Journal of Anesthesia (2021) 35:262–269
https://doi.org/10.1007/s00540-021-02910-2

ORIGINAL ARTICLE

Sugammadex versus neostigmine on postoperative pulmonary complications after robot-assisted laparoscopic prostatectomy: a propensity score-matched analysis

Jihion Yu[1] · Jun-Young Park[1] · Yongsoo Lee[1] · Jai-Hyun Hwang[1] · Young-Kug Kim[1]

Received: 19 July 2020 / Accepted: 14 February 2021 / Published online: 8 March 2021

Abstract

Purpose Robot-assisted laparoscopic prostatectomy (RALP) requires particular surgical conditions, such as carbon dioxide pneumoperitoneum and steep Trendelenburg positioning, which may have adverse effects on the respiratory system. The effect of sugammadex on postoperative pulmonary complications (PPCs) is controversial. Therefore, we evaluated the incidence of PPCs according to the type of neuromuscular blockade reversal agents in RALP.

Methods We retrospectively analyzed RALP patients. We compared the incidence of PPCs between patients receiving neostigmine (neostigmine group) and those receiving sugammadex (sugammadex group) as a neuromuscular blockade reversal agent. Propensity score-matched analysis was performed. Other postoperative outcomes, such as duration of hospital stays, major adverse cardiac events during hospital stays, and death during hospital stays, were also compared between the two groups.

Results The incidence of PPCs was 28.9% (137/474) in RALP. The incidence of PPCs was significantly lower in the sugammadex group than in the neostigmine group (18.6% [44/237] vs. 39.2% [93/237], $p < 0.001$). The incidence of atelectasis was significantly lower in the sugammadex group than in the neostigmine group (18.6% vs. 39.2%, $p < 0.001$). The incidence of pneumonia was not significantly different between the sugammadex and neostigmine groups after RALP (0.0% vs. 0.4%, $p > 0.999$). Besides these, other postoperative outcomes were not significantly different between the two groups.

Conclusions The incidence of PPCs after RALP was significantly lower in patients receiving sugammadex than in those receiving neostigmine. These results can provide useful information on the appropriate selection of neuromuscular blockade reversal agents in RALP.

Introduction

Robot-assisted laparoscopic prostatectomy (RALP) has a number of advantages, such as lower perioperative blood loss and transfusion rate and a shorter hospital stay, compared to open prostatectomy in patients with prostate cancer [1, 2]. RALP requires carbon dioxide pneumoperitoneum and steep Trendelenburg positioning. Carbon dioxide pneumoperitoneum can cause hypercarbia and respiratory acidosis. In addition, a steep Trendelenburg position can result in decreased lung volume, lung compliance, functional residual capacity, and vital capacity and increased ventilation–perfusion mismatch and peak airway pressure [3]. Furthermore, most patients undergoing RALP are elderly patients, who have lower lung compliance and pulmonary function [4]. These particular surgical conditions and patient characteristics may compromise the respiratory system and may cause a relatively high incidence of postoperative pulmonary complications (PPCs). Previous studies demonstrated that PPCs occurred in 30.9%–43.3% of patients who underwent RALP [5, 6].

Neostigmine can accelerate neuromuscular function recovery [7]. However, a previous study demonstrated that neostigmine was associated with increased PPCs, such as atelectasis, particularly when used without neuromuscular monitoring [8]. Conversely, sugammadex reportedly induces rapid and complete reversal of even deep neuromuscular blockade by selectively binding with rocuronium [9, 10]. Unlike neostigmine, sugammadex can reverse the effect

✉ Young-Kug Kim
kyk@amc.seoul.kr

[1] Department of Anesthesiology and Pain Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea

of neuromuscular blockade regardless of the depth of the neuromuscular block and reduce the postoperative residual neuromuscular blockade [11–13]. In addition, sugammadex rarely has muscarinic side effects [14]. Despite these advantages of sugammadex, its effect on postoperative outcomes, particularly PPCs, is controversial [15–18]. Moreover, little is known about the difference in the incidence of PPCs according to the type of neuromuscular blockade reversal agents in RALP, which can adversely affect the respiratory system.

Therefore, we compared the incidence of PPCs between patients receiving neostigmine (neostigmine group) and those receiving sugammadex (sugammadex group) as a neuromuscular blockade reversal agent in prostate cancer patients who underwent RALP requiring carbon dioxide pneumoperitoneum and steep Trendelenburg positioning.

