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Grip strength can be used to evaluate postoperative residual neuromuscular block recovery in patients undergoing general anesthesia

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Abstract

Background: Residual postoperative neuromuscular blockade is an important clinical issue. Neuromuscular monitoring is usually used to evaluate neuromuscular recovery in patients undergoing general anesthesia. However, this procedure is inconvenient and not widely adopted. We aimed to examine the correlation between grip strength and train-of-four ratio (TOFr) to examine whether assessing grip strength can be used clinically to monitor residual neuromuscular blockade.

Methods: One hundred twenty patients with ASA I or II scheduled for laparoscopic cholecystectomy under general anesthesia were enrolled in this study. All patients were randomly selected to receive standard anesthesia induction with either 0.6 mg·kg^{-1} rocuronium or 0.2 mg·kg^{-1} cisatracurium. Grip strength was tested in all patients using an electronic device before anesthesia and when TOFr values of 0.7, 0.8, and 0.9, and an hour later of TOFr value of 0.25. The time required for a change in TOFr values from 0.25 to 0.75 and 0.9 was evaluated. Spearman rank correlation analysis was performed to determine correlations between grip strength and TOFr.

Results: Spearman rank correlation analysis indicated that there was a significant correlation between grip strength and TOFr during patient recovery from general anesthesia (correlation coefficient for grip strength recovery [r_s] = 0.886). Subgroup analysis revealed that there were no differences in mean maximum grip value recovery between patients treated with rocuronium and those treated with cisatracurium when TOFr was 0.7, 0.8, and 0.9 or when the TOFr was 0.25 after 60 minutes (all $P > .05$). Recovery of TOFr from 0.25 to 0.75 and from 0.25 to 0.9 was longer in patients treated with rocuronium than in those treated with cisatracurium (both $P < .001$).

Conclusion: There was a strong correlation between grip strength and TOFr during recovery from general anesthesia. Evaluation of grip strength can be used as an additional strategy to evaluate postoperative residual neuromuscular blockade.

Abbreviations: PACU = post-anesthesia care unit, r_s = correlation coefficient for grip strength recovery, TOFr = train-of-four ratio.

Keywords: grip strength, postoperative residual neuromuscular blockade, train-of-four ratio

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1. Introduction

Residual neuromuscular blockade is one of the most serious clinical problems in postoperative settings. It may also lead to significant increases in respiratory morbidity and health-care utilization while putting patients at additional risk.[1,2] Even though the availability of new drugs and new protocols should help us prevent residual neuromuscular blockade, its incidence has not yet changed significantly.[2,3]

It is important that clinicians have information regarding variables that predict the duration of action of neuromuscular blocking drugs. The patient's ability to raise and maintain the head for 5 seconds, show the tongue, open the eyes, or cough, and adequate tidal ventilation are frequently used to predict postoperative muscle relaxant recovery. However, these assessments are often not performed correctly. In addition, the above tests do not solely exclude clinically significant residual curarization after general anesthesia.[4] A sustained tongue depressor test is most specific but has a sensitivity of only 13% to 22% for predicting a train-of-four (TOF) ratio <0.9.[5] Overall, physicians are unable to exclude residual paralysis using clinical tests unless the TOFr is <0.5.[6] Therefore, it is critical to use more objective methods to evaluate postoperative residual paralysis. TOF monitoring provides objective data following

treatment with neuromuscular blocking agents.[7] Acceleromyography is the most widely used quantitative neuromuscular monitoring technique, but requires specific equipment. In addition, this procedure is relatively complicated and leads to postoperative pain in patients.[6] Previous studies have reported that only about 10% of anesthetists routinely use quantitative TOF-Watch SX monitors to monitor neuromuscular function.[8,9]

Rocuronium and cisatracurium are often used in general anesthesia and intensive care medicine. Studies have shown that rocuronium leads to significantly longer muscle relaxation in elderly patients than in young adults.[3,10] The incidence of postoperative residual neuromuscular blockade has been reported to be approximately twice as high in elderly patients when compared to younger patients.[3] While repeated administration of cisatracurium during surgery does not lead to prolonged the duration and variability of duration of action.[8,11] Repeated administration of rocuronium increases the duration and variability of its clinical effects.[3,12]

In the current study, we aimed to determine the specific correlation between grip strength and TOFr during postoperative muscle relaxant recovery. We also compared postoperative grip strength recovery between patients subjected to general anesthesia with cisatracurium and those treated with rocuronium.

