

# Residual Neuromuscular Block in the Elderly

## Incidence and Clinical Implications

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### ABSTRACT

**Background:** Elderly patients are at increased risk for anesthesia-related complications. Postoperative residual neuromuscular block (PRNB) in the elderly, defined as a train-of-four ratio less than 0.9, may exacerbate preexisting muscle weakness and respiratory dysfunction. In this investigation, the incidence of PRNB and associated adverse events were assessed in an elderly (70 to 90 yr) and younger cohort (18 to 50 yr).

**Methods:** Data were prospectively collected on 150 younger and 150 elderly patients. Train-of-four ratios were measured on arrival to the postanesthesia care unit (PACU). After tracheal extubation, patients were examined for adverse respiratory events during transport to the PACU, for 30 min after PACU admission, and during hospital admission. Postoperative muscle weakness was quantified using a standardized examination, and PACU and hospital lengths of stay were determined.

**Results:** The incidence of PRNB was 57.7% in elderly and 30.0% in younger patients (difference, -27.7%; 99% CI, -41.2 to -13.1%;  $P < 0.001$ ). Airway obstruction, hypoxemic events, signs and symptoms of muscle weakness, postoperative pulmonary complications, and increased PACU and hospital lengths of stay were observed more frequently in the elderly (all  $P < 0.01$ ). Within each cohort, most adverse events were observed in patients with PRNB. Younger patients with PRNB received larger total doses of rocuronium than did those without it (60 vs. 50 mg,  $P < 0.01$ ), but there were no differences in rocuronium dose between elderly patients with PRNB and those without it (both 50 mg).

**Conclusion:** The elderly are at increased risk for PRNB and associated adverse outcomes. (ANESTHESIOLOGY 2015; 123:1322-36)

THE fastest growing segment of the population in the United States and European Union is the elderly.<sup>1</sup> Advances in medical care have increased life span, and a larger percentage of geriatric patients will require surgical procedures over the next several decades.<sup>1</sup> Although the safety of anesthesia has improved, the elderly are at increased risk of major morbidity and mortality.<sup>2</sup> Aging results in a gradual reduction of organ function, which limits the physiologic reserve of the cardiovascular, neurologic, respiratory, hepatic, and renal systems. This decline in organ function in the elderly may influence the pharmacokinetics and pharmacodynamics of an anesthetic agent, resulting in a prolonged effect and an increased risk of postoperative complications.

Age-appropriate dosing, monitoring, and reversal strategies are required if aminosteroid neuromuscular-blocking agents (NMBAs) are used in elderly patients, as these agents undergo a significant degree of organ-dependent elimination. A number of clinical studies have demonstrated that the time required to achieve full recovery of neuromuscular function is increased in patients older than 65 yr

### What We Already Know about This Topic

- Elderly patients are at greater risk for many postoperative complications and may have preexisting muscle weakness and respiratory dysfunction
- Whether the risk of postoperative neuromuscular residual block is greater in the elderly is not known

### What This Article Tells Us That Is New

- In a prospective study of 150 elderly and 150 younger patients, the incidence of postoperative residual neuromuscular block was high in both groups, but higher in the elderly (58% compared with 30%), associated with more frequent hypoxemia, postoperative pulmonary complications, and longer hospital length of stay in the elderly

administered with rocuronium or vecuronium.<sup>3-6</sup> A prolongation of neuromuscular recovery and reversal times in the geriatric patient may result in an increased risk for postoperative residual neuromuscular block (PRNB).<sup>3-6</sup> The presence of small degrees of muscle weakness after tracheal extubation may significantly affect recovery in this patient population,

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as the elderly have limited physiologic reserve. In particular, pharyngeal function and muscle strength may be impaired in patients older than 65 yr of age, and the residual effects of NMBAs may worsen this impairment.<sup>7</sup> At the present time, it is uncertain whether age is a risk factor for PRNB and complications related to incomplete neuromuscular recovery. In *post hoc* analyses, some previous investigations have observed an association between age and PRNB,<sup>8</sup> whereas others have not.<sup>9,10</sup>

The aim of this prospective, cohort-matched observational study was to determine the incidence of PRNB in geriatric patients (70 to 90 yr old) compared with that of a younger cohort of patients (18 to 50 yr old). In addition, both cohorts were followed after extubation to assess the effect of age on the incidence of adverse events generally attributed to PRNB. Postoperative complications occur more frequently in the elderly due to preexisting comorbidities and age-related muscle wasting.<sup>1,3</sup> Therefore, patients with PRNB (defined as a train-of-four [TOF] ratio < 0.9) in the elderly cohort and in the younger cohorts were compared with those in the same cohorts without PRNB (defined as a TOF ratio  $\geq$  0.9) to better assess the effect of residual muscle weakness on postoperative outcomes.

## Materials and Methods

### Study Population and Perioperative Management

This clinical trial was approved by the NorthShore University HealthSystem Institutional Review Board (Evanston, Illinois) and registered at ClinicalTrials.gov (NCT01545193, enrollment from June 2011 to September 2013). The study was conducted at a single tertiary medical center (NorthShore University HealthSystem) affiliated with the University of Chicago Pritzker School of Medicine, and written informed consent was obtained from all patients. Participants were recruited by reviewing operating room schedules to identify potentially eligible patients, who were then contacted by telephone on the day before surgery. Patients with American Society of Anesthesiologists (ASA) physical status I to III presenting for elective surgical procedures requiring general anesthesia with neuromuscular blockade were enrolled. Exclusion criteria were as follows: age less than 18 or more than 90 yr; use of drugs known to interfere with neuromuscular transmission; severe renal insufficiency (serum creatinine >2.0 mg/dl) or renal failure; severe hepatic dysfunction (liver function tests >50% above normal values); neurologic impairment likely to interfere with postoperative assessments; or patients found on preoperative screening examination to have symptoms or signs of muscle weakness. Obese patients were not excluded from enrollment. In addition, patients judged by the investigators to be incapable of completing an examination in the postanesthesia care unit (PACU) due to the nature of the surgical intervention (*e.g.*, prolonged procedures and highly invasive or painful operations) were excluded.

Data were prospectively collected on 300 eligible subjects. Patients were included in one of the two groups on the basis of age: a younger cohort (age 18 to 50 yr) or an elderly cohort (age 70 to 90 yr). In addition, patients within each age cohort were included in one of the two groups on the basis of the presence or absence of PRNB on admission to the PACU (TOF ratio < 0.9): a younger cohort with PRNB or one without PRNB and an elderly cohort with PRNB or one without PRNB.

Anesthetic management was standardized in both study cohorts. Monitoring consisted of a five-lead electrocardiogram, pulse oximetry, capnography, a manual blood pressure cuff, central temperature monitoring (nasopharyngeal or esophageal), and bispectral index monitoring (BIS<sup>®</sup> system; Aspect Medical Systems, USA). A peripheral nerve stimulator (qualitative monitor to allow assessment of a TOF count of 0 to 4) was used in all patients. Anesthesia was induced with propofol 1.0 to 2.0 mg/kg, lidocaine 30 to 50 mg, fentanyl 50 to 100  $\mu$ g/kg, and rocuronium 0.6 mg/kg (ideal body weight was used in obese patients). Anesthesia was maintained with sevoflurane 0.5 to 3.0%, with the concentration adjusted to maintain systemic blood pressure within 20% of baseline values. Bispectral index monitoring was used in all patients to standardize depth of anesthesia (values between 40 and 60). Hypotension was treated with phenylephrine (80  $\mu$ g), ephedrine (5 to 10 mg), or a fluid bolus, as clinically indicated. Hypertension was treated by increasing the concentration of sevoflurane. Additional doses of fentanyl, up to 2  $\mu$ g kg<sup>-1</sup> h<sup>-1</sup>, were administered at the discretion of the anesthesia care team. Hydromorphone 1 to 2 mg was given at the conclusion of surgery in procedures associated with moderate to severe pain. Antiemetic prophylaxis consisted of ondansetron 4 mg and dexamethasone 4 to 8 mg in high-risk patients. Ventilation was adjusted to achieve end-tidal carbon dioxide values of 30 and 34 mmHg. An upper extremity forced-air warming blanket was used to maintain core temperatures greater than 35°C and hand temperatures greater than 32°C.