Materials and methods

Patients

This was a large, retrospective, observational single-center study of patients who underwent RALP at the Asan Medical Center between January 2019 and March 2020. Patients with incomplete medical records were excluded. This study was approved by the institutional review board at the Asan Medical Center (approval no. 2020–0607), which waived the requirement for written informed consent.

Intraoperative and postoperative protocols

Before the induction of anesthesia, routine monitoring, which included pulse oximetry, electrocardiography, noninvasive blood pressure, end-tidal carbon dioxide concentration, bispectral index (BIS), and train-of-four (TOF) count and ratio, was performed. General anesthesia was induced with 4–5 mg/kg thiopental sodium or 1.5–2 mg/kg propofol. For muscle relaxation, 0.5–0.8 mg/kg rocuronium was used. Radial arterial catheterization was performed to continuously monitor arterial blood pressure. General anesthesia was maintained with 1–3 vol% sevoflurane or 4–6 vol% desflurane with 1–5 ng/mL remifentanil under continuous infusion. Medical air with 50% oxygen was supplied. Tidal volume was adjusted at 6–8 mL per ideal body weight, and the respiratory rate was adjusted to maintain an end-tidal carbon dioxide concentration of 30–40 mmHg while not surpassing a maximum peak airway pressure of 30 cmH_2O. Positive end-expiratory pressure was not applied, and recruitment maneuvers were not performed. The BIS was maintained at 40–60. Rocuronium was administered intermittently to maintain a TOF count of ≤ 2 throughout the surgery. Mean arterial blood pressure was maintained at > 65 mmHg, and heart rate was maintained at 60–100 bpm by administering fluid or a vasopressor/inotropic. The administered fluid was either crystalloid, such as plasma solution A (CJ Pharmaceutical; Seoul, Korea) or Plasma-Lyte 148 (Baxter; Deerfield, IL, USA), or colloid, such as 6% hydroxyethyl starch. The administered vasopressor or inotropic was phenylephrine or ephedrine. Red blood cells were transfused when the hemoglobin level was < 8 g/dL. After skin closure, 40 μg/kg of neostigmine and 8 μg/kg of glycopyrrolate mixture were administered after the TOF count increased to 4; alternatively, 2 mg/kg of sugammadex was administered after TOF count was ≥ 2 to reverse the neuromuscular blockade, as per the anesthesiologist's preference. In addition, extubation was performed when the BIS was > 90 and the TOF ratio was $> 90\%$.

RALP was carried out according to the standard technique of our institution using the da Vinci™ robot system (Intuitive Surgical; Sunnyvale, CA, USA) [19, 20]. Abdominal pressure was maintained at 15 mmHg by insufflating carbon dioxide gas into the intraperitoneal cavity. Patients were positioned in the steep Trendelenburg position (45°). Six trocars were placed, and the prostate was dissected with a transperitoneal antegrade approach. A nerve-sparing procedure was performed, and vesicourethral anastomosis was performed with continuous sutures. Low-risk patients underwent selective pelvic lymph node dissection, and high-risk patients underwent routine pelvic lymph node dissection as described [21]. All RALPs were performed by five highly experienced surgeons.

Not all patients received epidural anesthesia for postoperative pain management. Patients received meperidine 25 mg intravenously upon request from postoperative day 0 to discharge. In addition, all patients routinely received a non-steroidal anti-inflammatory drug (nimesulide) 100 mg orally twice a day from postoperative day 1 to discharge. All patients were encouraged to actively cough and practice deep breathing during postoperative days. From the first postoperative day to the day of discharge, patients were encouraged to ambulate the ward and exercise an inspirometer.

Definition of PPCs

PPCs were defined as the development of one or more of the following within postoperative 7 days [22, 23]: (1) atelectasis defined by computed tomography or chest radiograph; (2) pneumonia defined using US Centers for Disease Control criteria; (3) acute respiratory distress syndrome using the Berlin consensus definition; and (4) pulmonary aspiration with clear clinical history and radiological evidence.

Data collection

Patient demographics and preoperative data included age, body mass index, American Society of Anesthesiologists physical status, comorbidities (hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, cerebrovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, and interstitial pneumonia), smoking history, Gleason score, anti-hormonal therapy application, preoperative laboratory parameters (white blood cell count, neutrophil percentage, lymphocyte percentage, hemoglobin concentration, platelets count, serum albumin level, aspartate aminotransferase, alanine aminotransferase, serum creatinine level, glomerular filtration rate (GFR), serum uric acid level, and serum C-reactive protein level), and pre-induction O_2 saturation. Intraoperative data included inhalation agent type, rocuronium and remifentanil amounts, anesthesia and operation times, infused crystalloid amount, colloid administration rate, red blood cell transfusion rate, and pelvic lymph node dissection. Postoperative data included the meperidine amount. Postoperative outcomes included PPCs, duration of hospital stays (the days from RALP to discharge), major adverse cardiac events during hospital stays, and death during hospital stays. Major adverse cardiac events were defined as one or more of the following: acute myocardial infarction, congestive heart failure, arrhythmia, or nonfatal cardiac arrest [24].

