54	192	
Age (yr)	59 (18–95)	56 (12–92)	NS
Gender			
Male	21	91	NS
Female	33	103	
ASA (median)	2	2	NS
Creatinine (μ mol litre ⁻¹)	87 (40)	90 (50)	NS
Liver failure	2.8 (0.2)	2.5 (0.2)	NS
Neostigmine dose (mg)	197 (90)	196 (97)	NS
Temperature at PACU arrival (°C)	36.3	36.5	NS
Neuromuscular blocking agents used			
Vec	49 (90%)	149 (78%)	0.032
Cis	5 (10%)	43 (22%)	

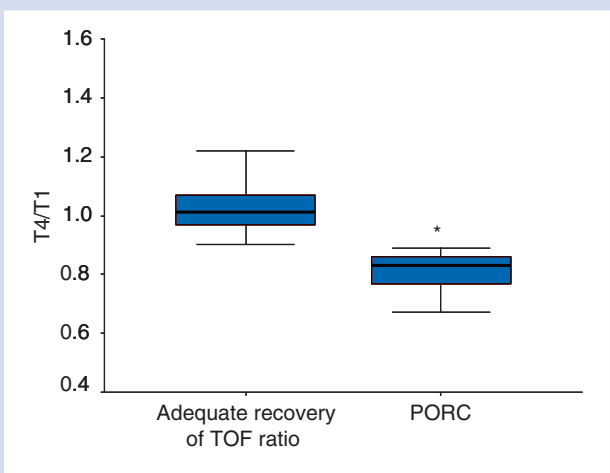
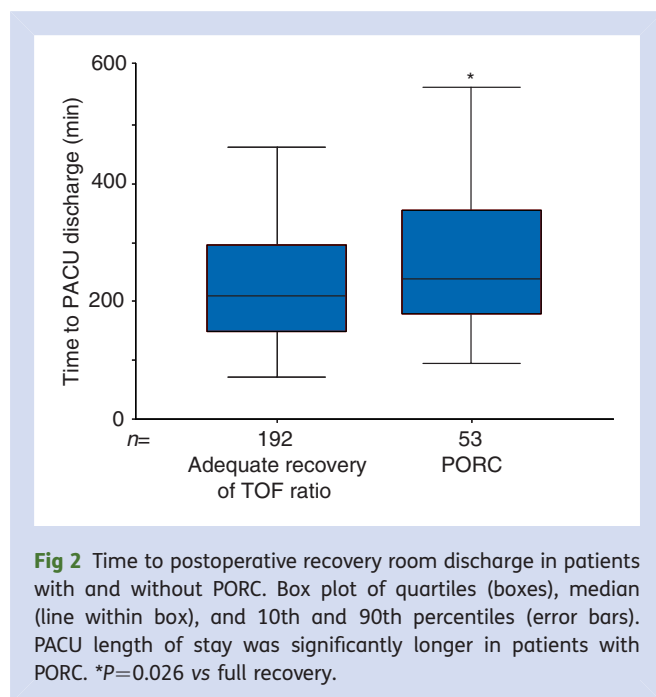


Fig 1 TOF (T4/T1) ratio in patients with and without adequate recovery of the TOF ratio. Box plot of quartiles (boxes), median (line within box), and 10th and 90th percentiles (error bars). The 10th percentile in patients with and without PORC was 0.9 and 0.65, respectively. **P*<0.05 vs adequate recovery of TOF ratio.

The PACU discharge readiness time was also significantly longer in patients with PORC (224 (173) min), compared with patients with adequate recovery of neuromuscular transmission (149 (64) min, *P*=0.025).

The mean PACU length of stay for patients with and without PORC was 323 and 243 min, respectively. The probability, based on our queuing model,¹³ of there being a queue to enter the PACU depends on the arrival rate (number of patients per hour entering the PACU), the PACU



length of stay, and the total number of PACU beds. We calculated the probability of a patient having to wait to enter the PACU assuming that all PACU patients had length of stay similar to our patients without PORC. Assuming that no patients had PORC, the probability of at least one patient waiting to enter the PACU during the day is 55%. If all patients experienced PORC and had the same prolongation of their stay as observed in our sample, this probability would increase to 95%.

We did not observe effects of PORC on oxygen saturation on arrival in PACU, and oxygen supplementation on arrival did not differ between groups. Nine patients (4.52%) required a nasal trumpet, and an oral airway or jaw thrust was needed in 6.25% of patients on arrival without differences between groups. No serious respiratory complications requiring re-intubation of the trachea occurred in either group.

Discussion

The main finding of our study is that PORC is an independent predictor of postoperative recovery room length of stay. The magnitude of the effect of PORC on PACU length of stay is likely to impact patient flow through the operating theatres.

