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Impact of Shorter-acting Neuromuscular Blocking Agents on Fast-track Recovery of the Cardiac Surgical Patient

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Background: **Residual paralysis associated with the use of long-acting muscle relaxants can delay recovery from anesthesia and surgery. The authors tested the hypothesis that use of shorter-acting neuromuscular blocking agents is associated with reductions in tracheal extubation times and intensive care unit (ICU) length of stay in patients undergoing cardiac surgery with cardiopulmonary bypass.**

Methods: **One hundred ten patients scheduled for elective coronary artery bypass grafting or single valve surgery were randomized prospectively to receive either pancuronium or rocuronium intraoperatively. Anesthetic management and muscle relaxant maintenance dosing were standardized. In the ICU, the time required to wean ventilatory support, the duration of tracheal intubation, and length of stay were recorded. Subjects were asked to quantify generalized muscle weakness as they awakened in the ICU and again after tracheal extubation.**

Results: **Complete data were collected on 51 patients in the pancuronium group and 52 patients in the rocuronium group. No differences were found between the groups in anesthetic, surgical, or ICU management. Significant increases in the duration of weaning of ventilatory support were observed in patients who received pancuronium (median, 180 min; range, 50–780 min) compared with the rocuronium group (median, 110 min; range, 45–250 min). Tracheal extubation was significantly delayed in the pancuronium group (median, 500 min; range, 240–1,305 min) compared with the rocuronium group (median, 350 min; range, 210–1,140 min). Subjects in the pancuronium group experienced more mild to severe weakness in the ICU. However, the choice of muscle relaxant did not influence ICU length of stay.**

Conclusion: **The use of shorter-acting neuromuscular blocking agents in patients undergoing cardiac surgery with cardiopulmonary bypass is associated with reductions in tracheal extubation times and symptoms of residual paresis.**

APPROXIMATELY half a million patients undergo cardiac surgical procedures in the United States annually.[1] Changing reimbursement patterns have motivated physicians and hospital administrators to implement strategies to make more efficient use of limited facilities and resources. An important component of cost reduction in cardiac surgical patients has been the development of fast-track cardiac anesthesia, which promotes early tracheal extubation and reductions in intensive care unit (ICU) length of stay (LOS). Fast-track cardiac anesthesia has been demonstrated to be safe and cost-effective.[2]

In the past, the use of high-dose narcotic anesthesia was advocated for cardiac surgical patients. This anesthetic technique made prolonged mechanical ventilation after surgery mandatory. Early investigations of fast-track cardiac anesthesia focused on limiting the dose of opioid analgesics in the operating room to achieve prompt recovery in the ICU.[3] The impact of shorter-acting neuromuscular blocking agents on extubation times and ICU LOS after cardiac surgery has not been examined in a prospective, randomized study.

In patients undergoing noncardiac surgery, a high incidence of residual neuromuscular block has been observed in the postoperative period.[4,5] When neuromuscular function was monitored in the ICU after cardiac surgery, the majority of patients who received pancuronium demonstrated significant residual block.[6,7] Because intermediate-acting muscle relaxants are associated with a more rapid recovery of muscle strength, some investigators have advocated the use of these agents in cardiac patients scheduled for early tracheal extubation.[8]

The objective of this study was to determine the influence of shorter-acting neuromuscular blocking agents on recovery from cardiac surgery. We tested the hypothesis that the use of rocuronium, when compared with pancuronium, would be associated with a reduction in the duration of weaning from mechanical ventilatory support and in the duration of tracheal intubation. The impact of shorter-acting agents on ICU and total hospital LOS was also examined. In addition, each study subject was asked to quantify the severity of muscle weakness they were experiencing in the ICU before and after tracheal extubation.

