# STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

**Official title: Postoperative Urinary Retention After Reversal of Neuromuscular Block by Neostigmine versus Sugammadex in Patients Undergoing Laparoscopic Cholecystectomy: A Randomized Controlled Trial**

**NCT number: NCT05794503**

**IRB Approved Document date: 08-05-23**

**Form A**

| IRB # | STU-2022-1201 |
|---|---|

**PROTOCOL FORM / RESEARCH DESCRIPTION**

If an item does not apply to your research project, indicate that the question is "**not applicable**" – do not leave sections blank

**Click once on the highlighted entry in each box to provide your response.** Click the item number/letter or word, if hyperlinked, for detailed instructions for that question. If your response requires inserting a table, picture, etc, you may need to first delete the box that surrounds the answer and then insert your table or other special document.

**1. Purpose and objectives.** *List the purpose and objectives:*

Objective 1:
To determine the incidence of postoperative urinary retention after reversal of rocuronium-induced neuromuscular blockade by neostigmine versus sugammadex in patients undergoing laparoscopic cholecystectomy.

Primary Hypothesis:
Subjects who are reversed with sugammadex will have 70% less postoperative urinary retention compared to subjects who are reversed with neostigmine.

**2. Background.**

- Describe past experimental and/or clinical findings leading to the formulation of your study.
- For research involving investigational drugs, describe the previously conducted animal and human studies.
- For research that involves FDA approved drugs or devices, describe the FDA approved uses of this drug/device in relation to your protocol.
- Attach a copy of the approved labeling as a product package insert or from the Physician's Desk Reference.

You may reference sponsor's full protocol or grant application (section number and/or title) or if none, ensure background includes references.

Please respond to all components of this item, or clearly indicate which components are not applicable.

**a. Background**

The incidence of postoperative urinary retention (POUR) after surgery varies widely from 3-50% and depends on various patient- and procedural-related factors [1, 2]. In an era of fast-track surgery and enhanced recovery, urinary retention has emerged as one of the most common barriers to successful same-day discharge. Risk factors for POUR include male gender, age >50, prolonged surgery, excessive intraoperative fluids, and use of anticholinergics [3]. POUR can contribute to a prolonged PACU stay, patient discomfort, and unplanned hospital admission. Acute urinary retention can impair renal glomerular and tubular function [4]. POUR is usually treated with urethral catheterization, which is uncomfortable, and can increase the risk for infection and trauma to the urogenital tract [5]. It is estimated that POUR accounts for between 20-25% of unplanned inpatient admissions following planned outpatient surgery [6, 7].

Adequate muscle relaxation is necessary for laparoscopic procedures. Residual neuromuscular blockade is common and has been proven to lead to a multitude of adverse effects including increased postoperative pulmonary complications, longer length of hospital stay, and decreased quality of recovery [8, 9]. At present, it is recommended that all patients

who receive neuromuscular blocking agents be given reversal agents unless they have a documented TOF >90% prior to extubation [10].

Neostigmine (an acetylcholinesterase inhibitor) is frequently used for reversal of neuromuscular blockade. However, it is associated with significant muscarinic side effects (i.e., bradycardia) and must be co-administered with an anticholinergic such as glycopyrrolate. Contraction of the detrusor and internal urethral sphincter are controlled by parasympathetic stimulation via muscarinic receptors so blockade of these receptors by glycopyrrolate can induce urinary retention [11]. Numerous studies have found that administration of glycopyrrolate intraoperatively increase the risk of POUR [11, 12].

Sugammadex is a selective relaxant binding agent which does not have any cholinergic effects and thus does not contribute to POUR. Previous studies have found that the use of sugammadex was associated with a lower incidence of POUR in patients undergoing total knee arthroplasty, inguinal hernia repair, and laparoscopic cholecystectomy [13-15].