During the procedure, rocuronium redoses (5 to 10 mg) were given to maintain a TOF count of 2 to 3. Clinicians were instructed to avoid administration of rocuronium during the last 30 min of surgery. Neuromuscular blockade was antagonized with neostigmine 50  $\mu$ g/kg and glycopyrrolate at completion of surgical wound closure, at a TOF count of at least 3. Tracheal extubation was performed when standard clinical criteria were met, which included tests of muscle strength (5-s head lift or hand grasp and adequate tidal ventilation), the ability to follow commands, and absence of fade with TOF stimulation using a peripheral nerve stimulator. Site of monitoring (adductor pollicis or eye muscles) was at the discretion of the anesthesia team. After tracheal extubation, the patient was transferred to the PACU. Use of oxygen therapy during transport to the PACU was at the discretion of the anesthesia care team.

### Perioperative Data

Immediately upon admission to the PACU, TOF ratios were quantified using acceleromyography (TOF-Watch SX<sup>®</sup>; Bluestar Enterprises, USA). After skin cleansing, two surface electrodes were positioned over the ulnar nerve at the wrist. A hand adapter (TOF-Watch Handadapter<sup>®</sup>; Bluestar Enterprises) that applied a constant preload to the thumb was secured to the hand with tape. An acceleration transducer was attached to the distal phalanx of the thumb *via* the hand adapter. The hand was positioned on the transport cart to prevent movement of fingers other than the thumb during each assessment. The evoked response of the adductor pollicis to TOF stimulation was then measured. The current intensity was 50 mA in all subjects. Two consecutive TOF measurements (separated by 15 s) were obtained, and the average of the two values was recorded. If measurements differed by more than 10%, additional TOF measurements were obtained (up to four TOF values), and the closest two ratios were averaged. All TOF measurements were obtained by investigators experienced with acceleromyography monitoring. Residual neuromuscular block was defined as a TOF ratio less than 0.9. Patients with TOF ratios between 0.9 and 0.7 were considered to have moderate block, and those with TOF ratios less than 0.7 were classified as having severe neuromuscular block.

Immediately after tracheal extubation, Sp<sub>o</sub><sub>2</sub> (saturation of peripheral oxygenation) was measured with a handheld pulse oxymeter (Rad-5; Masimo, USA). During the time between extubation and PACU admission, oxygen saturation was continuously monitored by an investigator, and oxygenation variables were recorded (Sp<sub>o</sub><sub>2</sub> postextubation, lowest observed Sp<sub>o</sub><sub>2</sub>, hypoxemic episodes [Sp<sub>o</sub><sub>2</sub> ≤94%], and Sp<sub>o</sub><sub>2</sub> at PACU arrival). During the same time, patients were continuously assessed for evidence of airway obstruction and need for treatment of airway obstruction. Peripheral oxygen saturation was recorded every minute for the first 30 min of the PACU admission (Philips IntelliVue MP70, USA); moderate hypoxemia was defined as Sp<sub>o</sub><sub>2</sub> values of 94% to 90% and severe hypoxemia as Sp<sub>o</sub><sub>2</sub> values of less than 90%. PACU nurses documented the need for additional oxygen therapy (>2 l/min), the requirement for physical or verbal stimulation to maintain Sp<sub>o</sub><sub>2</sub> greater than 93%, the lowest observed Sp<sub>o</sub><sub>2</sub> value during the admission, and any episodes of airway obstruction until the time of discharge. Aldrete scores were measured and recorded every 10 min and the times until discharge criteria were met (score ≥8 of 10) and until actual discharge achieved was noted.

Within 10 min of PACU admission, a standardized examination for 11 signs and 16 symptoms of muscle weakness was conducted by a trained research assistant.<sup>11</sup> If the level of consciousness was reduced due to the residual effects of volatile anesthetics or opioids, verbal or tactile stimulation was used to facilitate completion of the examination. Each patient was requested to perform 11 tests of muscle strength (signs). Symptoms of muscle paresis were defined as

subjective difficulty in completing each of the tests. In addition, patients were questioned about five symptoms of muscle weakness unrelated to the 11 previous tests. Subjective perception of overall weakness on a 11-point scale (0 = no weakness and 10 = most severe weakness experienced) was assessed and recorded. To quantify the severity of weakness in each of the cohorts, a total number of symptoms (0 to 16) and signs (0 to 11) score was determined for each patient. The same examination was repeated 20 min after the first one was completed.

During the hospitalization, patients were prospectively followed for any pulmonary complications, which were defined as the presence of atelectasis or pneumonia on a chest radiograph. The decision to obtain a chest radiograph was at the discretion of the surgical service. Hospital length of stay was recorded in all cohorts.

Preoperative demographic data were recorded from the electronic medical record. The electronic anesthesia record was used to determine the type of surgical procedure, perioperative temperatures, and patterns of rocuronium administration. A data collection sheet was used to record additional neuromuscular management information (TOF count at reversal and time from neostigmine administration until extubation, PACU admission, and TOF ratio measurements). Patients were prospectively followed and hospital charts reviewed to determine the incidence of pulmonary complications and hospital length of stay.

### Statistical Analysis

In previous investigations using similar protocols, nearly one third of patients under the age of 70 yr had TOF ratios less than 0.9 on admission to the PACU.<sup>12,13</sup> We hypothesized that approximately 50% of patients in the elderly group would have PRNB. For the sample size calculation, the proportion in the younger cohort was assumed to be 0.33 while that in the elderly cohort was assumed to be 0.33 under the null hypothesis and 0.50 under the alternative hypothesis. Group sample sizes of 143 in each cohort was predicted to achieve 80% power to detect a difference between the group proportions of 0.17 using a two-sided Fisher exact probability test, with the significance level of the test targeted at 0.05. Patients were enrolled in blocks of 20 subjects to reduce the potential effects of changes in practice patterns over time (*e.g.*, once 20 younger patients were enrolled, further data collection on this cohort would not occur until 20 elderly patients were enrolled).

The primary outcome variable, residual neuromuscular blockade, was summarized as the number patients in a cohort with residual neuromuscular blockade and the percent of all the patients in that cohort that they represent. These data were compared between cohorts using the Pearson chi-square test, and the 99% CIs for the differences in percentages were calculated using the Miettinen and Nurminen method (NCSS statistical software [2015], USA). Secondary outcome variables that were characterized by

nominal data (e.g., airway obstruction) are summarized as the number patients in each category and the percent of all the patients in that group that they represent. These variables were compared between groups using Pearson chi-square test or, when at least one of the cells of the contingency table had an expected N less than 5, Fisher exact test (NCSS). Variables that were characterized by ordinal data and non-normally distributed continuous data (e.g., overall weakness and total rocuronium dose) are summarized as median and interquartile range. These variables were compared between groups using the Mann–Whitney U test (StatsDirect, United Kingdom). Median differences and their 99% CIs were calculated where reported. Variables that were characterized by normally distributed continuous data are summarized as mean and SD. These variables were compared between the randomized groups using the unpaired *t* test (NCSS). Two separate analyses were performed on collected data. The elderly cohort was compared with the younger cohort, and those patients within each age cohort with PRNB were compared with those within the same age cohort without PRNB.

Given the large number of comparisons being made, the criterion for rejection of the null hypothesis was a two-tailed test with *P* value less than 0.01 to help in minimizing the chance of a type I error.

## Results

### Elderly and Young Cohorts

Patient demographic data are presented in table 1. The proportions of males and females and the weight and height of the patients in the younger cohort and the elderly cohort were similar. The two cohorts differed in ASA physical status and in most comorbidities, as might be expected given the difference in the ages of the patients in the two cohorts. Surgical procedures were similar, with the exception of more plastic surgical procedures in the younger cohort and more thoracic and urologic procedures in the elderly cohort. Perioperative data are presented in table 2. Anesthesia duration, blood loss, and crystalloid volume did not differ between groups. No differences in dosing of rocuronium (total dose, number of redoses, and dosing in the last 45 min) or reversal of rocuronium (TOF count at reversal and neostigmine administration to extubation time) were observed between the cohorts. The time from neostigmine administration until PACU arrival and TOF measurements did not differ between cohorts although lower temperatures were observed in the elderly cohort ( $36.4 \pm 0.4$  vs.  $36.6 \pm 0.5$ ,  $P = 0.002$ ). The incidence of PRNB (TOF ratio < 0.9), the primary outcome, was significantly higher in the elderly cohort (57.7%) than that in the younger cohort (30%,  $P < 0.001$ ). Severe PRNB (TOF ratio < 0.7) was observed in 16.8% of the elderly group and in 6.0% of the young group ( $P = 0.004$ ).