Methods

Patients

After obtaining approval from the institutional review board of Evanston Northwestern Healthcare and written informed consent of the involved patients, we studied 110 consecutive patients scheduled for early tracheal extubation. Any patient presenting for elective coronary artery bypass grafting or single valvular repair or replacement surgery requiring cardiopulmonary bypass (CPB) was eligible for enrollment. Patients were excluded from the study if any of the following criteria were met: (1) ejection fraction less than 30%; (2) severe chronic pulmonary disease (defined as shortness of breath after one or two flights of stairs or the need for home oxygen

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therapy); (3) obesity (body mass index > 30); (4) renal insufficiency (serum creatinine > 1.6 mg/dl); (5) severe hepatic disease (any liver function tests > 1.5 times the upper limit of normal); (6) chronic neuromuscular disease; (7) preoperative use of drugs that influence metabolism of muscle relaxants; (8) preoperative use of inotropic agents or an intraaortic balloon pump. In addition, patients were excluded from further data analysis in the operating room if more than one inotropic drug was required or if an intraaortic balloon pump was placed.

Anesthetic Management

Patients were randomly allocated to receive either pancuronium or rocuronium according to a computer-generated randomization code. The randomization assignment was concealed in an envelope until the patient entered the operating room.

Premedication consisted of 1–4 mg intravenous midazolam in the holding area. A radial arterial catheter and pulmonary artery catheter were placed during local anesthesia. Additional monitoring consisted of electrocardiography, noninvasive blood pressure measurements, pulse oximetry, capnography, and transesophageal echocardiography in selected patients. Anesthetic induction consisted of 5–10 μg/kg fentanyl, with the addition of 1–4 mg/kg thiopental or 0.2–0.4 mg/kg etomidate if required. Muscle relaxation was achieved with either 0.1–0.12 mg/kg pancuronium or 0.6–0.8 mg/kg rocuronium. Anesthesia was maintained with isoflurane 0.2–2% before, during, and after CPB. A total of 5 mg midazolam was administered before CPB, and another 5 mg was provided during rewarming from CPB. Additional bolus doses of fentanyl, up to a total dose of 15 μg/kg, could be administered in the operating room. Increases in systolic blood pressure or heart rate were treated by increasing the isoflurane concentration or with 50–150 μg fentanyl. Nitroglycerin or nitroprusside infusions were used if these measures were unsuccessful. Hypotension was treated with volume replacement, ephedrine, or phenylepherine, as indicated.

Maintenance dosing of muscle relaxants was determined on the basis of peripheral nerve stimulation of the facial nerve. The temporal branch of the facial nerve was stimulated, and the response at the muscles surrounding the eye was observed. One or two responses to train-of-four (TOF) stimulation were maintained throughout the intraoperative period. When required, 20–30% of the initial dose of muscle relaxant was provided as a bolus to achieve this goal. No muscle relaxants were administered during the last half-hour of the case.

Surgical Management

All patients underwent a median sternotomy and CPB. Standard coronary artery bypass grafting or single valvular surgery was performed by one of four surgeons who were blinded to group assignment. Hypothermic CPB (temperatures of 30–34°C) with a membrane oxygenator and crystalloid prime was used in all patients. Mean pressures of 50–70 mmHg and blood flows of 2.4–2.8 $l \cdot min^{-1} \cdot m^{-2}$ were maintained during CPB. The use of vasoactive drugs was at the discretion of the anesthesiologist managing the case. Patients were actively rewarmed to 37°C before removal of the aortic crossclamp and weaning from CPB.

Intensive Care Unit Care

Propofol sedation was initiated at sternal closure. An infusion of 25–75 $\mu g \cdot kg^{-1} \cdot min^{-1}$ was maintained until criteria for weaning of ventilatory support were met, at which time the infusion was terminated or the rate significantly reduced. No additional narcotics were provided to patients during the study period in the ICU. Mechanical ventilatory parameters were standardized in the ICU (respiratory rate, 8 breaths/min; fraction of inspired oxygen, 0.5; tidal volume, 10–12 ml/kg; positive end-expiratory pressure, +5 cm H_2O). ICU care was standardized, and weaning from ventilatory support, tracheal extubation, and ICU discharge were accomplished when strictly defined criteria were met (Appendix). Weaning and extubation were initiated when all the criteria listed in the Appendix were reached. ICU staff treating the patient were blinded to group assignment.