**b. Current practice**

Current practice at Parkland shows that about half of patients undergoing laparoscopic cholecystectomy are reversed with sugammadex and half are reversed with neostigmine. The incidence of POUR in these patients is unknown because there have not been any formal studies to evaluate this outcome. There are no prospective, randomized studies evaluating the incidence of POUR from reversal of neuromuscular blockade with neostigmine versus sugammadex in patients undergoing laparoscopic cholecystectomy. Most previous studies have been retrospective or did not examine POUR as the primary outcome.

**3. Study Design.**
Describe the study design (e.g., single/double blind, parallel, crossover, etc.) Consider inserting a scheme to visually present the study design.

This study is intended to be a single-site, prospective, randomized, controlled study that intends to enroll a total of 230 patients undergoing laparoscopic cholecystectomy at Parkland Hospital. Patients will be randomized to receive either neostigmine or sugammadex for reversal of rocuronium-induced neuromuscular blockade. A standardized anesthetic protocol that is usual and customary for the type of operation the patient is having will be provided to the anesthesia teams of enrolled subjects. The remainder of the anesthetic care of the subject will not deviate from the standard of care. To account for protocol deviations and patient dropout, up to 250 randomization envelopes will be made and enrollment will continue until there are 230 completed enrollments.

**Criteria for Inclusion of Subjects:**

- 18-80 years old
- Undergoing laparoscopic cholecystectomy
- Anticipated surgical duration <2 hours
- ASA physical status classification 1-3
- Willing and able to consent in English or Spanish
- No personal history of neuromuscular disease

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**Criteria for Exclusion of Subjects:**

- Preoperative urinary catheter
- History of problems with urination
- Current use of anticholinergic medications (e.g., antihistamines, phenothiazines, antidepressants, antipsychotics)
- Current UTI or urogenital problem (incontinence, known bladder retention, prostate hypertrophy)
- Planned intraoperative insertion of a urinary catheter
- ESRD (eGFR <30 mL/min)
- ESLD (AST or ALT > 3x reference range)
- Planned postoperative intubation/ventilation or admission to ICU
- Allergy to sugammadex, neostigmine, glycopyrrolate, or rocuronium
- Pregnant or nursing women
- "Stat" (emergent) cases
- Known or suspected neurological condition (e.g., Alzheimer's, h/o of stroke, multiple sclerosis, Parkinson's)
- Patients on toremifene (a selective estrogen receptor modulator)
- Women on oral contraceptives who do not wish to use a non-hormonal method of contraception for 7 days following surgery

**4. Research Plan / Description of the Research Methods:**

**4.a.** Provide a **comprehensive narrative** describing the **research methods**.

1) Provide the **order in which tests/procedures will be performed**,
2) Provide the **setting** for these events and a description of the **methods used to protect privacy** during the study.
3) Provide the **plan for data analysis** (include as applicable the **sample size calculation)**

Please respond to all components of this item, or clearly indicate which components are not applicable.

**1) Order in which tests/procedures will be performed**

*Screening and Informed Consent:*

A member of the research team will use a screening form to look for surgical patients that meet all the inclusion and exclusion criteria. He/she will approach potential subjects in the preoperative area and the study will be explained in detail in a private room. Enrolled patients will be randomly assigned to the neostigmine or sugammadex groups in a 1:1 ratio using a web-based randomization code. These assignments will be written and put into an envelope which will be given to the anesthesia provider to open once a patient is consented.

*Baseline Subjective Measures:*

In the preoperative area, and demographic information will be gathered from Epic.

*Anesthesia Protocol:*

The anesthesia team that will be caring for the patient during surgery will be given the protocol for the study, which standardizes the general anesthetic technique. A study member will provide the anesthesia team with an envelope containing which group the patient has been randomized into (neostigmine versus sugammadex). If the patient has been randomized to the neostigmine group, the drug will be drawn from the Pyxis per usual practice. If the patient has been randomized to the sugammadex group, an order will be sent to investigational drug services pharmacy (IDS) to draw up the sugammadex (see attachment, IDS order form). IDS Pharmacy will only be providing sugammadex if the patient has been randomized to that group.