Adverse airway events are presented in tables 2 and 3. A higher percentage of elderly patients developed airway obstruction during transport to the PACU compared with

the younger group (18.8 vs. 7.3%,  $P = 0.003$ ). Despite a greater use of oxygen therapy in the elderly cohort, the percentage of patients with moderate hypoxemic episodes in the PACU was higher (38.3 vs. 17.3%,  $P < 0.001$ ), and median lowest  $\text{SpO}_2$  values were lower in this group.

Elderly patients had a higher median number of symptoms of muscle weakness at both PACU admission (4 [1 to 8] vs. 2 [0 to 5],  $P = 0.003$ ) and 20 min later (2 [0 to 4] vs. 0 [0 to 2],  $P < 0.001$ ) than did the younger cohort (table 4 and appendix 1). More signs of muscle weakness were also present in the elderly cohort at both assessment times ( $P = 0.002$  to 0.006).

Aldrete scores were lower in the elderly cohort from 40 to 60 min ( $P = 0.005$  to  $< 0.001$ , data not presented). Although time to meeting discharge criteria did not differ between groups, patients in the elderly group remained longer in the PACU (92 min [67 to 125 min] vs. 73 min [56 to 102 min];  $P = 0.001$ ) (table 2). Compared with the patients in the younger cohort, those in the elderly cohort had a higher incidence of pulmonary complications (15.4 vs. 2%,  $P < 0.001$ ) and a longer hospital length of stay (1.25 days [0.25 to 3 days] vs. 0.25 days [0.25 to 1.25 days];  $P < 0.001$ ) (table 2).

### Elderly and Younger Cohorts, Stratified for the Presence or Absence of PRNB

Patients with PRNB within the younger cohort and within the elderly cohort did not differ strikingly in sex, age, weight, height, ASA physical status, number of preexisting medical conditions, or type of surgical procedure from those without PRNB within the same age cohort (table 5). Perioperative data are presented in table 6. There were no differences observed in anesthesia duration, crystalloid use, blood loss, or temperature in the operating room or in the PACU between patients with and without PRNB within the younger cohort and within the elderly cohort. Patients in the younger cohort with PRNB received more rocuronium (60 mg [50 to 75 mg]) than did those in the younger cohort without PRNB (50 mg [40 to 65 mg],  $P < 0.01$ ) and those with PRNB were redosed more often in the last 45 min (28.9 vs. 5.7%,  $P < 0.001$ ) than were those without PRNB. In contrast, no differences in rocuronium dosing were observed in elderly patients with and without PRNB. The times from neostigmine administration until extubation, PACU arrival, and TOF measurements did not differ between patients with and without PRNB in each age cohort.

Airway events are presented in tables 6 and 7. The percentage of patients with hypoxemic events ( $\text{SpO}_2 \leq 94\%$ ) during transport from the operating room to PACU was significantly higher in those group with PRNB (29.1% elderly and 22.2% younger) compared with that in those group without PRNB within the same age cohort (4.8% elderly and 2.9% younger, both  $P < 0.001$ ). Airway obstruction was also observed more in patients with PRNB during transport (30.2% elderly and 22.2% younger) compared with that observed in those without PRNB in the same age cohort

**Table 1.** Patient Characteristics

	Younger Cohort	Elderly Cohort
Number	150	149
Residual neuromuscular blockade (TOF < 0.9)	45 (30.0%)	86 (57.7%)
Sex (male:female)	52 (34.7%):98 (65.3%)	65 (43.6%):84 (56.3%)
Age (yr)	38 (30 to 46)	75 (72 to 80)
Weight (kg)	73.1 (61.6 to 86.2)	74.6 (63.8 to 83.8)
Height (cm)	167.6 (162.6 to 175.3)	165.1 (160.0 to 174.0)
ASA physical status		
1	48 (32.0%)	0 (0%)
2	92 (61.3%)	80 (53.7%)
3	10 (6.7%)	69 (46.3%)
Smoking history	17 (11.3%)	8 (5.4%)
Drinking history	2 (1.3%)	6 (4.0%)
Hypertension	17 (11.3%)	106 (71.1%)
Coronary artery disease	0 (0%)	29 (19.5%)
Congestive heart failure	0 (0%)	3 (2.0%)
Arrhythmia	4 (2.7%)	19 (12.8%)
COPD	1 (0.7%)	14 (9.4%)
Asthma	15 (10.0%)	17 (11.4%)
Sleep apnea	10 (6.7%)	16 (10.7%)
Chronic renal insufficiency	0 (0%)	13 (8.7%)
Thyroid disease	17 (11.3%)	34 (22.8%)
Diabetes mellitus	5 (3.3%)	21 (14.1%)
Transient ischemic attack	0 (0%)	7 (4.7%)
Operative procedures		
General	60 (40.0%)	53 (35.6%)
Ear, nose, and throat	27 (18.0%)	13 (8.7%)
Gynecologic	28 (18.7%)	23 (15.4%)
Neurologic	0 (0%)	1 (0.7%)
Orthopedic	5 (3.3%)	7 (4.7%)
Plastic	29 (19.3%)	10 (6.7%)
Thoracic	3 (2.0%)	14 (9.4%)
Urologic	1 (0.7%)	24 (16.1%)
Vascular	1 (0.7%)	9 (6.0%)

Data are number of patients (%) or median (interquartile range).

ASA = American Society of Anesthesiologists; COPD = chronic obstructive pulmonary disease; drinking history = more than two alcoholic drinks per day; elderly cohort = age 70 to 90 yr; TOF = train-of-four; younger cohort = age 18 to 50 yr.

(3.2% elderly and 1.0% younger, both  $P < 0.001$ ). Similarly, the percentage of patients with moderate hypoxemia in the PACU was higher if PRNB was present (52.3 *vs.* 19.1% elderly, 33.3 *vs.* 10.5% younger, both  $P < 0.001$ ).

Most symptoms and signs of muscle weakness were observed in patients with PRNB (table 8 and appendix 2). The median number of symptoms was higher in patients with PRNB compared with that in those without PRNB at both PACU admission (6 [4 to 11] *vs.* 1 [0 to 3] in the younger cohort; 6 [4 to 12] *vs.* 0 [0 to 2] in the elderly cohort) and 20 min later (2 [1 to 5] *vs.* 0 [0 to 1] in the younger cohort;

3 [2 to 5] *vs.* 0 [0 to 1] in the elderly cohort, all  $P < 0.001$ ). Overall weakness on a 0 to 10 scale was significantly higher in patients with PRNB compared with that in those without PRNB at both PACU admission (5 [4 to 6] *vs.* 2 [1 to 3] in the younger cohort; 6 [5 to 8] *vs.* 1.5 [1 to 3] in the elderly cohort) and 20 min later (3 [2 to 5] *vs.* 1 [0 to 2] in the younger cohort; 4 [3 to 5] *vs.* 1 [0 to 2] in the elderly cohort, all  $P < 0.001$ ).

Aldrete scores were lower in younger patients with PRNB compared with the scores in those without PRNB at 30 through 60 min of PACU admission (all  $P < 0.01$ , data not shown). In the elderly group, Aldrete scores were lower in those with PRNB at all times except at the 30- and 60-min assessments (all  $P < 0.01$ , data not shown). Despite differences in Aldrete scores, the presence or absence of residual block did not significantly affect PACU recovery times (table 7). No differences in the incidences in pulmonary complications were observed between patients with and without PRNB in the elderly cohort (20.9 *vs.* 7.9%) or younger cohort (4.4 *vs.* 1.0%) (table 7). Hospital length of stay was longer in patients in the younger group with PRNB (1.0 day [0.25 to 1.75 days] *vs.* 0.25 day [0.25 to 1.0 day] without PRNB,  $P < 0.01$ ) but not in the elderly group with PRNB (1.5 days [0.5 to 3.25 days] *vs.* 1.0 day [0.25 to 2.0 days] without PRNB) (table 7).

