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Original Article

# Prevalence and Risk Factors of Postoperative Residual Curarization in Patients Arriving at Postanesthesia Care Unit after General Anesthesia: A Prospective Cohort Study

Min Xie, Dong-Xin Wang, and Zhi-Yu Geng


## ABSTRACT

**Background:** Postoperative residual curarization (PORC) following the use of neuromuscular blocking drugs (NMBDs) remains a significant problem. The purpose of this study was to determine the prevalence and risk factors of PORC in patients who were admitted to postanesthesia care unit (PACU) after general anesthesia during our routine clinical practice.

**Methods:** This was a prospective, observational cohort study. Patients who were admitted to PACU after general anesthesia were enrolled. Neuromuscular function was monitored using acceleromyography and train-of-four (TOF) stimulation. A TOF ratio of less than 0.9 was defined as having PORC. Multivariate Logistic regression analysis was performed to identify risk factors of PORC.

**Results:** A total of 542 patients completed the study. PORC occurred in 30.6% (166/542) of patients. Increasing age (odds ratio [OR] 1.211, 95% confidence interval [CI] 1.068-1.374, P=0.003), combined use of two different non-depolarizing NMBDs during surgery (OR 1.693, 95% CI 1.138-2.520, P=0.009) and hypothermia at PACU arrival (OR 1.778, 95% CI 1.043-3.032, P=0.035) were associated with increased risk of PORC, whereas administration of neostigmine at the end of surgery (OR 0.341, 95% CI 0.164-0.709, P=0.004) and prolonged time interval from last dose of NMBDs to PACU arrival (OR 0.326, 95% CI 0.215-0.496, P<0.001) were associated with decreased risk of PORC. Patients with PORC at PACU arrival had prolonged PACU stay, increased occurrence of adverse events during PACU stay and increased rate of PORC at PACU discharge.

**Conclusions:** PORC was common in patients who were admitted to PACU after general anesthesia. Increasing age, combined use of two different non-depolarizing NMBDs during surgery and hypothermia at PACU arrival were associated with increased risk of PORC.


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Neuromuscular blocking drugs (NMBDs) are frequently used in patients undergoing general anesthesia. Postoperative residual curarization (PORC) is defined as unnecessary neuromuscular block caused by incomplete invalidation or reversion of NMBDs (1). Short- or intermediate-acting NMBDs have been used more extensively nowadays, which has led to an apparent decline of PORC (2, 3). However, according to recent studies, PORC remains a disturbing problem.

The existence of PORC causes a series of clinical problems, such as prolonged length of stay in the postanesthesia care unit (PACU) (4, 5), reduced efficiency of health care delivery, increased economic burdens of patients (5), and elevated risk of postoperative complications (6-8). The later may include hypoxemia, atelectasis, and acute respiratory failure. It is the duty of physicians and nurses in the PACU to diagnose and treat PORC correctly. Previous studies mainly focused on the prevalence of PORC produced by various kinds of NMBDs in special conditions (4, 9-11). The purpose of our study was to investigate the prevalence and risk factors of PORC in patients arriving at PACU after general anesthesia during daily clinical practice in our institution.

## MATERIALS AND METHODS

This was a prospective, observational cohort study. The study protocol was approved by the Clinical Research Ethics Committee of Peking University First Hospital (No. 2009181). Written informed consent was obtained from each patient or the surrogate of patient.

### Patient Recruitment

The study was conducted in the PACU of Second Operation Center of Peking University First Hospital from May 25 to August 25, 2009. This study included consecutive patients aged 18 years and older who were admitted to the PACU after general anesthesia in combination with NMBDs. Patients were excluded if they were unconscious before surgery or were admitted to the intensive care unit (ICU) after surgery.

### General Data Collection

Baseline characteristics, including age, gender, body mass index, and American Society of Anesthesiologists classification were collected. Intraoperative data including method of airway management during anesthesia, type of anesthesia maintenance, name and dose of NMBDs used, duration of anesthesia, duration of surgery, and administration of reversal drugs of NMBDs were recorded. Postoperative data including train-of-four (TOF) ratio and body temperature were documented both at PACU arrival and discharge. The length of stay in PACU was also recorded.