Data Collection

Preoperative and intraoperative data were recorded to compare the two groups. The primary outcome variable was the duration of tracheal intubation in the ICU. The time required to wean ventilatory support (from the initiation of reduced mechanical ventilation until tracheal extubation) and the total LOS in the ICU were also recorded. As subjects awakened after termination of the propofol sedation, but before tracheal extubation, they were asked to quantify the intensity of the muscle weakness they were experiencing. Generalized muscle weakness was quantified on a three-point scale, with 3 = no weakness, 2 = mild weakness, and 1 = severe weakness. Subjects were again asked to evaluate the severity of muscle weakness they were experiencing 15 min after tracheal extubation. Total hospital LOS was also measured.

Statistical Analysis

The sample size for this study was based on statistics from our institution. In the previous 50 cardiac patients who received pancuronium, the average duration of tracheal intubation was 7.5 ± 2.5 h. We hoped to observe a reduction in tracheal extubation times of at least 1 h in subjects who received rocuronium. A power analysis determined that we could detect ($\alpha = 0.05$, 80% power) this difference between groups if 50 patients were enrolled in each group.

Table 1. Baseline Characteristics

	Rocuronium Group	Pancuronium Group
Preoperative history		
Number	52	51
Age (yr)	70 (38–84)	71 (27–84)
Gender (M/F)	39:13	42:9
Weight (kg)	81 (45–116)	85 (46.5–115)
Height (cm)	172 (142–185)	172 (142–191)
Previous MI	18	15
MI within 3 months	3	4
Previous CHF	5	6
Hypertension	42	36
Diabetes	11	5
Peripheral vascular disease	5	5
Cerebrovascular disease	1	2
Smoking history	18	16
Presenting for CABG	41	42
Presenting for valvular surgery	11	9
Reoperations	5	3
Preoperative medications		
α-Adrenergic blocker	34	41
Calcium channel blocker	13	14
ACE inhibitor	16	15
Digitalis preparation	4	4
Diuretic	8	9
Nitrates	8	14
Heparin	4	7

Data are median (range) or number of patients. No significant differences among the groups were present.

MI = myocardial infarction; CHF = congestive heart failure; CABG = coronary artery bypass grafting; ACE = angiotensin-converting enzyme.

Table 2. Intraoperative Variables

	Rocuronium (n = 52)	Pancuronium (n = 51)
Drugs used		
Total fentanyl (μg/kg)	12.3 (7.4–19.8)	13.5 (7.6–20.5)
Total midazolam (μg/kg)	123.5 (98.9–185.1)	117.6 (70.5–176.5)
Muscle relaxant (mg/kg)	2.24 ± 0.48	0.20 ± 0.03
Dopamine use	4	4
Dobutamine use	4	3
Milrinone use	0	1
Epinephrine use	0	1
Aminocaproic acid use	14	20
Aprotinin use	3	2
Intraoperative volume infusion		
Crystalloids (ml)	3,100 (1,300–4,500)	2,900 (2,000–4,500)
Erythrocytes (units)	0 (0–3)	0 (0–3)
Platelets (units)	0 (0–2)	0 (0–2)
Fresh frozen plasma (units)	0 (0–2)	0 (0–2)
Surgical data		
Duration CPB (min)	119 (60–210)	110 (25–220)
Duration surgery (min)	242 (160–375)	250 (140–430)
Duration anesthesia (min)	297 (210–440)	300 (170–470)
First case of day	40	40
Second case of day	12	11
Saphenous vein grafts (n)	3 (1–4)	3 (0–4)
Internal mammary artery revascularization	39	37

Data are median (range) or number of patients. No significant differences among the groups were present.

CPB = cardiopulmonary bypass.

Nominal data were compared between treatment groups using the chi-square test. Ordinal data were compared using the Mann–Whitney rank sum test. Because nearly all of the interval data failed the Kolmogorov-Smirnov test for normality of the underlying population, these data were also compared using the Mann–Whitney rank sum test. The number of patients in each group with no weakness and with mild or severe weakness on awakening and after extubation were also compared with the chi-square test. The criterion for rejection of the null hypothesis was $P < 0.05$.