## Discussion

Residual neuromuscular block is commonly observed postoperatively in patients administered NMBAs. Studies have demonstrated that approximately 40% of patients administered intermediate-acting NMBAs have TOF ratios less than 0.9 in the PACU.<sup>14</sup> Patients with incomplete neuromuscular recovery have a higher risk of airway obstruction, hypoxemic events, impaired pulmonary function, unpleasant symptoms of muscle weakness, and prolonged PACU length of stay.<sup>7,11–13,15</sup> In the present investigation, we observed that the incidence of PRNB was approximately twice as high in elderly patients (58%) as it was in younger patients (30%). Despite similar neuromuscular management, elderly patients had a higher incidence of hypoxemic events, airway obstruction, and unpleasant symptoms of muscle weakness. In addition, PACU and hospital length of stay was increased in the elderly patients as was the incidence of postoperative pulmonary complications. In both the elderly and younger cohorts, however, the majority of adverse events (hypoxemia, airway obstruction, and symptoms of muscle weakness) were observed in patients with TOF ratios less than 0.9.

Only one previous observational investigation examined the incidence of residual block in the elderly as a primary endpoint.<sup>16</sup> TOF ratios less than 0.9 were observed in 89% of the elderly patients ( $\geq 65$  yr) and in 77% of the younger patients (19 to 57 yr) (statistical significance not presented). Furthermore, 18% of the elderly patients had hypoxemic events and required ventilation support *versus* 8% of the younger patients ( $P < 0.05$ ). Neuromuscular monitoring

**Table 2.** Residual Neuromuscular Blockade and Other Perioperative Data

	Younger Cohort	Elderly Cohort	Difference (99% CI)	P Values
Residual neuromuscular blockade (TOF < 0.9)	45 (30.0%)	86 (57.7%)	-27.7% (-41.2% to -13.1%)	<0.001
TOF ratio in PACU	0.93 (0.88 to 1.00)	0.86 (0.75 to 0.95)	0.08 (0.04 to 0.12)	<0.001
0.7 < TOF ratio < 0.9	36 (24.0%)	61 (40.9%)	-16.9% (-30.4% to -3.0%)	0.003
TOF ratio < 0.7	9 (6.0%)	25 (16.8%)	-10.8% (-20.9% to -1.4%)	0.004
Anesthesia duration (min)	140.5 (109 to 195)	153 (116 to 223)	-14 (-34 to 6)	0.067
Blood loss (ml)	30 (20 to 100)	50 (25 to 180)	-5 (-20 to 0)	0.076
Crystalloid volume (ml)	1,275 (1,000 to 1,600)	1,200 (1,000 to 1,800)	0 (-200 to 150)	0.791
Temperature at end of procedure (°C)	36.1 ± 0.7	35.9 ± 0.5	0.2 (0 to 0.4)	0.005
Total rocuronium dose (mg)	50 (40 to 70)	50 (40 to 70)	0 (-5 to 10)	0.490
Number of rocuronium redoses	1 (0 to 2)	1 (0 to 3)	0 (0 to 0)	0.566
Rocuronium dose in last 45 min of procedure	19 (12.6%)	16 (10.7%)	1.9% (-8.1% to 12.0%)	0.604
TOF count at reversal	4 (4 to 4)	4 (4 to 4)	0 (0 to 0)	0.010
Time from neostigmine administration to extubation (min)	11 (8 to 17)	13 (8 to 20)	-1 (-3 to 1)	0.190
SpO <sub>2</sub> postextubation (%)	100 (99 to 100)	100 (98 to 100)	0 (0 to 0)	0.060
Oxygen use during transport	111 (74.0%)	135 (90.6%)	-16.6% (-28.0% to -5.4%)	<0.001
Lowest SpO <sub>2</sub> during transport to PACU (%)	99 (97 to 100)	98 (96 to 99)	1 (0 to 2)	<0.001
SpO <sub>2</sub> ≤ 94% during transport to PACU	13 (8.7%)	28 (18.8%)	-10.1% (-20.8% to 0.2%)	0.011
Airway obstruction during transport to PACU	11 (7.3%)	28 (18.8%)	-11.5% (-22.0% to -1.5%)	0.003
Treatment of airway obstruction during transport to PACU	10 (6.7%)	22 (14.8%)	-8.1% (-18.0% to 1.2%)	0.024
SpO <sub>2</sub> at PACU arrival (%)	99 (97 to 100)	98 (96 to 99)	1 (0 to 2)	<0.001
Temperature at PACU arrival (°C)	36.6 ± 0.5	36.4 ± 0.4	0.2 (0 to 0.3)	0.002
Time neostigmine to PACU arrival (min)	17.5 (13 to 23)	19 (14 to 25)	-1 (-3 to 1)	0.196
Time from neostigmine administration to TOF measurement (min)	19.5 (15 to 25)	21 (16 to 28)	-2 (-4 to 1)	0.068

Data are reported as number of patients (%), median (interquartile range), or mean ± SD. Data reported as number of patients (%) were compared using Pearson chi-square test or, when at least one of the cells of the contingency table had an expected number < 5, Fisher exact probability test, whereas data reported as median (interquartile range) were compared using the Mann-Whitney U test and data reported as mean ± SD were compared by the unpaired *t* test. Number = 150 in the younger cohort and 149 in the elderly cohort.

Elderly cohort = age 70 to 90 yr; PACU = postanesthesia care unit; SpO<sub>2</sub> = arterial oxygen saturation measured by pulse oximetry; TOF = train-of-four; younger cohort = age 18 to 50 yr.

**Table 3.** PACU and Hospitalization Variables

	Younger Cohort	Elderly Cohort	Difference (99% CI)	P Values
Number with episodes of SpO <sub>2</sub> 90–94% in PACU	26 (17.3%)	57 (38.3%)	-20.9% (-33.7% to -7.7%)	<0.001
No. of SpO <sub>2</sub> 90–94% episodes in PACU	0 (0 to 0)	0 (0 to 3)	0 (0 to 0)	<0.001
Number with episodes of SpO <sub>2</sub> < 90% in PACU	2 (1.3%)	3 (2.0%)	-0.7% (-6.4 to 4.7%)	0.068
No. of SpO <sub>2</sub> < 90% episodes in PACU	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.634
Number requiring additional oxygen therapy in PACU	35 (23.3%)	61 (40.9%)	-17.6% (-31.0 to -3.7%)	0.001
Number requiring stimulation to maintain SpO <sub>2</sub> > 93% in PACU	9 (6.0%)	31 (20.8%)	-14.8% (-25.4 to -4.9%)	<0.001
Lowest SpO <sub>2</sub> in PACU (%)	96 (95 to 98)	95 (93 to 97)	2 (1 to 2)	<0.001
Airway obstruction	3 (2.0%)	3 (2.0%)	0% (-5.9 to 5.8%)	>0.999
Treat airway obstruction	0 (0%)	3 (2.0%)	-2.0% (-7.6 to 2.3%)	0.123
Time until PACU discharge criteria met (min)	55.5 (42 to 81)	61 (50 to 84)	-5 (-13 to 2)	0.083
Time until PACU discharge (min)	73 (56 to 102)	92 (67 to 125)	-14 (-26 to -3)	0.001
Any pulmonary complication during hospitalization	3 (2.0%)	23 (15.4%)	-13.4% (-22.8 to -5.7%)	<0.001
Hospital length of stay (days)	0.25 (0.25 to 1.25)	1.25 (0.25 to 3)	-0.75 (-1 to -0.25)	<0.001

Data reported as number of patients (%) were compared using Pearson chi-square test or, when at least one of the cells of the contingency table had an expected number < 5, Fisher exact probability test, and data reported as median (interquartile range) were compared using the Mann-Whitney U test. N = 150 in the younger cohort and 149 in the elderly cohort.

Elderly cohort = age 70 to 90 yr; PACU = postanesthesia care unit; SpO<sub>2</sub> = arterial oxygen saturation measured by pulse oximetry; younger cohort = age 18–50 yr.

**Table 4.** Muscle Strength Assessment, Symptoms, and Signs at PACU Admission and 20 Min Thereafter

	Younger Cohort	Elderly Cohort	Difference (99% CI)	P Values
General weakness				
PACU admission	87 (58%)	107 (72%)*	-14% (-28 to 0%)	0.010
20 min later	54 (36%)	89 (60%)	-24% (-38 to -9%)	<0.001
Overall weakness				
PACU admission	3 (1 to 5)	4 (2 to 7)*	-1 (-2 to 0)	<0.001
20 min later	1 (0 to 3)	3 (1 to 5)	-1 (-2 to -1)	<0.001
Number of symptoms score				
PACU admission	2 (0 to 5)	4 (1 to 8)	-1 (-3 to 0)	0.003
20 min later	0 (0 to 2)	2 (0 to 4)	-1 (-1 to 0)	<0.001
Number of signs score				
PACU admission	0 (0 to 0)	0 (0 to 2)	0 (0 to 0)	0.002
20 min later	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.006

Data are number of patients (%) or median (interquartile range). Data reported as number of patients (%) were compared using Pearson chi-square test or, when at least one of the cells of the contingency table had an expected number < 5, Fisher exact probability test, and data reported as median (interquartile range) were compared using the Mann-Whitney U test. N = 150 in the younger cohort and 149 in the elderly cohort, except where indicated. Overall weakness graded on an 11-point scale (0 = no weakness and 10 = most severe weakness experienced).