### Monitoring and Management of Patients in the PACU

Routine monitoring included electrocardiogram, blood pressure and pulse oxygenation. Oxygen was administered via mask. During the study period, body temperature was also monitored by putting a temperature probe (Mon-a-therm, Tyco, Mexico) in the armpit. Temperature reading was recorded when it became constant for more than 5 minutes. Hypothermia was defined as a core body temperature less than 36℃. Patients who developed hypothermia may be passively rewarmed with warmed blankets (Warm Touch, Mallinckrodt Medical, MO, USA).

Neuromuscular function was monitored by a trained investigator (M-Xie) using acceleromyography (TOF-Watch, Organon, New Zealand). The TOF model (electric current intensity 50 mA, pulses interval 0.5 second, 4 pulses duration 0.2 ms) was chosen to stimulate the ulnar nerve. Four evoked responses at the thumb were recorded as T1, T2, T3, T4, and T4/T1 was defined as TOF ratio. Two consecutive TOF stimulations were performed and the results were recorded at 15-second intervals. If the difference was less than 0.1, the average was documented as the final TOF ratio at that time; if the difference was more than 0.1, the stimulation was repeated once again and the average of the nearest two TOF ratios was defined as the final TOF ratio at that time. TOF monitoring was performed at least twice for each patient, i.e., at PACU arrival and discharge. The rates of residual paralysis were calculated using two thresholds of TOF ratio of less than 0.7 and 0.9. However, a TOF ratio $<0.9$ was defined as having PORC.

Muscle relaxant antagonist (neostigmine) and other treatments (such as analgesics, antiemetics,

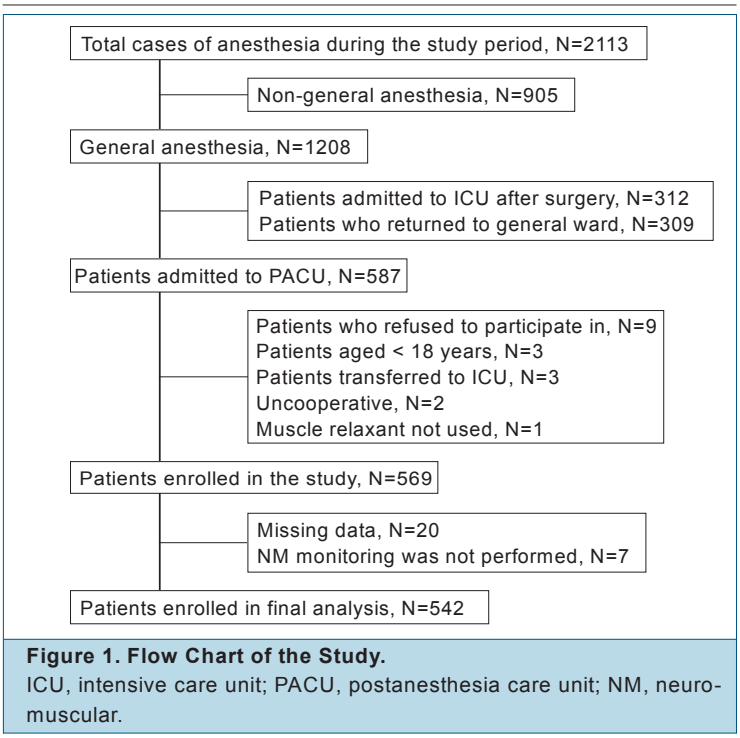


**Figure 1. Flow Chart of the Study.**
ICU, intensive care unit; PACU, postanesthesia care unit; NM, neuromuscular.

antihypertensive drugs and vasopressors) were administered according to the order of the attending anesthesiologists. In our routine clinical practice, neostigmine was administered at the end of surgery and extubation of the trachea was performed. Occasionally, patients with endotracheal intubation or laryngeal mask airway were sent to the PACU and were extubated in the PACU.

The attending anesthesiologist was responsible for making the decision of PACU discharge. The patients could not be discharged from PACU until the modified Aldrete score reached 9 or above. For patients whose TOF ratio was less than 0.9 at PACU discharge, monitoring of vital signs was continued and oxygen was administered in the general wards. All patients were followed up at 24 hours after surgery.

### Statistical Analysis

Continuous variables are expressed as means ± standard deviation or median (interquartile range). Data were compared using independent two-sample t-test or Mann-Whitney U test. Categorical variables are presented as number of patients (percentage). Data were compared using chi-square test. Variables that differed in univariate analyses ($P<0.15$) were included in a multivariate Logistic regression model to determine the independent predictors of PORC using a backward (Wald) stepwise procedure. Two-sided P values of less than 0.05 was regarded as statistically significant. Statistical analysis were performed with the SPSS 14.0 software (SPSS Inc., Chicago, USA).