Statistical analysis

Continuous variables were examined by Student's t-test or the Mann–Whitney U test and are expressed as mean ± standard deviation. Categorical variables were examined by the chi-square test or the Fisher's exact test and are expressed as number (percent). All variables including demographic and preoperative data were compared between the neostigmine and sugammadex groups before propensity score matching. The 1:1 propensity score-matched analysis was performed by the nearest neighbor method with a 0.2 caliper size to identify the impact of the neuromuscular blockade reversal agent on PPCs. The propensity score was examined by multiple logistic regression analysis using the following variables: age, body mass index, American Society of Anesthesiologists physical status, comorbidities (hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, cerebrovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, and interstitial pneumonia), smoking history, Gleason score, anti-hormonal therapy application, preoperative laboratory parameters (white blood cell count, neutrophil percentage, lymphocyte percentage, hemoglobin concentration, platelets count, serum albumin level, aspartate aminotransferase, alanine aminotransferase, serum creatinine level, GFR, serum uric acid level, and serum C-reactive protein level), pre-induction O_2 saturation, and inhalation agent. The standardized mean difference was examined to determine the balance between the two groups, and the standardized mean difference of <0.2 was considered to have a sufficient balance between groups. After 1:1 propensity score matching, intraoperative data and postoperative outcomes were compared by McNemar's test for categorical variables and the paired t-test for continuous variables. A p value of <0.05 was considered statistically significant. All statistical analyses were conducted by SPSS® version 21.0 software (IBM; Armonk, NY, USA).

Results

Of the 914 patients who underwent RALP between January 2019 and March 2020, 906 patients were included. Eight patients were excluded due to incomplete medical records. Among these 906 patients, 258 patients received neostigmine and 648 patients received sugammadex as the neuromuscular blockade reversal agent. After 1:1 propensity score matching, patients were divided into the neostigmine group ($n=237$) and the sugammadex group ($n=237$) (Fig. 1).

Before 1:1 propensity score matching, the parameters of hypertension, diabetes mellitus, interstitial pneumonia, anti-hormonal therapy, pre-induction O_2 saturation, and inhalation agent were significantly different between the two

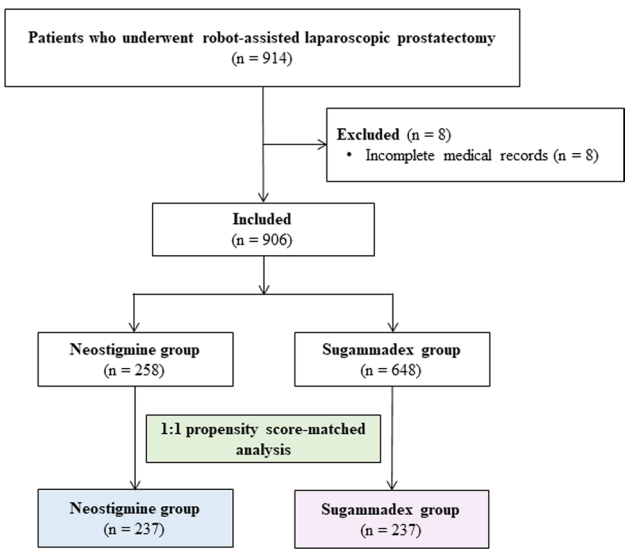

Fig. 1 Flowchart of the study's patients. In total, 914 patients who underwent robot-assisted laparoscopic prostatectomy were evaluated, and 906 patients were included in this study. Patients were divided into the neostigmine group and sugammadex group, and propensity score-matched analysis was performed. The neostigmine group included patients receiving neostigmine as a neuromuscular blockade reversal agent. The sugammadex group included patients receiving sugammadex as a neuromuscular blockade reversal agent

groups (Table 1). After 1:1 propensity score matching, none of the covariates were significantly different, and all were well-balanced with a standardized mean difference of < 0.2 between the two groups (Table 1). After 1:1 propensity score matching, the intraoperative and postoperative data including rocuronium and remifentanil amounts, anesthesia and operative times, crystalloid amount, colloid administration rate, red blood cell transfusion rate, pelvic lymph node dissection, and postoperative meperidine amount were not significantly different between the two groups (Table 2).