\* N = 148.

Elderly cohort = age 70 to 90 yr; PACU = postanesthesia care unit; younger cohort = age 18 to 50 yr.

and anticholinesterase reversal were not used in any patient, which likely accounted for the high incidence of incomplete neuromuscular recovery. Only a few clinical investigations have examined the association between age and residual neuromuscular block in *post hoc* analyses. In a recent study designed to examine the perioperative variables associated with PRNB, multivariate regression analysis did not identify age as a risk factor for PRNB.<sup>9</sup> In contrast, a similar, but larger, study (n = 134) reported that the only factors associated with TOF recovery were age and time elapsed from the last administration of rocuronium.<sup>8</sup>

Residual neuromuscular block in the elderly may be attributable to the physiologic changes of aging that alter the pharmacokinetics of NMBAs. Age-related reductions in cardiac output, renal and hepatic function, muscle mass, and ability to regulate temperature are present in most patients 70 yr old or older.<sup>3</sup> Several studies have examined the pharmacokinetic properties of rocuronium in the geriatric surgical patient. Duration of action and spontaneous recovery times were significantly longer in patients older than 70 yr compared with that in a younger patient population.<sup>4,5</sup> Furthermore, in the elderly, duration of neuromuscular block after each maintenance dose of rocuronium was prolonged and increased gradually with time.<sup>6</sup> More variability in recovery times has also been documented in elderly patients administered rocuronium compared with younger subjects.<sup>17,18</sup> These data suggest that dosing and reversal practices involving steroidal NMBAs should be modified in patients older than 70 yr.<sup>4-6,17,18</sup> In the present investigation, however, neuromuscular management did not differ between the young and elderly; total rocuronium dose, number of redoses, dosing during the last 45 min of the procedure, TOF count at reversal, and time between reversal and extubation were all similar between groups. These findings suggest that clinicians may be unaware of the need to alter management of neuromuscular block on the basis of age.

A higher incidence of adverse respiratory events was observed in the elderly cohort. These findings are not unexpected. Decreases in vital capacity, maximum voluntary ventilation, and total lung capacity occur in geriatric patients, while functional residual capacity and closing volume increase.<sup>3</sup> Pharyngeal dysfunction is often present in geriatric patients, increasing the risk of airway obstruction and aspiration in the setting of minimal neuromuscular block.<sup>7</sup> In an investigation of awake volunteers older than 65 yr, pharyngeal dysfunction was observed in 37% of swallows.<sup>7</sup> Misdirected swallowing and tracheal aspiration may account, in part, for the higher incidence of critical respiratory events and postoperative pulmonary complications, which have been reported in elderly.<sup>19,20</sup> Furthermore, geriatric patients may undergo surgical procedures with a higher risk of pulmonary complications (more patients in the elderly cohort underwent thoracic and urologic procedures). In the current study, hypoxemic events and airway obstruction occurred more frequently in the elderly group after tracheal extubation. The need for additional oxygen therapy, as well as for stimulation to maintain oxygenation, was also higher in this cohort. Furthermore, postoperative pulmonary complications occurred in 15% of the elderly patients but in only 2% of younger patients ( $P < 0.001$ ).

In addition to age, PRNB is an important risk factor for adverse respiratory events. Pharyngeal dysfunction, upper airway obstruction, reduced upper esophageal sphincter tone, and an increased risk of aspiration have been documented in awake volunteers with TOF ratios less than 0.9.<sup>7,21,22</sup> Clinical investigations have found an association between PRNB and postoperative airway obstruction,<sup>23</sup> hypoxemic events,<sup>16,23,24</sup> respiratory muscle weakness,<sup>25</sup> acute respiratory events,<sup>23,26</sup> and pulmonary complications.<sup>27</sup> As both age and PRNB are important risk factors for adverse respiratory events,<sup>28,29</sup> patients in each age cohort were further stratified into those

**Table 5.** Patient Characteristics

	Younger Cohort, No Residual Neuromuscular Blockade	Younger Cohort, Residual Neuromuscular Blockade	Elderly Cohort, No Residual Neuromuscular Blockade	Elderly Cohort, Residual Neuromuscular Blockade
Number	105	45	63	86
Sex (male:female)	41 (39.0%): 64 (61.0%)	11 (24.4%): 34 (75.6%)	26 (41.3%): 37 (58.7%)	39 (45.3%): 47 (54.7%)
Age (yr)	36.5 ± 10.0	37.5 ± 8.3	76.6 ± 4.6	75.9 ± 4.8
Weight (kg)	75.3 ± 19.2	84.5 ± 31.0	72.4 ± 17.6	76.1 ± 14.1
Height (cm)	168.9 ± 11.6	166.8 ± 7.7	167.6 ± 9.7	166.8 ± 9.7
ASA physical status				
1	40 (38.1%)	8 (17.8%)	0 (0%)	0 (0%)
2	62 (59.0%)	30 (66.7%)	34 (54.0%)	46 (53.5%)
3	3 (2.9%)	7 (15.6%)	29 (46.0%)	40 (46.5%)
Smoking history	12 (11.4%)	5 (11.1%)	2 (3.2%)	6 (7.0%)
Drinking history	2 (1.9%)	0 (0%)	3 (4.8%)	3 (3.5%)
Hypertension	7 (6.7%)	10 (22.2%)	43 (68.3%)	63 (73.3%)
Coronary artery disease	0 (0%)	0 (0%)	13 (20.6%)	16 (18.6%)
Congestive heart failure	0 (0%)	0 (0%)	2 (3.2%)	1 (1.2%)
Arrhythmia	1 (1.0%)	3 (6.7%)	7 (11.1%)	12 (14.0%)
COPD	1 (1.0%)	0 (0%)	5 (7.9%)	9 (10.5%)
Asthma	10 (9.5%)	5 (11.1%)	9 (14.3%)	8 (9.3%)
Sleep apnea	4 (3.8%)	6 (13.3%)	6 (9.5%)	10 (11.6%)
Chronic renal insufficiency	0 (0%)	0 (0%)	5 (7.9%)	8 (9.3%)
Thyroid disease	13 (12.4%)	4 (8.9%)	17 (27.0%)	17 (19.8%)
Diabetes mellitus	2 (1.9%)	3 (6.7%)	5 (7.9%)	16 (18.6%)
Transient ischemic attack	0 (0%)	0 (0%)	5 (7.9%)	2 (2.3%)
Operative procedures				
General	37 (35.2%)	23 (51.1%)	25 (39.7%)	28 (32.6%)
Ear, nose, and throat	22 (21.0%)	5 (11.1%)	9 (14.3%)	4 (4.7%)
Gynecologic	19 (18.1%)	9 (20.0%)	9 (14.3%)	14 (16.3%)
Neurologic	0 (0%)	0 (0%)	0 (0%)	1 (1.2%)
Orthopedic	5 (4.8%)	0 (0%)	2 (3.2%)	5 (5.8%)
Plastic	23 (21.9%)	6 (13.3%)	6 (9.5%)	4 (4.7%)
Thoracic	1 (1.0%)	2 (4.4%)	5 (7.9%)	9 (10.5%)
Urologic	0 (0%)	1 (2.2%)	5 (7.9%)	19 (22.1%)
Vascular	1 (1.0%)	0 (0%)	4 (6.3%)	5 (5.8%)

Data are mean ± SD, median (range), or number of patients (%).

ASA = American Society of Anesthesiologists; COPD = chronic obstructive pulmonary disease; drinking history = more than two alcoholic drinks per day; elderly cohort = age 70 to 90 yr; younger cohort = age 18 to 50 yr.

with (TOF < 0.9) and without (TOF ≥ 0.9) PRNB. During transport to the PACU, hypoxemia and upper airway obstruction occurred frequently in patients with PRNB (22 to 30%) in contrast to those without PRNB (1 to 5%) (in both age cohorts). Similarly, during the PACU admission, moderate hypoxemia was observed in a high percentage of patients with PRNB (33 to 52%) compared with patients with more complete neuromuscular recovery (11 to 19%) (in both age cohorts). Although a higher incidence of pulmonary complications was observed in elderly patients with PRNB (21 vs. 8% without PRNB), this difference was not statistically significant.