Subjects will receive 0.6 mg/kg of rocuronium for neuromuscular paralysis for induction. Additional rocuronium will be given in 0.15 mg/kg increments to facilitate neuromuscular relaxation. All patients will have the depth of neuromuscular block monitored quantitatively at the adductor pollicis with a TwitchView electromyography-based device (Blink, Seattle, WA) that provides real time feedback of the strength of contraction and graphically displays the relevant ratios. Assessments of depth of neuromuscular blockade will be recorded into the patient's electronic medical record every 15 minutes following intubation. Maintenance of anesthesia will be with sevoflurane in 50% oxygen. All patients will have a forced air warming device (e.g., Bair Hugger, 3M, Maplewood, MN) used to maintain normothermia throughout the surgery.

At the end of surgery, reversal of neuromuscular blockade will be achieved with either neostigmine or sugammadex and the patient will be extubated when the TOF ≥0.9. If the patient has been randomized into the sugammadex group, it will be prepared into a syringe by a pharmacist in Investigational Drug Service (IDS) Pharmacy. Sugammadex will be provided to IDS Pharmacy from the study sponsor, Merck. IDS Pharmacy will only be responsible for providing sugammadex, and only if the patient has been randomized to that group. The remaining aspects of the anesthetic will be standardized and not differ from the standard of care for all patients.

Patients will then be taken to the PACU and monitored according to established guidelines.

*Randomization & Dosing:*

Patients will be randomized to one of two groups for neuromuscular blockade and reversal of neuromuscular paralysis:

1. **Group 1**- rocuronium + neostigmine (NEO group)
    a. Induction: 0.6 mg/kg rocuronium
    b. Maintenance: additional boluses of 0.15 mg/kg rocuronium
    c. Reversal:
        i. TOF 0-1 twitch- delay reversal
        ii. TOF <0.4- 50-70 mcg/kg neostigmine (max 5 mg) + 10 mcg/kg glycopyrrolate (max 1 mg)
        iii. TOF 0.4-0.9- 20-40 mcg/kg neostigmine + 5 mcg/kg glycopyrrolate

2. **Group 2**- rocuronium + sugammadex (SUG group)
    a. Induction: 0.6 mg/kg rocuronium
    b. Maintenance: additional boluses of 0.15 mg/kg rocuronium

c. Reversal:
   i. TOF < 2 twitches- 4 mg/kg sugammadex
   ii. TOF ≥ 2 twitches- 2 mg/kg sugammadex

The statistician will make randomization envelopes by using a random number generator. These envelopes will be provided to the anesthesia team after subjects are consented. The anesthesia team will be responsible for opening the envelope to discover which group the patient has been randomized to. The words 'neostigmine' or 'sugammadex' will be printed on a piece of paper and placed in an opaque manila envelope that bears a unique subject number. If the patient has been randomized into the neostigmine group, the anesthesia provider will draw up the drug from the Pyxis. If the patient has been randomized into the sugammadex group, the study team will contact the IDS Pharmacy and they will provide sugammadex. It is solely the responsibility of the research team to contact IDS Pharmacy in order to retrieve sugammadex.

*PACU Assessment:*
A blinded, trained research assistant will observe and record all parameters from the time the patient arrives in the PACU until they are discharged from the PACU. Any drugs given in the PACU will be recorded. The patient will be asked to void 45 minutes after PACU arrival. Post void residual will be obtained with an ultrasound. The bladder scan will be administered 60 min after arrival to the PACU.

POUR will be defined as:
1. Inability to spontaneously urinate and a bladder volume ≥ 300 mL [16-17]
2. Postvoid residual > 150 mL [18-19]
3. Need for insertion of Foley catheter or straight catheter [20]

*Data Sources:*
Protected health information including name, medical record number, and date of birth will be recorded and stored securely in an IRB approved, secured REDCap database.