Table 1 Demographic and clinical data before and after propensity score matching

Variables	Before propensity score matching				After propensity score matching			
	Neostigmine group ($n=258$)	Sugammadex group ($n=648$)	SMD	p value	Neostigmine group ($n=237$)	Sugammadex group ($n=237$)	SMD	p value
Age (years)	65.7 ± 7.5	66.0 ± 6.7	0.044	0.566	65.9 ± 7.3	66.0 ± 6.9	0.021	0.835
Body mass index (kg/m^2)	25.1 ± 2.9	25.0 ± 2.8	− 0.009	0.740	25.1 ± 3.1	25.0 ± 2.9	− 0.018	0.848
ASA physical status			− 0.115	0.143			0.059	0.652
≤ 2	226 (87.6)	589 (90.9)			209 (88.2)	213 (89.9)		
3	32 (12.4)	59 (9.1)			28 (11.8)	24 (10.1)		
Hypertension	123 (47.7)	199 (30.7)	− 0.367	< 0.001	112 (47.3)	118 (49.8)	0.055	0.648
Diabetes mellitus	47 (8.2)	202 (31.2)	0.279	< 0.001	46 (19.4)	44 (18.6)	− 0.018	0.906
Coronary artery disease	18 (7.0)	38 (5.9)	− 0.047	0.542	18 (7.6)	14 (5.9)	− 0.072	0.572
Atrial fibrillation	9 (3.5)	11 (1.7)	− 0.139	0.130	9 (3.8)	9 (3.8)	0.000	> 0.999
Cerebrovascular disease	16 (6.2)	26 (4.0)	− 0.111	0.164	12 (5.1)	12 (5.1)	0.000	> 0.999
Chronic kidney disease	2 (0.8)	4 (0.6)	− 0.020	> 0.999	2 (0.8)	1 (0.4)	− 0.054	> 0.999
COPD	15 (5.8)	24 (3.7)	− 0.112	0.203	11 (4.6)	8 (3.4)	− 0.067	0.629
Interstitial pneumonia	33 (12.8)	48 (7.4)	− 0.205	0.014	28 (11.0)	21 (8.9)	− 0.080	0.542
Smoking			0.136	0.061			0.029	0.845
Non/Ex-smoker	244 (94.6)	587 (90.6)			224 (94.5)	222 (93.7)		
Current smoker	14 (5.4)	61 (9.4)			13 (5.5)	15 (6.3)		
Gleason score			0.068	0.387			0.065	0.545
≤ 7	217 (84.1)	528 (81.5)			201 (84.8)	195 (82.3)		
≥ 8	41 (15.9)	120 (18.5)			36 (15.2)	42 (17.7)		
Anti-hormonal therapy	2 (0.8)	49 (7.6)	0.256	< 0.001	2 (0.8)	3 (1.3)	0.016	> 0.999
White blood cell (μL)	6012.0 ± 1380.1	6007.7 ± 1521.2	− 0.003	0.969	5946.8 ± 1339.8	5974.3 ± 1455.8	0.018	0.835
Neutrophil (%)	56.0 ± 9.0	56.6 ± 8.7	0.069	0.352	56.3 ± 9.1	56.6 ± 8.3	0.033	0.717
Lymphocyte (%)	32.9 ± 8.4	32.6 ± 7.8	− 0.035	0.638	32.8 ± 8.3	32.6 ± 7.5	− 0.024	0.800
Hemoglobin (g/dL)	14.2 ± 1.3	14.3 ± 1.2	0.112	0.140	14.1 ± 1.3	14.1 ± 1.2	0.007	0.942
Platelet (10^3/μL)	214.1 ± 48.9	221.0 ± 55.5	0.125	0.080	213.5 ± 48.1	217.5 ± 56.1	0.070	0.409
Albumin (g/dL)	3.95 ± 0.30	3.98 ± 0.27	0.112	0.141	3.95 ± 0.31	3.97 ± 0.29	0.068	0.511
AST (IU/L)	22.9 ± 6.2	23.9 ± 8.0	0.126	0.070	22.9 ± 6.1	23.4 ± 7.2	0.066	0.392
ALT (IU/L)	22.9 ± 10.2	23.8 ± 12.0	0.077	0.274	22.9 ± 10.2	24.0 ± 10.4	0.094	0.205
Creatinine (mg/dL)	0.97 ± 0.20	0.97 ± 0.53	0.004	0.949	0.96 ± 0.19	0.94 ± 0.19	− 0.046	0.160
GFR (mL/min/1.73m^2)	81.6 ± 13.8	82.9 ± 13.8	0.091	0.215	82.0 ± 13.4	83.7 ± 13.5	0.120	0.178
Uric acid (mg/dL)	5.3 ± 1.2	5.4 ± 1.3	0.062	0.382	5.3 ± 1.2	5.4 ± 1.4	0.087	0.347
CRP (mg/dL)	0.16 ± 0.21	0.18 ± 0.38	0.067	0.309	0.16 ± 0.22	0.16 ± 0.23	0.001	0.981
Pre-induction O_2 saturation	99.0 ± 0.2	98.4 ± 0.6	− 1.075	< 0.001	99.0 ± 0.1	99.0 ± 0.1	0.000	> 0.999
Inhalation agent			− 0.197	0.011			0.084	0.475
Sevoflurane	185 (71.7)	516 (79.6)			173 (73.0)	165 (69.6)		
Desflurane	73 (28.3)	132 (20.4)			64 (27.0)	72 (30.4)		