Signs and symptoms of muscle weakness in the PACU were observed more frequently in the elderly group compared with these in the younger group. Fewer patients in the elderly cohort were able to perform a 5-s head lift, smile, or breathe deeply. Specific symptoms of muscle weakness,

such as difficulty smiling or swallowing, blurry vision, and general weakness, were also observed more frequently in this group. Postoperative muscle weakness is not unexpected in the elderly. Muscle performance in the postoperative period can be affected by age-related muscle wasting.<sup>30</sup> The inflammatory response to surgery can further impair muscle performance and produce symptoms of weakness.<sup>30</sup> Another potential cause of postoperative muscle weakness is PRNB.<sup>11</sup> Awake subjects with TOF ratios less than 0.9 have described a variety of unpleasant symptoms of weakness that can persist for hours after full neuromuscular recovery.<sup>31</sup> An association between PRNB, symptoms of muscle weakness, and poorer patient-perceived quality of recovery has also been reported in surgical patients.<sup>11</sup> We observed that most symptoms and signs of muscle weakness were present in patients with objective measures of residual neuromuscular block. Overall weakness scores, measured on a 0 to 10 scale, were



**Table 6.** Perioperative Data

	Younger Cohort, No Residual Neuromuscular Blockade	Younger Cohort, Residual Neuromuscular Blockade	Elderly Cohort, No Residual Neuromuscular Blockade	Elderly Cohort, Residual Neuromuscular Blockade
Number	105	45	63	86
TOF ratio in PACU	0.97 (0.93 to 1.02)	0.82 (0.74 to 0.87)*	0.97 (0.93–1.00)	0.765 (0.65 to 0.84)*
Anesthesia duration (min)	133 (98 to 190)	160 (132 to 213)	146 (103 to 199)	163 (119 to 240)
Blood loss (ml)	25 (20 to 100)	50 (25 to 125)	30 (20 to 150)	50 (25 to 200)
Crystalloid volume (ml)	1,200 (1,000 to 1,700)	1,300 (1,000 to 1,600)	1,200 (900 to 1,500)	1,400 (1,000 to 2,000)
Temperature at end of procedure (°C)	36.1±0.7	36.1±0.8	35.9±0.6	35.9±0.5
Total rocuronium dose (mg)	50 (40 to 65)	60 (50 to 75)†	50 (30 to 60)	50 (40 to 70)
Number of rocuronium redoses	1 (0 to 2)	2 (1 to 3)	1 (0 to 2)	2 (0 to 3)
Rocuronium dose in last 45 min of procedure	6 (5.7%)	13 (28.9%)*	6 (9.5%)	10 (11.6%)
TOF count at reversal	4 (4 to 4)	4 (4 to 4)	4 (4 to 4)	4 (4 to 4)
Time neostigmine to extubation (min)	11 (8 to 17)	12 (7 to 19)	13 (8 to 19)	13 (7 to 20)
SpO <sub>2</sub> postextubation (%)	100 (99 to 100)	100 (99 to 100)	99 (98 to 100)	100 (98 to 100)
Oxygen use during transport	73 (69.5%)	38 (84.4%)	56 (88.9%)	79 (91.9%)
Lowest SpO <sub>2</sub> during transport to PACU (%)	99 (98 to 100)	99 (96 to 100)	98 (97 to 100)	97 (94 to 99)†
SpO <sub>2</sub> ≤ 94% during transport to PACU	3 (2.9%)	10 (22.2%)*	3 (4.8%)	25 (29.1%)*
Airway obstruction during transport to PACU	1 (1.0%)	10 (22.2%)*	2 (3.2%)	26 (30.2%)*
Treatment of airway obstruction during transport to PACU	1 (1.0%)	9 (20.0%)*	0 (0%)	22 (25.6%)*
SpO <sub>2</sub> at PACU arrival (%)	99 (97 to 100)	100 (98 to 100)	98 (96 to 100)	97 (96 to 99)
Temperature at PACU arrival (°C)	36.6±0.4	36.6±0.7	36.5±0.3	36.4±0.4
Time neostigmine to PACU arrival (min)	17 (13 to 21)	18 (15 to 25)	19 (13 to 26)	19.5 (14 to 24)
Time neostigmine to TOF measurement (min)	19 (15 to 23)	22 (17 to 27)	20 (16 to 29)	22 (16 to 27)

Data are number of patients (%), median (interquartile range), or mean ± SD. Data reported as number of patients (%) were compared using Pearson chi-square test or, when at least one of the cells of the contingency table had an expected number < 5, Fisher exact probability test while data reported as median (interquartile range) were compared using the Mann–Whitney U test, and data reported as mean ± SD were compared by the unpaired *t* test.

\* *P* < 0.001 vs. patients in the same age group with no residual neuromuscular blockade. † *P* < 0.01 vs. patients in the same age group with no residual neuromuscular blockade.

Elderly cohort = age 70 to 90 yr; PACU = postanesthesia care unit; SpO<sub>2</sub> = arterial oxygen saturation measured by pulse oximetry; TOF = train-of-four; younger cohort = age 18 to 50 yr.

approximately three to four times greater in patients with TOF ratios less than 0.9 compared with the scores in those with TOF ratios 0.9 or greater. Similarly, more symptoms of muscle weakness were present in patients with PRNB (median 2 to 6) compared with patients without PRNB (median 0 to 1). Although signs of muscle weakness were more common in patients with PRNB, the median total number of signs was low in all patient cohorts (0 to 1). As noted in previous investigations, standard tests of muscle strength used by anesthesiologists (head lift and hand grasp) are insensitive in detecting PRNB.<sup>32</sup>

A large observational study reported that the only independent predictors of PACU length of stay were age and the presence of PRNB (TOF ratios < 0.9).<sup>33</sup> In the current study, time until PACU discharge was longer in the elderly cohort compared with the younger cohort. In contrast, the presence of PRNB did not significantly alter PACU length of stay in these patients. Aged patients are also at increased risk for prolonged hospital length of stay due to the presence of preexisting comorbidities and the need for increasingly

complex surgical procedures.<sup>1,2</sup> The length of the hospital admission was longer in geriatric surgical patients than that in younger patients; however, the presence or absence of PRNB did not affect the total length of time in the hospital in the elderly cohort (1.5 days with PRNB *vs.* 1 day without PRNB). Larger studies are needed to determine whether PRNB affects these important economic outcome measures.

There are limitations to the present investigation. First, an observational study design can only find associations, not causality. It is possible that unmeasured variables in the PRNB cohorts influenced the findings. Second, calibration of the TOF-Watch SX<sup>®</sup> (Bluestar Enterprises) was not performed, and TOF ratio values were not normalized. When acceleromyography is used as described, TOF ratios should recover to 1.0 to more reliably exclude residual paralysis.<sup>34,35</sup> Third, the intraoperative neuromuscular monitoring site (eye muscles or adductor pollicis) may influence the risk of PRNB<sup>36</sup>; these data were not recorded in the investigation. Fourth, our observations may not apply to centers where sugammadex is freely available. Rapid reversal (2.9 min) of

**Table 7.** PACU and Hospitalization Variables

	Younger Cohort, No Residual Neuromuscular Blockade	Younger Cohort, Residual Neuromuscular Blockade	Elderly Cohort, No Residual Neuromuscular Blockade	Elderly Cohort, Residual Neuromuscular Blockade
Number	105	45	63	86
No. with episodes of SpO <sub>2</sub> 90–94% in PACU	11 (10.5%)	15 (33.3%)*	12 (19.1%)	45 (52.3%)*
Number of SpO <sub>2</sub> 90–94% episodes in PACU	0 (0 to 0)	0 (0 to 2)†	0 (0 to 0)	1 (0 to 4)*
No. with episodes of SpO <sub>2</sub> < 90% in PACU	0 (0%)	2 (4.4%)	1 (1.6%)	2 (2.3%)
Number of SpO <sub>2</sub> < 90% episodes in PACU	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
No. requiring additional oxygen therapy in PACU	22 (21.0%)	13 (28.9%)	21 (33.3%)	40 (46.5%)
No. requiring stimulation to maintain SpO <sub>2</sub> > 93% in PACU	5 (4.8 %)	4 (8.9%)	10 (15.9%)	21 (24.4%)
Lowest SpO <sub>2</sub> in PACU (%)	97 (95 to 98)	96 (93 to 99)	96 (94 to 97)	94 (92 to 97)
Airway obstruction	1 (1.0%)	2 (4.4%)	0 (0%)	3 (3.5%)
Treat airway obstruction	0 (0%)	0 (0%)	0 (0%)	3 (3.5%)
Time until PACU discharge criteria met (min)	54 (42 to 73)	59 (46 to 84)	58 (50 to 71)	64 (48 to 91)
Time until PACU discharge (min)	69 (51 to 96)	83 (63 to 105)	77 (60 to 110)	96 (71 to 139)
Any pulmonary complication during hospitalization	1 (1.0%)	2 (4.4%)	5 (7.9%)	18 (20.9%)
Hospital length of stay (days)	0.25 (0.25 to 1.0)	1.0 (0.25 to 1.75)†	1.0 (0.25 to 2.0)	1.5 (0.5 to 3.25)

Data are reported as number of patients (%) or as median (interquartile range). Data reported as number of patients (%) were compared using Pearson chi-square test or, when at least one of the cells of the contingency table had an expected number < 5, Fisher exact probability test, and data reported as median (interquartile range) were compared using the Mann–Whitney U test.

