

## **Study**

This study is a single center, randomized, controlled, and double-blinded trial. The protocol of this study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (No B-1701-1378-006) and registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT#03039543). Informed consents were obtained from all patients before the conduction of the study.

## **Patients**

Patients aged more than 19 years who are American Society of Anesthesiologists (ASA) physical status I and II and scheduled to undergo elective TURB were included for this trial. Exclusion criteria are a history of neuromuscular, renal, or hepatic disease, a body mass index (BMI) of  $< 18.5$  or  $> 30.0 \text{ kg/m}^2$ , and treatment with drugs known to interfere with neuromuscular function.

## **Randomization and intervention**

Randomization is conducted by a person who was not involved in the study using a computer - generated randomization code (Random Allocation Software, version 2.0). The result of randomization was sealed in an opaque envelope, which was delivered to the anesthesiologist who is in charge of the patient. Patients, surgeons and outcome assessors for recovery profiles were blinded to the group assignment. However, the anesthesiologist responsible for the patients during surgery was not blinded to the assigned group. From a table of random numbers, a total of 108 patients undergoing elective TURB are randomized into either moderate NMB group ( $n = 54$ ) or deep NMB group ( $n = 54$ ).

Moderate NMB group: During maintenance of anesthesia, added bolus doses of intravenous rocuronium (5–10 mg) were used to maintain moderate NMB (TOF count of 1 or 2) if needed. After the surgery, patients were reversed with 2 mg/kg sugammadex at a TOF count of 1 or 2.

Deep NMB group: During maintenance of anesthesia, added bolus doses of intravenous rocuronium (5–10 mg) were used to maintain deep NMB (TOF count of 0 with PTC of 2) if needed. After the surgery, patients were reversed with 4 mg/kg sugammadex at PTC of 2.

## **Anesthesia**

Premedication was administered with intravenous midazolam (0.02 mg/kg) as a premedication at the reception area of operating theater and then transferred to the operating room. In the operating room, standard monitoring, including electrocardiography, noninvasive arterial pressure measurements, and pulse oximetry was placed. The level of NMB was monitored using acceleromyography (TOF-Watch® SX, Organon Ireland Ltd., a subsidiary of Merck & Co., Inc., Swords, Co. Dublin, Ireland) at the adductor pollicis muscle. The TOF ratio was recorded for each patient every 5 min during the operation. The TOF-watch was calibrated in each patient before performing the measurements. The stimulation current was set to 30 mA and the TOF-watch SX was calibrated in the calibration 1 mode. During induction of anesthesia, patients received propofol (2 mg/kg) and alfentanil and the I-gel™ (Intersurgical Ltd, Wokingham, UK) was inserted after the administration of 0.6 mg/kg rocuronium in both groups. Anesthesia was maintained with desflurane while monitoring the bispectral index (A-2000 BISTM monitor; Aspect Medical Systems, Inc., Natick, MA, USA) between 40-60. A bolus dose of intravenous rocuronium (5–10 mg) was used to maintain moderate (moderate NMB group, TOF count of 1 or 2) or deep (deep NMB group, TOF count of 0 with PTC of 2) NMB if needed. At the end of the operation, the surgeon rated the endoscopic surgical condition on a 5-point scale (1 = extremely poor, 2 = poor, 3 =

acceptable, 4 = good, 5= optimal, **Table 1**) [9]. Patients in moderate NMB group are reversed with 2 mg/kg sugammadex at a TOF count of 1 or 2 (group A) and patients in the deep NMB group are reversed with 4 mg/kg sugammadex at PTC of 2 (group B). Patients were extubated when spontaneous ventilation of the patient was adequate. After the surgery, patients were transferred to the post-anesthesia care unit (PACU)

Postoperative residual curarization (PORC, TOF ratio < 0.9) is recorded if it occurred. Patients were evaluated every 15 min using the modified Aldrete scoring system until ready for discharge from the PACU and the criterion used for patient discharge was the achievement of a modified Aldrete score of 9 [10]. Respiratory complication such as desaturation ( $\text{SpO}_2 < 90\%$ ) or respiratory depression ( $\text{RR} < 8$ ) and other adverse events including postoperative nausea and/or vomiting (PONV) were recorded during PACU stay.

### **Outcome measurement**

Primary outcome was the endoscopic surgical condition that was evaluated right after the operation by the surgeon (Table 1), who was blinded to the group assignment. Secondary outcomes were recovery profiles including the postoperative residual curarization (PORC, TOF ratio < 0.9), respiratory complications, recovery time (PACU discharge, a modified Aldrete score of 9) and other postoperative adverse events.

### **Sample size**

The sample size was calculated based on the preliminary data using G\*Power 3.1.2 (Heinrich-Heine University, Düsseldorf, Germany). The proportion of optimal endoscopic surgical condition (score 5) during TURB was 30 % after the use of moderate NMB ( $n = 10$ ) and 30% increase of optimal endoscopic surgical condition by deep NMB was considered to

be clinically significant. Fifty four (54) patients per group was calculated with  $\alpha = 0.05$  and  $\beta = 0.2$ , allowing for a 10 % drop-out rate.

### **Statistical analysis**

Statistical analysis is performed using SPSS 21 (SPSS Inc., Chicago, IL, USA) and the test of normal distribution was assessed with the Shapiro–Wilk test. Chi-square test or Fisher’s exact test was used for the analysis of incidence variables (gender, ASA physical class, additional rocuronium, surgical condition score, PORC, respiratory complications and other adverse events). Student’s t test is used to compare normally distributed continuous variables (age, weight, height, BMI, operation time, anesthesia time, propofol, alfentanil, rocuronium, and recovery time). All values presented are number of patients (%) or mean (SD). A p values  $< 0.05$  were considered to indicate statistical significance.

Table 1. Surgical condition score (Ref 7 by Martini et al.)

Score	Surgical condition
1.	Extremely poor conditions The surgeon is unable to work because of coughing or because of the inability to obtain an endoscopic view because of inadequate muscle relaxation. Additional neuromuscular blocking agents must be given
2.	Poor conditions There is an endoscopic view but the surgeon is severely hampered by inadequate muscle relaxation with continuous muscle contractions, movements, or both with the hazard of tissue damage. Additional neuromuscular blocking agents must be given
3.	Acceptable conditions There is a wide endoscopic view but bladder contractions, movements, or both occur regularly causing some interference with the surgeon's work. There is the need for additional neuromuscular blocking agents to prevent deterioration
4.	Good conditions There is a wide endoscopic working field with sporadic muscle contractions, movements, or both. There is no immediate need for additional neuromuscular blocking agents unless there is the fear of deterioration
5.	Optimal conditions There is a wide endoscopic working field without any movement or contractions. There is no need for additional neuromuscular blocking agents

Surgical conditions were evaluated right after the surgery by the surgeon, who was blinded to the group assignment.