## RESULTS

### Patient Recruitment

During the study period, 569 patients met the inclusion/exclusion criteria. Among them, 542 completed all PACU monitoring and postoperative follow-up and were included in the final analysis (Figure 1). The baseline and perioperative variables of these patients were presented in table 1.

### Prevalence and Risk Factors of PORC

At PACU arrival, the percentages of patients with TOF ratios of less than 0.7 and 0.9 were 12.7% (69/542) and 30.6% (166/542), respectively. At PACU discharge, the results were 0.4% (2/542) and 3.7% (20/542), respectively (Figure 2).

Univariate analyses revealed that 11 of all recorded baseline and perioperative variables were associated with higher occurrence of PORC at PACU arrival ($P<0.15$). After testing for multicolinearity, two variables (duration from last dose of NMBDs to extubation and body temperature at PACU arrival) were excluded from further analysis. At last, nine variables were included in multivariate Logistic regression analysis. Multiple Logistic regression analysis identified five independent predictors of PORC at PACU arrival, among them, increasing age, combined use of two different non-depolarizing NMBDs during surgery and existence of hypothermia at PACU arrival were associated with increased risk of PORC, whereas administration of neostigmine at the end of surgery and prolonged duration from last dose of NMBDs to PACU arrival were associated with decreased risk of PORC (Table 2).

### Outcomes and Adverse Events Associated with PORC in the PACU

The length of stay in PACU was significantly longer in patients with PORC at PACU arrival than in those without. At PACU discharge, a signifi-

cantly higher proportion of patients with PORC at PACU arrival than of those without had PORC. The overall incidence of adverse events during patients' stay in PACU was 9.8% (53/542). The incidences of use of oropharyngeal airway and any adverse events during PACU stay were significantly higher in patients with PORC at PACU arrival than in those without (Table 3).

## DISCUSSION

Our study found that 30.6% of our patients who were admitted to the PACU after general anesthesia had PORC. Increasing age, administration of two different non-depolarizing NMBDs during surgery and existence of hypothermia at PACU arrival were associated with increased risk of PORC, whereas administration of neostigmine at the end of surgery and long-time interval from last dose of NMBDs to PACU arrival were associated with decreased risk of PORC. Currently, use of the criteria of PACU discharge, like modified Aldrete score, could not guarantee the full recovery from the effects of NMBDs (12, 13).

NMBDs are frequently used in patients undergoing general anesthesia in order to facilitate endotracheal intubation and surgery. However, their use is associated with higher risk of PORC which increases the incidence of postoperative complications. In 1979, Viby-Mogenson et al. (10) reported that 42% of their patients in PACU had PORC (TOF ratio<0.7) after using succinylcholine followed by the long-acting NMBDs (d-tubocurarine, gallamine or pancuronium). With the development of short- and mediate-acting NMBDs, the incidence rate of PORC is decreasing rapidly but is still a problem that cannot be ignored (3, 14-17). In the present study, only mediate-acting NMBDs were used and the prevalence rate of PORC in a routine PACU practice was reported.

Clinical signs (such as the grip strength, ability to perform a 5-second head lift and ability to withhold the tongue depressor between the incisor teeth) can be used to identify the presence of PORC. However, the acceleromyography and the resulting TOF ratio are more sensitive to detect PORC and are regarded as golden standard. The criteria of TOF ratio to diagnose PORC is also changing. In 1970, Ali et al.(18) reported that conscious patients with TOF ratio of less than 0.7 had impaired respiratory function. From that time, a TOF ratio of less than 0.7 was