2. Methods

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Jiaxing University (Ethical Committee number CZJE 201601) on August 11, 2016. All patients provided prior written informed consent for participation in the study. One-hundred twenty patients (age, 19–70 years; weight, 45–85 kg) were enrolled in this study from April 2017 to July 2017. All patients had American Society of Anesthesiologists (ASA) physical status I or II and were scheduled for laparoscopic cholecystectomy. Patients with neuromuscular diseases, hand disabilities, morbid obesity (body mass index $\geq$30 kg/m^2), pregnancy, preoperative use of medication with the potential to interfere with neuromuscular transmission within the last 72 hours, severe liver or kidney diseases, electrolyte or acid-base disorders, alteration of plasma protein fraction or endocrine disease with effects on metabolic rate, or any known allergy against the drugs used in the study, those predicted to have difficulty with the maintenance of the airway, and those predicted to require intubation were excluded from the study.

All patients fasted for 6 to 8 hours before the surgery. After the patients entered the operating room, ASA monitoring was performed and end-tidal CO_2 levels were measured. After an intravenous cannula was placed in the antecubital vein in the elbow not intended for neuromuscular monitoring, a 10 mL/kg Ringer's lactate solution was preloaded before the induction of anesthesia. The patients were then placed supine on the operating table. Grip strength of the dominant hand was measured using an electronic device (Electronic Hand Dynamometer EH101; Camry, China) 3 times. Patients were requested to exert maximum grip strength and the maximum value for grip strength was recorded for each 1-minute interval (Fig. 1). Neuromuscular function was monitored by assessing the contraction of the adductor policies muscle using acceleromyography (TOF-Watch SX; Organon, Ireland). After skin cleansing, 2 surface electrodes were positioned over the ulnar nerve at the wrist. A hand adapter that applied a constant preload to the thumb was secured to the hand using tape. An acceleration transducer was attached to the distal phalanx of the thumb via

Figure 1. Electronic grip strength test. Flow diagram: flow diagram outlining the study procedure.

the hand adapter. The hand was positioned on the transport cart to prevent movement of fingers other than the thumb during each assessment. The ulnar nerve was stimulated with TOF stimulation (4 pulses 200 μs in duration, at a frequency of 2 Hz) at 15 seconds intervals, the current intensity was 50 mA. Skin temperature over the adductor pollicis muscle was maintained at >32°C by wrapping the arm in cotton wool. The patients were intravenously anesthetized with midazolam (0.05 mg/kg), sufentanil (0.6 μg/kg), and propofol (2.0 mg/kg). After anesthesia induction and loss of consciousness and prior to neuromuscular drug administration, the accelerometer was calibrated using 0.2-ms supra-maximal square wave impulses delivered at 0.1 Hz. There were no calibration difficulties in any of the patients. After the loss of the eyelash reflex, the patients were treated with 0.6 mg/kg rocuronium or 0.2 mg/kg cisatracurium by an anesthesiologist within approximately 5 to 6 seconds. Tracheal intubation was preformed when no response to nerve stimulation was observed on the TOFr display. The evoked response of the adductor pollicis to TOF stimulation was then measured. The resulting TOFrs were obtained using TOF Watch SX at the T1 level relative to the T4 level. T4/T1 differing by 5% or less were used for analysis. When the difference in the TOFr between the 2 stimuli was >5%, we applied additional TOF stimuli until we achieved 2 subsequent TOF readings differing by 5% or less. The mean of the 2 consecutive T4/T1 values was used for the analysis.

Anesthesia was maintained using 3 to 4 mg·kg^{-1}·h^{-1} propofol and 0.15 to 0.2 μg·kg^{-1}·min^{-1} remifentanil. Repeat doses of rocuronium (0.15 mg/kg) or cisatracurium (0.05 mg/kg) were

administered until the twitch height (T1/T0) reached 0.2. Emergency equipment and drugs were available at all times. During the operation, intravenous ephedrine (6 mg) or atropine (0.5 mg) were administered if the mean arterial pressure was decreased by >25% when compared to pre-induction values. Antiemetic prophylaxis consisted of ondansetron (4 mg) and dexamethasone (4–8 mg) in high-risk patients. Ventilation was assisted to maintain end-tidal CO_2 levels between 35 and 45 mmHg. Body temperature was monitored using an esophageal probe and maintained at 35°C or higher using a warming blanket. The appropriate hand and forearm were wrapped in cotton to prevent peripheral temperature from falling below 32°C.