Results

Fifty-five patients were randomized to each group. Of the 110 patients enrolled in the study, 4 were excluded from the statistical analysis when surgical reexploration was required because of excessive bleeding, 1 was excluded after an intraaortic balloon pump was placed in the operating room, and 2 were excluded when more than one inotropic agent was needed to separate from CPB. Fifty-one patients in the pancuronium group and 52 patients in the rocuronium group completed the study.

There were no statistically significant differences between the groups with respect to age, height, weight, gender distribution, preexisting medical conditions, preoperative medications, or type of surgical procedure (table 1). Intraoperative data are presented in table 2. The use of fentanyl, midazolam, inotropic agents, antifibrinolytic drugs, crystalloids, and blood products did not differ between groups. There were no differences between the groups in surgical management, duration of surgery, CPB time, or time of ICU admission (early *vs.* late afternoon). Core temperature was greater than 35.5°C in all subjects on arrival to the ICU.

Significant differences between the groups were observed in the ICU (table 3). The median time required to wean ventilatory support was significantly reduced in the rocuronium group (median, 110 min; range, 45–250 min) compared with the pancuronium group (median, 180 min; range, 50–780 min). Statistically significant reductions in the median time from ICU admis-

Table 3. Postoperative Recovery

	Rocuronium	Pancuronium	*P* Value
First patient movement (min)	85 (1–485)	200 (5–480)	0.001
Duration of ventilatory weaning (min)	110 (45–250)	180 (50–780)	< 0.001
ICU arrival until extubation (min)	350 (210–1,140)	500 (240–1,305)	< 0.001
ICU discharge (h)	23 (14.5–42)	23 (18–72)	NS
Hospital discharge (days)	5 (4–32)	5 (4–41)	NS

Data are median (range).

ICU = intensive care unit; NS = not significant.

Table 4. Muscular Weakness in the ICU

	None	Mild or Severe
On awakening in the ICU (before extubation)		
Rocuronium (n = 52)	27 (52)	25 (48) mild = 21; severe = 4
Pancuronium (n = 51)	6 (12)	45 (88) mild = 26; severe = 19
15 min after extubation		
Rocuronium (n = 52)	38 (73)	14 (27) mild = 13; severe = 1
Pancuronium (n = 51)	12 (24)	39 (76) mild = 37; severe = 2

Values are expressed as number of patients (%) experiencing none, mild, or severe muscular weakness (3 = none, 2 = mild, and 1 = severe).

$P < 0.001$ rocuronium *versus* pancuronium on awakening in the intensive care unit (ICU) and 15 min after extubation.

sion until tracheal extubation occurred in patients who received rocuronium (median, 350 min; range, 210–1,140 min) *versus* those who received pancuronium (median, 500 min; range, 240–1,305 min). The two study groups experienced a similar ICU LOS (23 h in both groups) and total hospital LOS (5 days in both groups).

Subjects who received pancuronium noted significantly more muscle weakness in the ICU (table 4). On awakening in the ICU and after tracheal extubation, a significantly higher percentage of patients in the pancuronium group experienced mild or severe weakness. Subjects who received rocuronium in the operating room were more likely to be free of any symptoms of residual paralysis in the ICU.

Discussion

In our study of cardiac surgical patients randomized to receive either pancuronium or rocuronium, we demonstrated that the use of a shorter-acting neuromuscular blocking agent in the operating room was associated with a reduction in the duration of postoperative intubation. A significant reduction in the time required to wean patients from mechanical ventilatory support was also observed in subjects who received rocuronium. In addition, significantly fewer symptoms of residual muscle weakness occurred in the rocuronium group in the early postoperative period. However, these improvements in recovery were not associated with reductions in ICU or total hospital LOS.