\* *P* < 0.001 vs. patients in the same age group with no residual neuromuscular blockade. † *P* < 0.01 vs. patients in the same age group with no residual neuromuscular blockade.

Elderly cohort = age 70 to 90 yr; PACU = postanesthesia care unit; SpO<sub>2</sub> = arterial oxygen saturation measured by pulse oximetry; younger cohort = age 18 to 50 yr.

**Table 8.** Muscle Strength Assessment, Symptoms, and Signs at PACU Admission and 20 Min Thereafter

	Younger Cohort, No Residual Neuromuscular Blockade	Younger Cohort, Residual Neuromuscular Blockade	Elderly Cohort, No Residual Neuromuscular Blockade	Elderly Cohort, Residual Neuromuscular Blockade
Number	105	45	63	86
General weakness				
PACU admission	46 (44%)	41 (91%)*	24 (38%)†	83 (97%)*
20 min later	20 (19%)	34 (76%)*	12 (19%)	77 (90%)*
Overall weakness				
PACU admission	2 (1 to 3)	5 (4 to 6)*	1.5 (1 to 3)†	6 (5 to 8)*
20 min later	1 (0 to 2)	3 (2 to 5)*	1 (0 to 2)	4 (3 to 5)*
Number of symptoms score				
PACU admission	1 (0 to 3)	6 (4 to 11)*	0 (0 to 2)	6 (4 to 12)*
20 min later	0 (0 to 1)	2 (1 to 5)*	0 (0 to 1)	3 (2 to 5)*
Number of signs score				
PACU admission	0 (0 to 0)	1 (0 to 2)*	0 (0 to 0)	1 (0 to 3)*
20 min later	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)‡

Data are number of patients (%) or median (interquartile range). Data reported as number of patients (%) were compared using Pearson chi-square test or, when at least one of the cells of the contingency table had an expected number < 5, Fisher exact probability test, and data reported as median (interquartile range) were compared using the Mann–Whitney U test. Overall weakness graded on an 11-point scale (0 = no weakness, 10 = most severe weakness experienced).

\* *P* < 0.001 vs. patients in the same age group with no residual neuromuscular blockade. † Number = 62. ‡ *P* < 0.01 vs. patients in the same age group with no residual neuromuscular blockade.

Elderly cohort = age 70 to 90 yr; PACU = postanesthesia care unit; younger cohort = age 18 to 50 yr.

a moderate neuromuscular block is possible in the elderly when sugammadex is administered.<sup>37</sup>

In conclusion, the incidence of PRNB was significantly higher in patients aged 70 to 90 yr than it was in patients aged 18 to 50 yr. Elderly patients had a higher incidence of hypoxemic events, airway obstruction, and unpleasant symptoms of muscle weakness. Further analysis revealed that

the majority of these adverse events occurred in patients with PRNB. Careful dosing (fewer redoses), monitoring (routine qualitative), and reversal (early administration at a TOF count of 3 to 4) of neuromuscular blockade can reduce, but not eliminate, the risk of PRNB. The use of quantitative monitoring or sugammadex is required to ensure full recovery of neuromuscular function in the elderly surgical patient.

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## Competing Interests

Dr. Murphy has served on the advisory board and as a speaker for Merck (Kenilworth, New Jersey). The other authors declare no competing interests.

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**Appendix 1.** Muscle Strength Assessment at PACU Admission and 20 Min Thereafter

	Age 18 to 50 Yr	Age 70 to 90 Yr	Difference (99% CI)	P Values
<b>Five-second head lift</b>				
PACU admission				
Sign	15 (10%)	36 (24%)	-14% (-26 to -3%)	0.001
Symptom	30 (20%)	70 (47%)	-27% (-40 to -13%)	<0.001
20 min later				
Sign	5 (3%)	16 (11%)	-7% (-16 to 0%)	0.012
Symptom	19 (13%)	41 (28%)	-15% (-27 to -3%)	0.001
<b>Five-second hand grip</b>				
PACU admission				
Sign	3 (2%)	10 (7%)	-5% (-12 to 2%)	0.046
Symptom	16 (11%)	41 (28%)	-17% (-29 to -5%)	<0.001
20 min later				
Sign	0 (0%)	1 (1%)	-1% (-5 to 4%)	0.498
Symptom	6 (4%)	17 (11%)	-7% (-16 to 1%)	0.016
<b>Five-second eye opening</b>				
PACU admission				
Sign	10 (7%)	13 (9%)	-2% (-11 to 6%)	0.504
Symptom	47 (31%)	55 (37%)	-6% (-20 to 9%)	0.309
20 min later				
Sign	2 (1%)	4 (3%)	-1% (-7 to 4%)	0.448
Symptom	10 (7%)	16 (11%)	-4% (-13 to 5%)	0.212
<b>Five-second protrude tongue</b>				
PACU admission				
Sign	7 (5%)	14 (9%)	-5% (-13 to 3%)	0.110
Symptom	24 (16%)	36 (24%)	-8% (-20 to 4%)	0.078
20 min later				
Sign	0 (0%)	3 (2%)	-2% (-8 to 2%)	0.123
Symptom	7 (5%)	13 (9%)	-4% (-13 to 4%)	0.160
<b>Tongue depressor test</b>				
PACU admission				
Sign	7 (5%)	13 (9%)	-4% (-13 to 4%)	0.160
Symptom	23 (15%)	37 (25%)	-10% (-22 to 2%)	0.040
20 min later				
Sign	0 (0%)	3 (2%)	-2% (-8 to 2%)	0.123
Symptom	7 (5%)	12 (8%)	-3% (-12 to 4%)	0.213
<b>Ability to smile</b>				
PACU admission				
Sign	5 (3%)	12 (8%)	-5% (-13 to 3%)	0.078
Symptom	29 (19%)	46 (31%)	-12% (-24 to 1%)	0.021
20 min later				
Sign	0 (0%)	7 (5%)	-5% (-11 to 0%)	0.007
Symptom	9 (6%)	19 (13%)	-7% (-16 to 2%)	0.045

(Continued)