Neuromuscular blocking drug administration was stopped approximately 30 minutes prior to the completion of the operation. The surgery wound was administrated a certain amount of 0.5% ropivacaine for local analgesia at the end of the operation. After the cessation of intravenous anesthesia at the end of the surgery, the trachea was extubated when 4 responses to TOF stimulation were observed, the patient regained consciousness, and the anesthetist judged that neuromuscular function had recovered adequately for upper airway protection and spontaneous ventilation. After tracheal extubation, the patients were admitted to the post-anesthesia care unit (PACU) immediately. Electrocardiography, pulse oxygen saturation (SpO2), and TOF monitoring was continued after the operation.

The maximum grip strength of the dominant hand was measured again in all patients using the same methods as those used previously when the TOFr values reached 0.7, 0.8, and 0.9, and when the TOFr value was 0.25 after 60 minutes. Flumazenil (0.2 mg) was administered to patients who woke up with poor quality when the TOFr value was 0.7. The onset time and the times required for the recovery of TOFr from 0.25 to 0.75 and from 0.25 to 0.9 were recorded by an anesthesiologist who was blinded to group allocation. Patient characteristics, neuromuscular blocking agent used, estimated blood loss, total propofol and opioid consumption, duration of surgery, and recovery room stay duration were recorded. These data were obtained from the electronic medical record. In the PACU, SpO2 values <90% were considered indicative of hypoxia. Patients with hypoxia were treated with 6 L/min oxygen via a face mask once patency of the airway was ensured. Complications encountered during and after the operation were recorded. When the TOFr was ≥1.0 and the clinical tests were positive, the patients were transferred to the ward.

Intubation time was defined as the interval between the injection of neuromuscular blocking drugs and the time at which there was no response to TOF stimulation. The duration of TOF ≥0.9 was defined as the interval between extubation and the time at which the TOFr was 0.9. The duration of anesthesia was defined as the interval between anesthesia induction and tracheal extubation, and extubation time was defined as the interval between the end of the operation and tracheal extubation. The duration of surgery was defined as the interval between anesthesia induction and closure of the skin.

3. Statistical analysis

The primary outcome of the current study was the correlation between grip strength and TOFr during postoperative muscle relaxant recovery. The simple size was calculated by PASS (Version 11.0.10). A minimum sample size of 112 was required to achieve the desired statistical power level of 0.90 at a probability level of 0.05 with the effect size of 0.3. Quantitative data are expressed as means ± standard deviations, number (%), or mean (range), as appropriate. SPSS software for Windows version 19.0 (SPSS Inc.; Chicago, IL) was used to analyze the data. Spearman rank correlation analysis was performed to determine the correlation between muscle relaxant recovery and TOFr. Normalized TOFr values were used for all statistical analyses. Quantitative data were analyzed using independent-sample Student t tests. Categorical variables were analyzed using Chi-squared tests. P values <.05 were considered significant.

4. Results

Three patients were excluded from this study because we were unable to obtain reliable TOFr measurements from them. The remaining 117 patients were included in the study (flow diagram). The patients' characteristics are presented in Table 1.

There was a significant correlation between grip strength and TOFr during patient recovery from general anesthesia. The correlation coefficient for grip strength recovery (r_s) between grip strength and the TOFr was 0.886.

Subgroup analysis indicated that there was no difference in preoperative mean maximum grip strength between patients treated with rocuronium and those treated with cisatracurium (P=.612). There were no significant differences in mean maximum grip value recovery between patients treated with rocuronium and those treated with cisatracurium when the TOFr reached 0.7, 0.8, and 0.9, and when the TOFr was 0.25 after 60 minutes (all P >.05). Recovery of the TOFr from 0.25 to 0.75 and from 0.25 to 0.9 was prolonged in patients treated with rocuronium when compared to those treated with cisatracurium (both P <.001). The coefficient of determination (R^2) was 0.675 and 0.643 in patients treated with rocuronium and cisatracurium, respectively (Table 2; Figs. 2 and 3). No significant difference was found in the duration of PACU stay between patients treated with rocuronium and those treated with cisatracurium (Table 2).

5. Discussion

In this study, we investigated the correlation between grip strength and TOFr during postoperative muscle relaxant recovery in patients undergoing general anesthesia. We found an r_s value of 0.886. This indicated that the grip strength test can be used to largely predict postoperative muscle relaxant recovery. Subgroup analysis indicated that mean maximum grip strength was not significantly different at the same TOFr in patients treated with different muscle relaxants.

The primary finding of the present study was that grip strength was well correlated with TOF responses and was a reasonably reliable indicator to evaluate muscle relaxant recovery. In a

Table 1

General characteristics and measurements of patients.