Only one previous study has examined the impact of shorter-acting neuromuscular blocking agents on extubation times after cardiac surgery. Using a multicenter database, Butterworth *et al.*[9] examined a total of 1,094 patients undergoing primary coronary artery bypass grafting surgery. The investigators concluded that there were no differences between patients receiving pancuronium and vecuronium in duration of intubation or ICU LOS. This retrospective study had a number of limitations, including no standardization of anesthetic management of patients in the operating room and no defined criteria for weaning ventilatory support, extubation, and discharge while in the ICU. The current study attempted to address some of these limitations. Exclusion criteria and randomization ensured that comorbid factors were comparable between the two groups. Anesthetic management was similar in the groups, and dosing of muscle relaxants was determined on the basis of neuromuscular monitoring. Strict criteria were used to define when weaning from ventilatory support, extubation, and ICU discharge should be accomplished. In contrast to the findings of Butterworth *et al.*,[9] we observed reduced weaning and extubation times in patients who received an intermediate-acting muscle relaxant. Differences in study design may account for the differences in our results.

Two previous studies have examined residual neuromuscular block in cardiac patients in the postoperative period. Van Oldenbeek *et al.*[7] measured recovery of neuromuscular function in 20 patients who received pancuronium for cardiac surgery. TOF ratios were recorded every 5 min using electromyography until TOF ratios greater than 0.8 were obtained. At the time when criteria for discontinuation of sedation and extubation were met, when full recovery of neuromuscular function was assumed to have occurred, the median TOF ratio was only 0.23. On average, the time interval between the last dose of pancuronium and the observation of TOF ratios greater than 0.8 was more than 7 h. McEwin *et al.*[6] randomized 20 cardiac patients to receive either pancuronium or rocuronium in the operating room. On arrival to the ICU, neuromuscular activity was monitored using electromyography. TOF ratios less than 0.7 were measured in all of the subjects who received pancuronium at the time of ICU admission, and the mean TOF ratio was 0.03 in these patients. Severe residual weakness was present up to 7 h after the last dose of pancuronium. Only 4 of the 10 patients who received rocuronium had an initial TOF ratio less than 0.7, and a mean TOF ratio of 0.68 was observed in this group. These studies demonstrate that the use of pancuronium in cardiac patients is associated with considerable residual neuromuscular block, which may persist for many hours after CPB. In addition, the incidence and severity of residual paresis can be reduced with the use of shorter-acting muscle relaxants.

The studies of Van Oldenbeek *et al.*[7] and McEwin *et al.*[6] did not explain why prolonged muscle weakness occurred in the ICU in cardiac patients who received pancuronium. The investigators concluded that excessive dosages of muscle relaxants were used in these patients. Our data do not support this hypothesis. In the previous studies, neuromuscular monitoring was not used, and dosing of muscle relaxants was not standard-

ized. In the current study, neuromuscular monitoring was used to guide the administration of maintenance doses of neuromuscular blocking agents. The careful titration of muscle relaxants, based on the response to TOF nerve stimulation, resulted in larger total doses of pancuronium being provided to patients (0.20 mg/kg) than in the studies by Van Oldenbeek *et al.* (0.11 mg/kg)[7] or McEwin *et al.* (0.18 mg/kg).[6] Hypothermic CPB may also contribute to a significant prolongation of the effects of muscle relaxants. The duration of action of pancuronium and rocuronium during hypothermic CPB has been shown to be prolonged two[10] and four times,[11] respectively, compared with pre-CPB values. Multiple factors contribute to the increased duration of action of muscle relaxants during CPB, including enhanced sensitivity of the neuromuscular junction to muscle relaxants during hypothermia,[12] decreased drug metabolism and elimination by the liver and kidney,[13,14] altered volumes of distribution,[15] and decreased concentrations of calcium and magnesium.[16] Increased sensitivity of muscles to both pancuronium and rocuronium has been shown to persist into the post-CPB period. This impairment of neuromuscular function is present at the end of surgery, despite the maintenance of normothermia.[10,11] Alterations in the phamacokinetic and pharmacodynamic properties of muscle relaxants, induced by CPB, may therefore contribute to residual paresis after surgery.