**Parameters:**
1. Protected health information (PHI): name, medical record number, date of birth, phone number
2. Demographic information (age, weight, height, BMI), medical and surgical history, ASA status
3. Intraoperative parameters
   - Frequency and dose of all neuromuscular blocking and reversal agents
   - Intraoperative vitals (systolic, diastolic, and mean blood pressures, temperature, heart rate) at least every 3 minutes
   - ECG rhythm
   - Fluids administered
   - End-tidal concentration of anesthetic (e.g., sevoflurane)
   - Total intraoperative opioids
   - Length of surgery
   - The time from last neuromuscular blocking agent given to reversal agent (min)
   - Depth of neuromuscular blockade throughout the surgery at 15-minute intervals
   - Presence of hemodynamic changes, rash, erythema, or flushing after reversal agent given
4. PACU parameters

- Vitals during PACU stay (BP, temperature, HR, $SpO_2$) every 15 minutes
- The time when PACU discharge criteria are met
- Total PACU time (PACU arrival to actual discharge from PACU)
- Amount of urine voided
- Bladder volume at $T_{60}$

5. Adverse event monitoring
   - Critical respiratory adverse event including bronchospasm, atelectasis, pulmonary edema
   - Cardiovascular adverse events such as tachycardia, bradycardia, cardiac arrhythmias, hypotension, and hypertension
   - Major adverse postoperative events (pneumonia, reintubation, myocardial infarction, stroke)
   - Unplanned hospital admission
   - Readmission after discharge
   - Inability to void prior to discharge
   - Need for insertion of a bladder catheter
   - Development of urinary tract infection (UTI)

## 2) Setting and Methods used to Protect Privacy

*Setting*

The study will take place in the pre-operative rooms, the operating rooms, and the PACU at Parkland Hospital.

*Procedures to Maintain Confidentiality:*

A non-identifiable code will be assigned to the data collection sheet so that there is not a direct link to specific names. Patient IDs will be standardized in chronological order as subject 1, subject 2, etc. A key to the coding system will be maintained in a locked storage cabinet with limited access until all the data is collected and analyzed. Access to study data will be restricted to authorized study personnel only. Following the completion of the analysis and the project, the key to the coding system or subject identifiers themselves will be destroyed by shredding the documents so that there is no direct or indirect link to subject identifiers and information.

All data from the study will be kept on encrypted computers belonging to the University, which are stored in secured areas. All electronic study data will be password protected and passwords will be changed on a regular basis.

All data will be de-identified when exported from the REDCap database. Patient data will be analyzed without patient identifiers by assigning study ID subject numbers that are de-linked from patient identifiers. Signed consent forms, and HIPAA forms, will remain in a locked cabinet in the PI's office.

## 3) Plan for Data Analysis

*Statistics:*

The principal investigator will be responsible for analyzing the study data with a biostatistician. For the final analysis, the database will not be unblinded until enrollment, medical review, protocol violations, and data have been collected.

*Sample Size Justification:*

Sample size was calculated assuming the POUR incidence rates of 3% and 13% for the sugammadex and neostigmine groups, respectively. To detect a difference of 10% with 80% power and 5% Type I error rate (one-sided), the estimated sample size is 115 for each group.

The primary outcome is the incidence rates of postoperative urinary retention (POUR) of sugammadex and neostigmine groups. The difference of the incidence rates between groups will be analyzed using the z test with a significance level of 5%.

Based upon a sample size of n=115 patients per group, this study has 80% power and 5% Type I error rate (one-sided) to detect a 10% difference between groups in the incidence of POUR. This calculation is based on prior published research estimating the incidence of POUR to be 3% and 13% for the sugammadex and neostigmine groups, respectively.