Patient characteristics and measurements (n=117)	Value
Age, yr	49.8±10.5
Weight, kg	61.6±7.7
Sex, male/female	54/63
Extubation time, min	8.4±2.5
Duration of surgery, min	54.8±8.9
Duration of PACU stay, min	38.5±8.2
Maximum grip value, kg	32.0±7.5

Data are expressed as mean ± standard deviation.

Table 2

Subgroup analysis of grip value recovery and TOFr.

	Patients treated with rocuronium (n = 58)	Patients treated with cisatracurium (n = 59)	P value
Maximum grip value, kg	31.7 ± 7.1	32.4 ± 7.8	.612
Mean dose of NMBA, mg	39.1 ± 5.0	13.2 ± 1.4	—
Mean maximum grip value recovery			
0.7TOFr, %	63.9 ± 7.2	64.3 ± 8.3	.779
0.8TOFr, %	74.2 ± 6.8	74.7 ± 7.2	.696
0.9TOFr, %	84.7 ± 6.8	83.9 ± 6.5	.544
TOFr of 0.25 after 60 min, %	93.7 ± 5.9	93.8 ± 3.8	.872
TOF recovery from 0.25 to 0.75, min	20.9 ± 3.8	15.4 ± 2.5	<.001
TOF recovery from 0.25 to 0.9, min	30.4 ± 3.9	23.5 ± 3.2	<.001
The coefficient of determination, R^2	0.675	0.643	—
Duration of PACU stay, min	56.5 ± 7.2	54.2 ± 5.9	.069

Data are expressed as mean ± standard deviation unless otherwise indicated. 95% CI = 95% confidence interval, NMBA = neuromuscular blocking agents, TOFr = train-of-four ratio.

previous study, Kopman et al[7] found that when the TOFr was equal to 0.70, grip strength was decreased in all subjects. Specifically, at a TOFr of 0.70, the average grip strength was 59% of the control value. Grip strength increased to 83% of the control value at a TOFr of 0.90. These findings are similar to those of the current study. Grayling et al[9] and Murphy et al[13] have both studied the relationship between grip strength and TOFr but did not explore the specific correlation between grip strength and TOFr. Heier et al[14] have reported that hand grip does not reflect muscle relaxant recovery. This finding may have been due to a too-small sample size. In the study, we used a quantitative electronic grip measurement to determine the recovery of muscle strength after surgery in a simple and more convenient manner.

We included 2 types of neuromuscular blocking agents in the current study, namely rocuronium and cisatracurium. We performed a stratification analysis for the 2 types of neuromuscular blocking agents and found that the coefficient of determination between grip strength and TOFr was very similar in patients treated with rocuronium and those treated with cisatracurium. Of course, the grip strength values at the same TOFr were very similar in patients undergoing muscle relaxant recovery following treatment with rocuronium and cisatracurium. These results suggest that the specific type of neuromuscular blocker has no effect on the correlation coefficient between grip strength and TOFr.

During the stratification analysis, we found that TOFs recovery from 0.25 to 0.75 and from 0.25 to 0.9 were shorter in patients treated with cisatracurium than in those treated with rocuronium. This may be because the 2 neuromuscular blocking drugs are metabolized via completely different pathways in vivo.[10,15,16] A previous study has shown that there is greater variability in the duration of anesthesia when rocuronium is used than when cisatracurium is used, especially in elderly patients.[17] There was no difference between the groups in PACU stay duration after surgery. This may be due to the fact that laparoscopic cholecystectomy surgery is relatively short. As a result, almost no additional intraoperative muscle relaxants are needed, and neuromuscular blocking drug accumulation in the body is unlikely. The patients in our study were on average about 50 years old or younger. Some research indicates that age is a factor that may influence the duration of action of muscle relaxants and that age-related reductions in cardiac output, renal and hepatic function, muscle mass, and the ability to regulate temperature are present in most elderly patients.[3,10]

In current study, grip strength was tested at the TOFr values of 0.7, 0.8, and 0.9, and a TOFr of 0.25 after 60 minutes. Most patients had already recovered consciousness and were able to carry out the grip test when the TOFr had reached 0.7. Three patients completed the grip test after treatment with 0.2 mg flumazenil. In order to reduce the influence on the outcomes of the study caused by some factors, propofol and remifentanil were
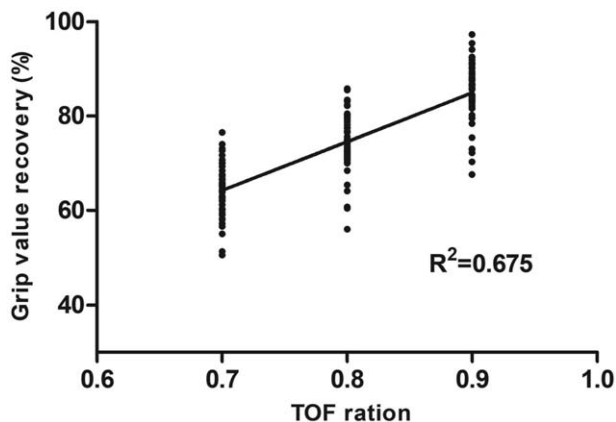