Recent studies have reported that residual neuromuscular block from intermediate-acting neuromuscular blocking agents may be present in up to two-thirds of the patients, particularly if no reversal agents are given. The practice of not administering reversal agents has been reported from many European institutions,^{1 2 12 18} although reversal of NMB is more widely used in the UK. In our institution, reversal agents are frequently used—78% of our study population received neostigmine [mean dose of 2.5 (1.2) mg]. This might explain why the incidence of PORC of 20%, while clinically meaningful, is somewhat lower in our investigation compared

with the results reported in European studies,^{1 2 12 18} but more closely reflects the results of a recent North American study.⁴

The length of stay in PACU has been used as a dependent variable to compare the outcome of different anaesthetic techniques and perioperative management strategies,^{19–21} but data on factors that contribute to length of stay are limited.²² In our study, age and PORC were associated with a longer length of stay. This is in contrast to Waddle and colleagues²² who reported that the duration of anaesthesia and anaesthetic technique predict PACU length of stay. Our study focused on patients receiving neuromuscular blocking agents, and we did not examine the effect of regional vs general anaesthesia on PACU length of stay. Older patients have a higher surgical mortality and risk of complications,²³ and an increased risk of unexpected postoperative intensive care unit admission.²⁴

To our knowledge, the effect of PORC on PACU length of stay has not yet been prospectively studied. A comparison of PACU stay after the use of long- or short-acting neuromuscular blocking agents found that the difference in mean recovery time between patients receiving short- and intermediate-acting relaxants (mivacurium, atracurium, and vecuronium) was 30 min less than those receiving long-acting relaxants (d-tubocurarine and pancuronium).¹⁷ Our data add to these findings by showing a direct association between PORC with PACU length of stay, even when intermediate-acting neuromuscular blocking agents are used.

We observed a higher incidence of PORC in patients who received vecuronium compared with cisatracurium, but the NMBD itself did not independently predict PACU length of stay. Possible reasons for the association between the neuromuscular blocking agent used and PORC include pharmacodynamic differences between cisatracurium and vecuronium, and a lack of experience of our anaesthetists with vecuronium, use of which was encouraged by departmental guidelines.

We examined the impact of the increasing effects of PORC on PACU discharge by calculating the consequences on operating theatre (OR) throughput. Our queuing model revealed that the differences in PACU length of stay between patients with and without PORC probably result in waiting times for patients to enter the PACU. Our system is congested, and waiting to leave the operating theatre because the PACU is full occurs on many days. If all patients had PORC which affected PACU time to the extent we observed, then waiting to leave the operating theatre would occur virtually every day.

The economic consequences of the PORC-induced delay in PACU discharge are difficult to evaluate and clearly depend on individual institutional factors including staffing models, PACU size and floor bed availability, and the average case duration and PACU length of stay. If, for example, the PORC-evoked PACU discharge delays occur early in the morning, the economic consequences might be negligible unless the magnitude of the delay exceeds a time threshold such that cases need to be cancelled or delayed because all

of the operating theatres are filled with patients waiting for PACU beds. On the other hand, if the PORC-induced increase in PACU length of stay occurs in the afternoon at the end of the allocated block time, then our institution has to pay incentive salaries for anaesthetists and nurses to recover patients in the OR. Both of these scenarios assume that the PACU currently is, or is near to becoming, a bottleneck in the patient flow. Thus, it is likely that PORC has economic consequences in congested operation theatre/PACU systems, but this must be determined for each institution.

The PACU discharge times are surprisingly long in our study, significantly longer than the PACU readiness times. This likely reflects the shortage of bed availability on the ward in our hospital which is critical to patients' PACU discharge, an issue that has been addressed by hospital leadership. We selected the PACU length of stay as the main criterion, because this variable should be more important than PACU readiness time in terms of costs. Our data show that the magnitude of the effects of partial paralysis on PACU readiness time and length of stay are similar, a finding that is in accord with the suggestion that the observed delay is attributable to PORC.

The results of our study have to be considered within the context of its limitations. This is an observational study. Our multiregression model controlled for many variables associated with prolonged PACU stay but we cannot exclude that other non-measured factors may have influenced the results of our study. Using a queuing model previously validated in our PACU/operating theatre suite, we first estimated the probability of a patient waiting to enter the PACU, assuming that all PACU patients had a length of stay similar to our patients without PORC. This is somewhat artificial because this sample of patients receiving neuromuscular blocking agents, but without PORC, is not representative of all cases, notably neglecting the brief ambulatory operations with short length of stay. Finally, the study took place during a Departmental change from using cisatracurium to vecuronium, and we did not randomize our patients to receive cisatracurium or vecuronium. Although all anaesthesia providers received training in the use of vecuronium, we cannot exclude that the drug was not optimally used. Although this will not alter our main finding on the consequences of PORC on PACU length of stay, it might change the incidence of PORC associated with vecuronium.

Our study has clinical implications. On the basis of our findings, our Departmental guidelines were changed to encourage the use of quantitative neuromuscular transmission monitoring on all patients receiving neuromuscular blocking agents. Future studies determine whether the implementation of quantitative neuromuscular transmission monitoring helps decrease the incidence of PORC, a suggestion that is supported by a recent study which showed that intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular block and adverse respiratory events in the PACU.⁴

In summary, PORC ($T_4/T_1 < 0.9$) was independently associated with increased PACU length of stay. Estimates

using the queuing model suggest that the delay in PACU discharge increases the likelihood of patients having to wait to enter the PACU.

Conflict of interest

None declared.

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