Residual muscle weakness associated with pancuronium likely contributed to the delays in weaning and extubation that were observed in these subjects, since the two groups were otherwise similar. To test this hypothesis, recovery of neuromuscular function was objectively measured in 10 patients using acceleromyography. On arrival in the ICU, TOF ratios were recorded by a blinded investigator, and values were determined once each hour until ventilatory weaning was initiated. The ulnar nerve was stimulated supramaximally, and the responses at the adductor pollicis measured using the TOF-Watch (Organon, Dublin, Ireland). The mean of three consecutive TOF ratios, repeated every 12 s, was used for each evaluation. All monitoring was conducted according to guidelines established for Good Clinical Research Practice in pharmacodynamic studies of neuromuscular transmission.[17] In the rocuronium group (n = 5), full recovery of neuromuscular function (a mean TOF ratio of 0.99 ± 0.04 SD) was observed in all of the patients by the time weaning of ventilation had commenced. Significant residual neuromuscular block was present in all of the patients who received pancuronium (n = 5) during the study period. Ideally, complete recovery of muscle strength should be present when the ventilatory weaning process is started. TOF ratios less than 0.4 were observed in all of the subjects in the pancuronium group at this time. Measurements obtained at the initiation of weaning demonstrated a mean TOF ratio of 0.21 ± 0.09 SD ($P < 0.001$ compared with the rocuronium group). Significant differences in recovery of neuromuscular function were present between the two groups, despite the observation that weaning was initiated significantly later in the patients who received pancuronium (mean ± SD: 291 ± 27 *vs.* 218 ± 21 min; $P < 0.01$). We are currently conducting a more definitive study examining the relation between shorter-acting muscle relaxants, TOF ratios in the ICU, and clinical signs and symptoms of residual paresis in postoperative cardiac surgical patients.

Patients were asked to quantify symptoms of residual paresis as they awakened in the ICU and after tracheal extubation. When compared with the rocuronium group, subjects who received pancuronium experienced significantly more mild to severe generalized muscle weakness. The majority of the patients in the rocuronium group were free of any symptoms of muscle weakness in the ICU. Kopman *et al.*[18] recently examined the subjective experience that accompanies residual neuromuscular block in volunteers. At TOF ratios of 0.70–0.75, volunteers described visual disturbances, facial weakness, an inability to maintain incisor teeth apposition, difficulty speaking and sitting up, and generalized weakness. A generalized fatigue and visual problems persisted at a TOF ratio of 0.85–0.90. In the current study, we only asked subjects to quantify their sensation of generalized muscle weakness; more detailed questions about weakness in specific muscle groups were not elicited. Despite this limitation, we were able to demonstrate that symptoms of residual paresis may be present for more than 8 h after ICU admission in cardiac patients who receive pancuronium. The use of shorter-acting neuromuscular blocking agents resulted in a significantly higher percentage of patients who were free of any symptoms of muscle weakness.

The choice of muscle relaxant did not influence ICU or total hospital LOS in our subjects. These results are not surprising. The results of previous studies suggest that there are limits below which a further reduction in intubation times will have no effect on ICU or hospital LOS.[19,20] Even when extubation occurs in the operating room immediately after surgery, instead of in the ICU, no reduction in ICU LOS was observed.[21] Transfer out of the ICU is affected by many factors other than clinical readiness. Most patients in the United States will spend the majority of the first postoperative day in the ICU, regardless of when tracheal extubation occurs.[9] Transfer to the ward occurs at most hospitals at relatively set times of the day centered on nursing shift changes. Clinicians are also reluctant to transfer patients out of the ICU in the middle of the night, because staffing ratios are typically lower at this time. At our institution, cardiac patients are usually transferred out of the ICU in the late morning after evaluations by the surgical and ICU staff. Furthermore, it is unlikely that residual muscle weakness would produce clinically significant symptoms on the

day after surgery, when patients were evaluated for ICU discharge.