**Table 1. Baseline and Perioperative Variables.**

| Variables | All patients (N=542) | Without PORC at PACU arrival[a] (N=376) | With PORC at PACU arrival[a] (N=166) | P value |
|---|---|---|---|---|
| Age (year) | 50.8 ± 15.9 | 49.5 ± 15.7 | 53.7 ± 16.0 | 0.005 |
| Gender (female) | 299 (55.1) | 210 (55.9) | 89 (53.6) | 0.629 |
| BMI (kg/m$^2$) | 23.6 ± 3.6 | 23.5 ± 3.6 | 24.0 ± 3.6 | 0.168 |
| ASA classification | | | | 0.031 |
| I | 107 (19.7) | 76 (20.2) | 31 (18.7) | |
| II | 416 (76.8) | 292 (77.7) | 124 (74.7) | |
| III | 19 (3.5) | 8 (2.1) | 11 (6.6) | |
| Airway control during anesthesia | | | | 0.119 |
| Endotracheal intubation | 488 (90.0) | 344 (91.5) | 144 (86.8) | |
| Laryngeal mask airway | 54 (10.0) | 32 (8.5) | 22 (13.3) | |
| Maintenance of anesthesia | | | | 0.172 |
| Total intravenous anesthesia | 46 (8.5) | 33 (8.8) | 13 (7.8) | |
| Combined intravenous-inhalational anesthesia | 352 (64.9) | 252 (67.0) | 100 (60.3) | |
| Combined epidural-general anesthesia | 144 (26.6) | 91 (24.2) | 53 (31.9) | |
| Use of NMBDs | | | | < 0.001 |
| Rocuronium | 451 (83.2) | 331 (88.0) | 120 (72.3) | |
| Atracurium | 10 (1.8) | 7 (1.9) | 3 (1.8) | |
| Both | 81 (14.9) | 38 (10.1) | 43 (25.9) | |
| Total dosage of NMBDs[b] | 3.6 ± 2.1 | 3.4 ± 1.9 | 4.0 ± 2.3 | 0.001 |
| Methods of NMBDs administration | | | | < 0.001 |
| Single bolus | 148 (27.3) | 118 (31.4) | 31 (18.7) | |
| Multiple boluses | 321 (54.7) | 225 (59.8) | 95 (57.2) | |
| Continuous infusion | 73 (13.5) | 33 (8.8) | 40 (24.1) | |
| Duration of anesthesia (hour) | 2.8 ± 1.4 | 2.9 ± 1.5 | 2.8 ± 1.4 | 0.692 |
| Duration of surgery (hour) | 2.0 ± 1.3 | 2.3 ± 1.3 | 2.2 ± 1.2 | 0.951 |
| Duration from last dose of NMBDs to extubation (hour) | 1.2 ± 0.6 | 1.3 ± 0.6 | 1.0 ± 0.6 | < 0.001 |
| Duration from last dose of NMBDs to PACU arrival (hour) | 1.4 ± 0.6 | 1.5± 0.6 | 1.2 ± 0.6 | < 0.001 |
| Administration of neostigmine at the end of surgery[c] | 504 (93.0) | 354 (94.1) | 150 (90.4) | 0.111 |
| Arriving at PACU with endotracheal tube/LMA | 19 (3.5) | 11 (2.9) | 8 (4.8) | 0.269 |
| Body temperature at PACU arrival (℃) | 36.0 ± 0.5 | 36.0 ± 0.5 | 35.8 ± 0.6 | < 0.001 |
| Hypothermia at PACU arrival[d] | 275 (50.7) | 172 (45.7) | 105 (63.3) | < 0.001 |

Variables are presented as means±standard deviation or number (percentage).
[a]Threshold of diagnosing PORC is the TOF ratio <0.9.
[b]Calculated as multiples of 95% effective dose.
[c]Neostigmine 2 mg and atropine 1 mg were administered to reverse the effect of non-depolarizing NMBDs.
[d]Body temperature <36 ℃ at PACU arrival.
PORC, postoperative residual curarization; BMI, body mass index; ASA, American Society Anesthesiologists; NMBDs, neuromuscular blocking drugs; PACU, postoperative care unit.

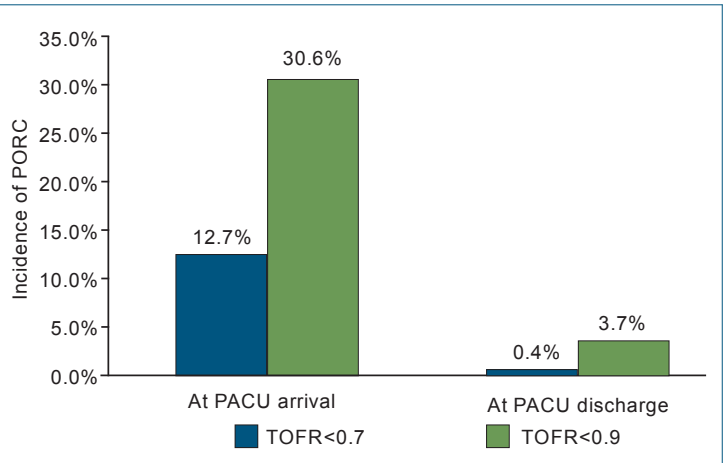


**Figure 2. Percentages of Patients with TOF Ratios Less Than 0.7 or 0.9 at Both PACU Arrival and Discharge.**
TOF, train-of-four; PACU, postoperative care unit.