**4.b. List of the study intervention(s) being tested or evaluated under this protocol**

☐ **N/A -** this study does not test or evaluate an intervention. Skip to item 4.d.

| # | Study intervention(s) being tested or evaluated under the protocol<br><br>*Add or delete rows as needed* | Affiliate<br><br>Place a check next to institution(s) where the intervention will be performed | Local Standard Practice?<br>Indicate whether the intervention is considered acceptable practice locally for applicable institutions |
|---|---|---|---|
| 1 | Rocuronium + neostigmine | ☐ UTSW | ☐ Yes |
| | | ☒ PHHS | ☒ Yes |
| | | ☐CMC | ☐ Yes |
| | | ☐THR | ☐ Yes |
| | | ☐TSRH | ☐ Yes |
| | | ☐ Other: _____ | ☐ Yes |
| 2 | Rocuronium + sugammadex | ☐ UTSW | ☐ Yes |
| | | ☒ PHHS | ☒ Yes |
| | | ☐CMC | ☐ Yes |
| | | ☐THR | ☐ Yes |
| | | ☐TSRH | ☐ Yes |
| | | ☐ Other: _____ | ☐ Yes |

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**4.c. Risk:Benefit Analysis of study interventions being tested or evaluated under this protocol**

For each study intervention identified in section 6b above, complete a risk:benefit analysis table.

*(Two tables are provided, copy & paste additional tables as needed or delete both tables if this study does not test an intervention)*

**4.c.**
**Study Intervention #1**
**Rocuronium + neostigmine**

| **List each group exposed to this intervention on a separate line.** (e.g., experimental, control, Arm A, Arm B, etc) **Or** state All Groups/Subjects | For each group, list the **benefits** of this intervention. (Benefits can be directly from the intervention or from a monitoring procedure likely to contribute to the subject's well being). If there are no benefits, state "none". |
|---|---|
| Group 1 (NEO) | None |
| | |

**If you are requesting a Waiver of Informed Consent, complete the table below.**

If you have a consent form, **list the reasonably foreseeable risks in the consent form (and do not complete this section).**

List the risks according to the probability (likely, less likely or rare) and magnitude (serious or not serious).
(include: 1) expected adverse events; 2) rare and serious adverse events; 3) all other psychological, social, legal harms)
Do not delete frequency. Frequency must be estimated because it will assist you with determining which adverse events will require prompt reporting.

| | **Not serious** | **Serious** |
|---|---|---|
| **Likely** These risks are expected to occur in more than **20** out of **100** subjects. | • | • |
| | **Not serious** | **Serious** |
| **Less likely** These risks are expected to occur in **5-20** subjects or less out of **100** subjects. | • | • |
| | | **Serious** |
| **Rare** These risks are expected to occur in less than **5** subjects out of **100** | | • |

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| **4.c.**<br>**Study Intervention #1**<br>**Rocuronium + neostigmine** | |
|---|---|
| **List each group exposed to this intervention on a separate line.**<br>(e.g., experimental, control, Arm A, Arm B, etc)<br>**Or** state All Groups/Subjects | For each group, list the **benefits** of this intervention. (Benefits can be directly from the intervention or from a monitoring procedure likely to contribute to the subject's well being). If there are no benefits, state "none". |
| Group 2 (SUG) | This study is not designed to directly benefit the study subjects who participate in this study, but there may be potential for a direct benefit to the patient if they receive sugammadex, based on available literature, which reports that sugammadex is more beneficial in reducing post operative urinary retention. |
| | |

**If you are requesting a Waiver of Informed Consent, complete the table below.**

If you have a consent form, **list the reasonably foreseeable risks in the consent form (and do not complete this section).**

List the risks according to the probability (likely, less likely or rare) and magnitude (serious or not serious).
(include: 1) expected adverse events; 2) rare and serious adverse events; 3) all other psychological, social, legal harms)
Do not delete frequency. Frequency must be estimated because it will assist you with determining which adverse events will require prompt reporting.

| | **Not serious** | **Serious** |
|---|---|---|
| **Likely**<br>These risks are expected to occur in more than **20** out of **100** subjects. | • | • |
| | **Not serious** | **Serious** |
| **Less likely**<br>These risks are expected to occur in **5-20** subjects or less out of **100** subjects. | • | • |
| | | **Serious** |
| **Rare**<br>These risks are expected to occur in less than **5** subjects out of **100** | | • |

**4.d**. List ALL other research procedures or components not listed in table 4.b.
***The combination of Tables 4b and 4d should account for all of the research procedures that will take place during this study.***