## Appendix 1. (Continued)

	Age 18 to 50 Yr	Age 70 to 90 Yr	Difference (99% CI)	P Values
Ability to swallow				
PACU admission				
Sign	6 (4%)	14 (9%)	-5% (-14 to 2%)	0.062
Symptom	35 (23%)	43 (29%)	-6% (-19 to 8%)	0.277
20 min later				
Sign	0 (0%)	4 (3%)	-3% (-9 to 2%)	0.060
Symptom	7 (5%)	21 (14%)	-9% (-19 to 1%)	0.005
Ability to speak				
PACU admission				
Sign	7 (5%)	14 (9%)	-5% (-13 to 3%)	0.110
Symptom	42 (28%)	53 (36%)	-8% (-21 to 6%)	0.160
20 min later				
Sign	2 (1%)	4 (3%)	-1% (-7 to 4%)	0.448
Symptom	13 (9%)	28 (19%)	-10% (-21 to 0%)	0.011
Ability to cough				
PACU admission				
Sign	9 (6%)	19 (13%)	-7% (-16 to 2%)	0.045
Symptom	42 (28%)	45 (30%)	-2% (-16 to 11%)	0.675
20 min later				
Sign	3 (2%)	3 (2%)	0% (-6 to 6%)	>0.999
Symptom	14 (9%)	27 (18%)	-9% (-19 to 2%)	0.027
Track object with eyes				
PACU admission				
Sign	22 (15%)	32 (21%)	-7% (-18 to 5%)	0.126
Symptom	50 (33%)	64 (43%)	-10% (-24 to 5%)	0.087
20 min later				
Sign	3 (2%)	13 (9%)	-7% (-15 to 0%)	0.010
Symptom	19 (13%)	35 (23%)	-11% (-22 to 1%)	0.015
Ability to breathe deeply				
PACU admission				
Sign	3 (2%)	14 (9%)	-7% (-16 to -1%)	0.006
Symptom	24 (16%)	42 (28%)	-12% (-24 to 0%)	0.011
20 min later				
Sign	0 (0%)	3 (2%)	-2% (-8 to 2%)	0.123
Symptom	10 (7%)	24 (16%)	-9% (-20 to 0%)	0.010
Blurry vision				
PACU admission	26 (17%)	44 (30%)*	-12% (-25 to 0%)	0.012
20 min later	18 (12%)	37 (25%)	-13% (-24 to -1%)	0.004
Double vision				
PACU admission	16 (11%)	27 (18%)*	-8% (-18 to 3%)	0.063
20 min later	9 (6%)	15 (10%)	-4% (-13 to 4%)	0.196
Facial weakness				
PACU admission	39 (26%)	59 (40%)*	-14% (-27 to 0%)	0.011
20 min later	16 (11%)	27 (18%)	-7% (-18 to 3%)	0.066
Facial numbness				
PACU admission	10 (7%)	22 (15%)*	-8% (-18 to 1%)	0.022
20 min later	4 (3%)	7 (5%)	-2% (-9 to 4%)	0.351

Data are number of patients (%). Data were compared using Pearson chi-square test or, when at least one of the cells of the contingency table had an expected  $N < 5$ , Fisher exact probability test.  $N = 150$  in the age 18- to 50-yr group and 149 in the age 70- to 90-yr group, except where indicated.

\*  $N = 148$ .

PACU = postanesthesia care unit.

**Appendix 2.** Muscle Strength Assessment at PACU Admission and 20 Min Thereafter

	Age 18 to 50 Yr, No Residual Neuromuscular Blockade	Age 18 to 50 Yr, Residual Neuromuscular Blockade	Age 70 to 90 Yr, No Residual Neuromuscular Blockade	Age 70 to 90 Yr, Residual Neuromuscular Blockade
N	105	45	63	86
Five-second head lift				
PACU admission				
Sign	0 (0%)	15 (33%)*	4 (6%)	32 (37%)*
Symptom	4 (4%)	26 (58%)*	9 (14%)	61 (71%)*
20 min later				
Sign	1 (1%)	4 (9%)	2 (3%)	14 (16%)
Symptom	1 (1%)	18 (40%)*	3 (5%)	38 (44%)*
Five-second hand grip				
PACU admission				
Sign	0 (0%)	3 (7%)	0 (0%)	10 (12%)†
Symptom	2 (2%)	14 (31%)*	3 (5%)	38 (44%)*
20 min later				
Sign	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Symptom	1 (1%)	5 (11%)†	0 (0%)	17 (20%)*
Five-second eye opening				
PACU admission				
Sign	3 (3%)	7 (16%)†	1 (2%)	12 (14%)†
Symptom	19 (18%)	28 (62%)*	8 (13%)	47 (55%)*
20 min later				
Sign	1 (1%)	1 (2%)	1 (2%)	3 (3%)
Symptom	3 (3%)	7 (16%)†	1 (2%)	15 (17%)†
Five-second protrude tongue				
PACU admission				
Sign	2 (2%)	5 (11%)	1 (2%)	13 (15%)†
Symptom	7 (7%)	17 (38%)*	4 (6%)	32 (37%)*
20 min later				
Sign	0 (0%)	0 (0%)	1 (2%)	2 (2%)
Symptom	1 (1%)	6 (13%)†	2 (3%)	11 (13%)
Tongue depressor test				
PACU admission				
Sign	2 (2%)	5 (11%)	0 (0%)	13 (15%)†
Symptom	7 (7%)	16 (36%)*	2 (3%)	35 (40%)*
20 min later				
Sign	0 (0%)	0 (0%)	1 (2%)	2 (2%)
Symptom	1 (1%)	6 (13%)†	0 (0%)	12 (14%)†
Ability to smile				
PACU admission				
Sign	0 (0%)	5 (11%)†	1 (2%)	11 (13%)
Symptom	12 (11%)	17 (38%)*	8 (13%)	38 (44%)*
20 min later				
Sign	0 (0%)	0 (0%)	2 (3%)	5 (6%)
Symptom	3 (3%)	6 (13%)	3 (5%)	16 (19%)
Ability to swallow				
PACU admission				
Sign	1 (1%)	5 (11%)†	3 (5%)	11 (13%)
Symptom	18 (17%)	17 (38%)†	7 (11%)	36 (42%)*
20 min later				
Sign	0 (0%)	0 (0%)	1 (2%)	3 (3%)
Symptom	3 (3%)	4 (9%)	2 (3%)	19 (22%)*

(Continued)

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## Appendix 2. (Continued)

	Age 18 to 50 Yr, No Residual Neuromuscular Blockade	Age 18 to 50 Yr, Residual Neuromuscular Blockade	Age 70 to 90 Yr, No Residual Neuromuscular Blockade	Age 70 to 90 Yr, Residual Neuromuscular Blockade
<b>Ability to speak</b>				
PACU admission				
Sign	1 (1%)	6 (13%)†	2 (3%)	12 (14%)
Symptom	20 (19%)	22 (49%)*	12 (19%)	41 (48%)*
20 min later				
Sign	1 (1%)	1 (2%)	1 (2%)	3 (3%)
Symptom	4 (4%)	9 (20%)†	5 (8%)	23 (27%)*
<b>Ability to cough</b>				
PACU admission				
Sign	2 (2%)	7 (16%)†	2 (3%)	17 (20%)†
Symptom	19 (18%)	23 (51%)*	8 (13%)	37 (43%)*
20 min later				
Sign	1 (1%)	2 (4%)	1 (2%)	2 (2%)
Symptom	5 (5%)	9 (20%)†	7 (11%)	20 (23%)
<b>Track object with eyes</b>				
PACU admission				
Sign	7 (7%)	15 (33%)*	2 (3%)	30 (35%)*
Symptom	20 (19%)	30 (67%)*	7 (11%)	57 (66%)*
20 min later				
Sign	2 (2%)	1 (2%)	0 (0%)	13 (15%)†
Symptom	7 (7%)	12 (27%)*	1 (2%)	34 (40%)*
<b>Ability to breathe deeply</b>				
PACU admission				
Sign	0 (0%)	3 (7%)	3 (5%)	11 (13%)
Symptom	9 (9%)	15 (33%)*	5 (8%)	37 (43%)*
20 min later				
Sign	0 (0%)	0 (0%)	0 (0%)	3 (3%)
Symptom	3 (3%)	7 (16%)†	2 (3%)	22 (26%)*
<b>Blurry vision</b>				
PACU admission	6 (6%)	20 (44%)*	3 (5%)‡	41 (48%)*
20 min later	5 (5%)	13 (29%)*	2 (3%)	35 (41%)*
<b>Double vision</b>				
PACU admission	6 (6%)	10 (22%)†	2 (3%)‡	25 (41%)*
20 min later	3 (3%)	6 (13%)	1 (2%)	14 (16%)†
<b>Facial weakness</b>				
PACU admission	14 (13%)	25 (56%)*	10 (16%)‡	49 (57%)*
20 min later	5 (5%)	11 (24%)*	3 (5%)	24 (28%)*
<b>Facial numbness</b>				
PACU admission	3 (3%)	7 (16%)†	3 (5%)‡	19 (22%)†
20 min later	1 (1%)	3 (7%)	1 (2%)	6 (7%)

Data are number of patients (%). Data were compared using Pearson chi-square test or, when at least one of the cells of the contingency table had an expected  $N < 5$ , Fisher exact probability test.

\*  $P < 0.001$  vs. patients in the same age group with no residual neuromuscular blockade. †  $P < 0.01$  vs. patients in the same age group with no residual neuromuscular blockade. ‡  $N = 62$ .

PACU = postanesthesia care unit.