**Table 2. Predictors of PORC at PACU Arrival.**

| Variables | Univariate analysis[a] | Multivariate Logistic regression analysis[b] | |
|---|---|---|---|
| | P value | OR (95%CI) | P value |
| Age (every 10 years increase) | 0.050 | 1.211 (1.068-1.374) | 0.003 |
| Preoperative ASA classification≥III | 0.031 | - | - |
| Use of laryngeal mask airway | 0.119 | - | - |
| Combined use of two different NMBDs | < 0.001 | 1.778 (1.043-3.032) | 0.035 |
| Continuous infusion of NMBDs | < 0.001 | - | - |
| Total dosage of NMBDs (every 1 ED95 increase) | 0.001 | - | - |
| Duration from last dose of NMBDs to extubation (every 1 hour increase)[c] | < 0.001 | - | - |
| Duration from last dose of NMBDs to PACU arrival (every 1 hour increase) | < 0.001 | 0.326 (0.215-0.496) | < 0.001 |
| Administration of neostigmine at the end of surgery | 0.111 | 0.341 (0.164-0.709) | 0.004 |
| Body temperature at PACU arrival (℃) | < 0.001 | - | - |
| Hypothermia at PACU arrival | < 0.001 | 1.693 (1.138-2.520) | 0.009 |

[a]Occurrence of PORC was modeled as a function of a single factor.
[b]Occurrence of PORC was modeled as a function of all factors that differed (P< 0.15) in the univariate analysis. Multivariate Logistic regression analysis was performed by using a backward (Wald) stepwise procedure. The cutoff P-values used for inclusion and deletion of a variable were 0.05 and 0.10, respectively.
[c]Variable was not included in the multivariate Logistic regression analysis.
PORC, postoperative residual curarization; PACU, postoperative care unit; ASA, American Society Anesthesiologists; NMBDs, neuromuscular blocking drugs; OR, odd ratio; CI, confidence interval.

set as the threshold of PORC. Since 1990s, studies found that a TOF ratio of less than 0.9 indicated pharyngeal dysfunction and increased risk of aspiration (6, 19-22). Therefore, a TOF ratio of less than 0.9 is suggested as a new threshold of PORC (23). In the present study, the percentages of patients with TOF ratios of less than both 0.7 and 0.9 were provided so that our results can be compared with the results of other studies. However, a TOF ratio of less than 0.9 was adopted as the threshold of PORC.

Because of the differences of diagnostic criteria and clinical situations, the reported prevalence rate of PORC varied widely (from 5% to 85%). In the study of Dabaene et al.(10), a single dose of intermediate-acting muscle relaxant (rocuronium or atracurium) was used and no reversal was administered, the prevalence rates of residual paralysis were 16% (TOF ratio<0.7) and 45% (TOF ratio<0.9) at PACU arrival, respectively. In our study, the prevalence rates of PORC were lower than the above ones, perhaps because of more prevalent use of reversal drugs. However, the prevalence rate of PORC at PACU arrival in our patients was still high and strict vigilance must be maintained against this problem.

In previous studies, the reported rate of PORC was lower when patients were discharged from PACU. In our study, the decision of PACU discharge was made by the attending anesthesiologists according to a modified Aldrete score. Our results showed that although all patients met the criteria of discharge, PORC still existed in a small number of patients (3.5%, TOF ratio<0.9 or 0.4%, TOF ratio<0.7). Therefore, use of the modified Aldrete score as the criteria of PACU discharge could not guarantee the full recovery from the effects of NMBDs. TOF monitoring should be used to assess the neuromuscular function of patients prior to discharge from PACU.

Our study identified three independent predictors associated with increased risk of PORC at PACU arrival, i.e., increasing age, combined use of two different non-depolarizing NMBDs and hypothermia. Therefore, special attention should be paid to elderly patients who are more susceptible to NMBDs. According to our results, combined use of two different non-depolarizing NMBDs is not recommended. The influence of hypothermia on the occurrence of PORC has also been reported by others (24), possibly due to the lower metabolic rate of NMBDs in hypother-

mic patients. Therefore, body temperature should be monitored and prophylactic rewarming measures should be used during the perioperative period to avoid hypothermia. And for patients with PORC in the PACU, the possible influence of hypothermia should be considered.