Consider grouping similar procedures under a single component (e.g., blood work, CT = safety assessments)

| # | Research component<br>• **individual procedures**<br>*example:*<br>**Eligibility Assessments**<br>• History and physical<br>• Laboratory tests<br>*Add or delete rows as needed* | **Column A**<br>**Local Standard Practice** Indicate the number of times each procedure will be performed as stipulated in the research plan **that would be performed if the participant were not participating in the study.** | **Column B**<br>**Research Only**<br>Indicate the number of times each procedure will be performed solely for research purposes *(meaning that the participant would not undergo the same number of procedures or would not undergo the procedure(s) at the same frequency if they were not participating in the study)* | **Column D**<br>**Risks**<br>**If you are requesting a Waiver of Informed Consent, complete the table below.**<br>List the reasonably expected risks for each procedure or group of procedures under the following categories as appropriate:<br>• Serious and likely;<br>• Serious and less likely;<br>• Serious and rare;<br>• Not serious and likely;<br>• Not serious and less likely |
|---|---|---|---|---|
| 1 | **Research Component** | | | |
| | Intraoperative vitals | Every 3 minutes | | Not serious and less likely |
| | PACU Bladder ultrasound | | 1 | Not serious and less likely |
| 2 | | | | |
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**5. Safety Precautions.** *(Describe safeguards to address the serious risks listed above.)*

**a.** Describe the procedures for protecting against or minimizing any potential risks for each of the more than minimal risk research procedures listed above.

**Potential Risks:**
The additional risks posed by participation in this study are not different than the usual risks associated with surgery and general anesthesia. There is a potential for a direct benefit to the patient if they receive sugammadex, based on available literature, which reports that sugammadex is superior to neostigmine for reversal of neuromuscular blockade [7-17]. The anesthetic management of subjects will not differ from the standard care. Patients will be randomized to receive either neostigmine or sugammadex for reversal of neuromuscular paralysis.

Risk of Sugammadex:
The most common adverse reactions after administration of sugammadex are nausea/vomiting, pain, hypotension, and headache. There is a 0.3% chance of an allergic reaction to sugammadex. Female subjects who are using oral contraceptives will be informed during the consenting process that they will need to use a non-hormonal method of contraception for 7 days if they are randomized to sugammadex. Women who do not wish to do this will not be enrolled in the study. Women who do choose to participate will be provided a letter (in English or Spanish) with this information and phone number of the PI if they have any additional questions.

Psychological Stress
There is minimal risk for psychological stress to the patient as a result of participation in this study. Subjects may refuse to answer any of the questions or take a break or stop participation in the study at any time.

**b.** Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse events, or unanticipated problems involving subjects.

**Subject Safety and Data Monitoring:**
Study oversight will include a Data Safety and Monitoring Board (DSMB). The DSMB will be chaired by a faculty member that is not the PI and will include specialists from different specialties including anesthesiology, critical care medicine, and surgery. The DSMB will meet quarterly as needed to review all patient enrollments. If necessary, the DSMB will meet more often to review specific study subjects, unanticipated events, protocol violations, and adverse events. All study subjects will be reviewed by the DSMB for any study-related adverse outcomes. A written record of all meetings will be kept. The IRB will be notified in writing of any adverse study-related outcomes.

*Blinding/Un-blinding:*
The patient and the postoperative evaluator will be blinded as to which reversal agent the patient receives. The anesthesia team taking care of the patient in the operating room will not be blinded, meaning they will know which reversal agent the patient receives. A member of the research team will provide the randomization envelopes to the anesthesia provider to open to determine which study group the patient has been assigned to. They will then contact IDS Pharmacy for the reversal drug, if necessary.