There are many potential benefits for the cardiac patient when the duration of weaning and tracheal extubation is reduced, even for as little as 1–3 h. At our institution, propofol sedation is terminated or significantly reduced when weaning of ventilatory support is initiated. The possibility of awareness and patient discomfort during this process may be reduced if the length of weaning is shortened. The transition from controlled ventilation to spontaneous ventilation and extubation results in rapid improvements in cardiac performance. Significant increases in left ventricular end-diastolic diameter, stroke work, and cardiac index occur in cardiac patients after extubation.[22] Earlier tracheal extubation may also reduce requirements for sedatives and analgesics,[19] permit earlier patient mobilization,[23] and improve pulmonary function by reducing intrapulmonary shunt and atelectasis.[24,25] However, these variables were not measured in this study. Finally, earlier tracheal extubation may produce improvements in the patients' perception of the perioperative experience. Patients undergoing a second cardiac operation report that early tracheal extubation is a far superior experience compared with 12–24 h of postoperative intubation.[26]

There are several limitations to the current study. First, investigators were not blinded in the operating room to the assignment of muscle relaxants. In a pilot study involving 10 subjects in which blinded syringes containing equipotent concentrations of either pancuronium or rocuronium were used, clinicians were able to easily determine which drug was administered on the basis of hemodynamic changes and duration of action. Therefore, no blinding in the intraoperative period was attempted. However, all endpoints in the study were predetermined and objective, and all ICU management occurred independently of the investigators. ICU physicians and nurses, who determined when criteria for weaning, extubation, and ICU discharge were met, were blinded to group assignment. Second, residual neuromuscular block was not reversed in the ICU. Reversal of residual paresis may have eliminated the differences between the groups. In the United States, however, muscle relaxants are seldom reversed in the ICU after cardiac surgery.[6,27] Many clinicians believe that neuromuscular function will spontaneously recover by the time weaning is initiated. No anticholinesterase agents were used in our study, because these drugs appear to be rarely used when postoperative intubation is anticipated. Third, we used facial nerve monitoring to determine when maintenance dosing of muscle relaxants should be provided to patients. The adductor pollicis was not monitored in the operating room because we did not have access to the hand during cardiac surgery. Because the muscles surrounding the eye are relatively resistant to nondepolarizing agents, the use of facial nerve monitoring may have resulted in comparative overdoses of relaxants. Although both groups would have received a relative overdose, the effect may have been more pronounced when the longer-acting agent was used.

In conclusion, we have shown that the use of shorter-acting muscle relaxants in patients undergoing cardiac surgical procedures with CPB was associated with reductions in the duration of ventilatory weaning and tracheal intubation. Symptoms of residual paresis were also reduced in subjects receiving shorter-acting agents. Despite these improvements in clinical recovery, no reduction in ICU or total hospital LOS was observed in subjects who received rocuronium.

Appendix

The following criteria were adapted from Cheng *et al.*[2]

Criteria for Weaning Mechanical Ventilatory Support

- Hemodynamic stability
- Absence of uncontrolled arrhythmias
- Central temperature greater than 36.0°C
- Chest tube drainage less than 100 ml in the past 2 h
- Arterial oxygen tension greater than 60 mmHg with a oxygen fraction less than 0.5
- *p*H greater than 7.3

Criteria for Tracheal Extubation

- All of the criteria for weaning ventilatory support met
- Negative inspiratory force greater than -20 cm H_20
- Patient responsive to simple commands

Criteria for Intensive Care Unit Discharge

- Patient alert and cooperative
- No inotropic support
- No significant arrhythmias
- Arterial oxygen saturation greater than 90% with inspired oxygen fraction less than 0.5
- Chest tube drainage less than 50 ml in the past 2 h
- No seizure activity
- Urine output greater than 0.5 $ml \cdot kg^{-1} \cdot ml^{-1}$

Criteria for Hospital Discharge

- Hemodynamically stable
- Stable cardiac rhythm
- Noninfected incisions and absence of elevated temperatures
- Patient is able to void and have bowel movements
- Independent ambulation and feeding

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