Our study also identified two independent predictors associated with decreased risk of PORC at PACU arrival, i.e., use of neostigmine at the end of surgery and prolonged time interval from the last dose of NMBDs to PACU arrival. These findings have been confirmed by others (10). Our results supported routine use of neostigmine at the end of surgery. In the present study, reversal of muscle relaxation was performed with neostigmine (2 mg) and atropine (1 mg) in 93% of patients. Theoretically, another dose of neostigmine/atropine could be administered in case of the occurrence of PORC in the PACU. This was not executed during the period of this study, but might be helpful in further reducing PORC at PACU discharge. According to our results, NMBDs should not be administered toward the end of surgery. Otherwise, the patient's condition should be monitored in the operating room and/or the PACU for longer durations in order to guarantee the safety. However, in consideration of the capacity of PACU and the efficiency of clinical work, it is not an optimal method to reduce the prevalence rate of POCR merely by extending patients′ length of stay in PACU.

In the present study, the length of stay in PACU was longer in patients with PORC than those without. A previous study reported that use of long-acting NMBDs was associated with prolonged PACU stay, perhaps because of the higher prevalence rate of PORC (4, 5). Despite of longer PACU stay, however, the prevalence rate of PORC at PACU discharge remained higher in patients with PORC at PACU arrival. This indicates that the clinical signs included in modified Aldrete score are not sensitive enough to detect PORC, further demonstration of the importance of TOF monitoring is needed. Again, our study found that the percentage of oropharyngeal airway use and the overall incidence of adverse events in PACU were higher in patients with PORC, which is consistent with previously reported results (25-27).

**Table 3. Outcomes and Adverse Events of Patients in the PACU.**

| | All patients (N=542) | Without PORC at PACU arrival[a] (N=376) | With PORC at PACU arrival[a] (N=166) | P value |
|---|---|---|---|---|
| Length of stay in PACU | 32 (20-48) | 30 (20-48) | 36 (22-50) | 0.041 |
| PORC at PACU discharge | 20 (3.7) | 1 (0.3) | 19 (11.4%) | < 0.001 |
| Occurrence of adverse events | | | | |
| Mild hypoxemia[b] | 17 (3.1) | 9 (2.4) | 8 (4.8) | 0.135 |
| Severe hypoxemia[c] | 16 (3.0) | 10 (2.7) | 6 (3.6) | 0.545 |
| Use of oropharyngeal airway | 17 (3.1) | 8 (2.1) | 9 (5.4) | 0.043 |
| Use of manual ventilation | 2 (0.4) | 2 (0.5) | 0 (0.0) | 0.346 |
| Reintubation | 1 (0.2) | 0 (0.0) | 1 (0.6) | 0.132 |
| Occurrence of any adverse events | 53 (9.8) | 29 (7.7) | 24 (14.5) | 0.018 |

Data are presented as median (interquartile range) or number (percentage).
[a]Threshold of diagnosing PORC is TOF ratio < 0.9.
[b]90%<$SpO_2$≤93% (with oxygen therapy).
[c]$SpO_2$≤90% (with oxygen therapy).
PACU, postoperative care unit; PORC, postoperative residual curarization.

In our patient population, the overall incidence of adverse events was 9.8%, slightly higher than the previously reported results (8). Several reasons might contribute to the phenomenon. Firstly, among all patients who underwent general anesthesia during the study period, 25.6% (309/1208) of patients were considered to be fully recovered and were sent back to the general ward directly from the operating room. As a result, only patients who were thought to be not fully recovered were sent to the PACU. It is reasonable that the incidence of adverse events in our patient population was also high. Secondly, the definitions of adverse events in different studies are not exactly the same. In the present study, mild hypoxemia was also recorded as adverse events.

In summary, PORC (TOF ratio<0.9) existed in 30.6% of our patients who were admitted to the PACU after general anesthesia. Increasing age, combined use of two different non-depolarizing NMBDs and hypothermia at PACU arrival were associated with increased risk of PORC, whereas use of neostigmine at the end of surgery and prolonged interval from last dose of NMBDs to PACU arrival were associated with decreased risk of PORC. The presence of PORC was associated with prolonged PACU stay, increased prevalence rate of PORC at PACU discharge and increased incidence of adverse events. Clinical

signs using modified Aldrete score, were not sensitive enough to detect the PORC.

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