Figure 2. Rank regression analysis between grip strength and TOFr in patients treated with rocuronium. R^2 = 0.675, P<.0001. R^2, the coefficient of determination.
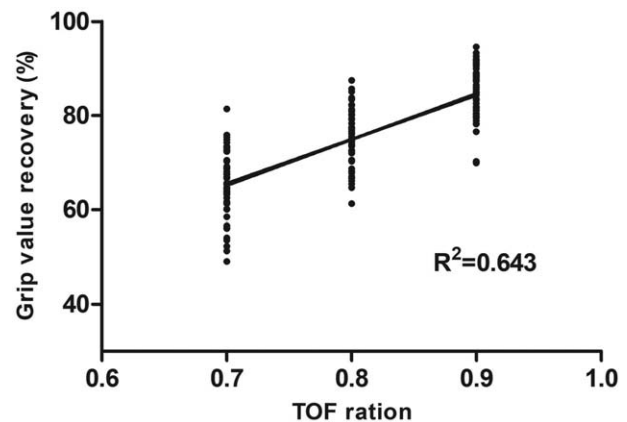

Figure 3. Rank regression analysis between grip strength and TOFr in patients treated with cisatracurium. R^2 = 0.643, P<.0001. R^2, the coefficient of determination.

selected for anesthesia maintenance, which with rapid onset and short duration, and patients can be quickly awake after surgery, with little impact on patient grip testing. Inhalation anesthesia was not adopted in this study, because inhalation anesthesia was found that it can increase the incidence and duration of neuromuscular blockade after surgery.[18] Body weight can also change the distribution volume of neuromuscular blocking in the body, AChE activity, and so on, thereby affecting the muscle relaxation effect.[19] In this study, patients with a body mass index greater than $30 \, kg/m^2$ were excluded from the study.

A previous study has shown that baseline TOFr as measured by Acceleromyography are usually >1.0 and vary widely among patients.[20,21] This means that an AMG reading of 0.9 does not always represent adequate recovery of neuromuscular function. A previous study indicates that calibrated and normalized baseline values can be more accurate measures used to detect residual paralysis.[22] We calibrated and normalized the baseline value. In order to increase accuracy, we adjusted the electronic grip lever to a comfortable position and used the maximum grip value as the outcome. To avoid postoperative agitation in patients with in accurate measurements, the patients were informed that the series of TOF stimulations may lead to pain. In addition, the surgery wound was given a certain amount of ropivacaine for local analgesia at the end of the operation to lessen the effect of pain on the grip strength measurement.

Given that the quantitative TOF-Watch SX monitors have not been routinely used to monitor neuromuscular function during the recovery of general anesthesia,[8,9] the grip test can be used to evaluate the recovery of neuromuscular function after surgery. To the extent, that it can avoid the harm caused by residual postoperative neuromuscular blockade.

There are limitations to the present study. First, the grip test is passive and can only be carried out when the patients are awake and in cooperation. Thus, we were unable to evaluate grip strength when the patients were not awake. Another limitation of our study was that we did not perform a stratification analysis on the effects of sex or age on muscle relaxant recovery as assessed using the grip test. Interestingly, Heier et al[23] have investigated residual neuromuscular blockade and reported sex-related differences in the relationship between TOFr and clinical manifestations. Third, children and elderly patients were excluded from this study. In the clinical process, children are often incoordinate,[24] and elderly patients are prone to cognitive impairment.[25] Thus, the results were not suitable for children and elderly patients. Forth, patients undergoing some surgeries were not suitable for testing the grip strength, such as upper limb surgery and partial brain surgery.

In summary, a strong correlation was found between grip strength and TOFr during patient recovery from general anesthesia. Grip strength provides an additional measure for the evaluation of postoperative residual neuromuscular blockade in the clinic.

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Author contributions

Conceptualization: Da-qing Pei.
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Validation: Qing-he Zhou.
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Writing – review & editing: Da-qing Pei.

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