**c.** Will the safeguards be different between/among groups?

☐ Yes ☒ a No

If yes, describe here

*All literature references.*

1. Huang, L., et al., *Risk factors for postoperative urinary retention in patients undergoing colorectal surgery: a systematic review and meta-analysis.* Int J Colorectal Dis, 2022. **37**(12): p. 2409-2420.
2. Sivasankaran, M.V., T. Pham, and C.M. Divino, *Incidence and risk factors for urinary retention following laparoscopic inguinal hernia repair.* Am J Surg, 2014. **207**(2): p. 288-92.
3. Ziemba-Davis, M., et al., *Identifiable Risk Factors to Minimize Postoperative Urinary Retention in Modern Outpatient Rapid Recovery Total Joint Arthroplasty.* J Arthroplasty, 2019. **34**(7S): p. S343-S347.
4. Mustonen, S., I. Ala-Houhala, and T.L. Tammela, *Proteinuria and renal function during and after acute urinary retention.* J Urol, 1999. **161**(6): p. 1781-4; discussion 1784-5.
5. Igawa, Y., J.J. Wyndaele, and O. Nishizawa, *Catheterization: possible complications and their prevention and treatment.* Int J Urol, 2008. **15**(6): p. 481-5.
6. Lau, H. and D.C. Brooks, *Predictive factors for unanticipated admissions after ambulatory laparoscopic cholecystectomy.* Arch Surg, 2001. **136**(10): p. 1150-3.
7. Awan, F.N., et al., *Factors involved in unplanned admissions from general surgical day-care in a modern protected facility.* Ir Med J, 2013. **106**(5): p. 153-4.
8. Murphy, G.S., et al., *Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit.* Anesth Analg, 2008. **107**(1): p. 130-7.
9. Sauer, M., et al., *The influence of residual neuromuscular block on the incidence of critical respiratory events. A randomised, prospective, placebo-controlled trial.* Eur J Anaesthesiol, 2011. **28**(12): p. 842-8.
10. Thilen, S.R., et al., *2023 American Society of Anesthesiologists practice guidelines for monitoring and antagonism of neuromuscular blockade: A report by the American Society of Anesthesiologists Task Force on Neuromuscular Blockade.* Anesthesiology, 2023. **138**(1): p. 13-41.

11. Scott, A.J., et al., *Prospective Risk Factor Analysis for the Development of Post-operative Urinary Retention Following Ambulatory General Surgery.* World J Surg, 2018. **42**(12): p. 3874-3879.
12. Walter, P.J., et al., *Perioperative anticholinergic medications and risk of catheterization after urogynecologic surgery.* Female Pelvic Med Reconstr Surg, 2014. **20**(3): p. 163-7.
13. Cha, J.-E., et al., *Sugammadex use can decrease the incidence of post-operative urinary retention by avoiding anticholinergics: a retrospective study.* Anesthesia and Pain Medicine, 2018. **13**(1): p. 40-46.
14. Valencia Morales, D.J., et al., *Urinary Retention Following Inguinal Herniorrhaphy: Role of Neuromuscular Blockade Reversal.* Surg Laparosc Endosc Percutan Tech, 2021. **31**(5): p. 613-617.
15. Han, J., et al., *Quality of Recovery after Laparoscopic Cholecystectomy Following Neuromuscular Blockade Reversal with Neostigmine or Sugammadex: A Prospective, Randomized, Controlled Trial.* J Clin Med, 2021. **10**(5).
16. Fitzgerald MP, Stablein U, Brubaker L. *Urinary habits among asymptomatic women*. Am J Obstet Gynecol, 2002. 187(5): p. 1384-1388.
17. Latini JM, Mueller E, Lux MM, Fitzgerald MP, Kreder KJ. *Voiding frequency in a sample of asymptomatic American men.* J Urol, 2004.172(3): p. 980-984.
18. Keskinen H, Helenius L, Pajulo O, Helenius IJ. *Postoperative urinary retention or difficulties to empty the bladder in young patients undergoing posterior spinal fusion for adolescent idiopathic scoliosis.* J Pediatr Surg, 2018. 53(8): p. 1542-1546.
19. Boulis NM, Mian FS, Rodriguez D, Cho E, Hoff JT. *Urinary retention following routine neurosurgical spine procedures.* Surg Neurol, 2001. 55(1): p. 23-28.
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