Continuous variables are presented as mean ± standard deviation and categorical variables as number (percent). The neostigmine group included patients receiving neostigmine as a neuromuscular blockade reversal agent. The sugammadex group included patients receiving sugammadex as a neuromuscular blockade reversal agent

SMD standardized mean difference, *ASA* American Society of Anesthesiologists, *COPD* chronic obstructive pulmonary disease, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *GFR* glomerular filtration rate, *CRP* C-reactive protein

Table 2 Intraoperative and postoperative data after propensity score matching

Variables	All patients ($n=474$)	Neostigmine group ($n=237$)	Sugammadex group ($n=237$)	p value
Rocuronium amount (mg)	77.5 ± 12.1	76.5 ± 13.4	78.5 ± 10.5	0.078
Remifentanil amount (mg)	0.98 ± 0.32	0.98 ± 0.28	0.98 ± 0.36	0.846
Anesthesia time (min)	168.9 ± 23.7	169.9 ± 23.7	167.8 ± 23.7	0.323
Operation time (min)	147.1 ± 60.7	144.3 ± 50.9	149.9 ± 69.2	0.310
Crystalloid amount (mL)	1011.3 ± 428.0	1005.6 ± 360.4	1016.9 ± 486.9	0.785
Colloid administration rate	7 (1.5)	3 (1.3)	4 (1.7)	> 0.999
Red blood cell transfusion rate	0 (0)	0 (0)	0 (0)	> 0.999
Pelvic lymph node dissection	422 (89.0)	207 (87.3)	215 (90.7)	0.280
Postoperative meperidine amount (mg)	15.5 ± 15.2	14.1 ± 14.8	16.8 ± 15.6	0.063

Continuous variables are presented as mean ± standard deviation and categorical variables as number (percent). The neostigmine group included patients receiving neostigmine as a neuromuscular blockade reversal agent. The sugammadex group included patients receiving sugammadex as a neuromuscular blockade reversal agent

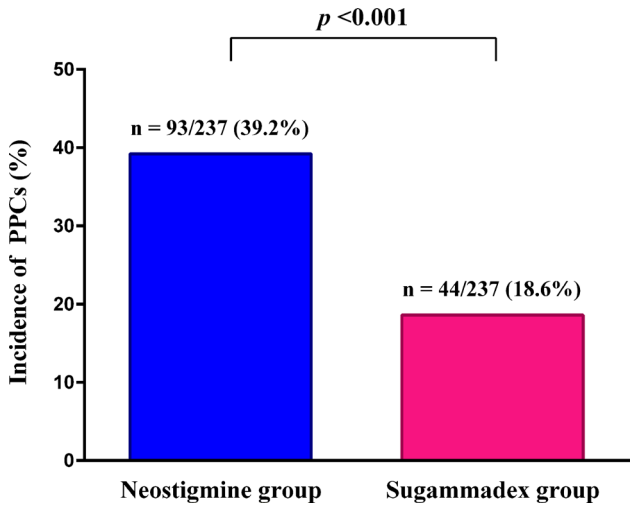

Fig. 2 Comparison of the incidence of PPCs between the neostigmine group and sugammadex group. The neostigmine group included patients receiving neostigmine as a neuromuscular blockade reversal agent. The sugammadex group included patients receiving sugammadex as a neuromuscular blockade reversal agent. *PPC* postoperative pulmonary complication

The overall incidence of PPCs was 28.9% (137/474) in RALP. The incidence of PPCs was significantly lower in the sugammadex group than in the neostigmine group (18.6% vs. 39.2%, $p<0.001$) (Fig. 2). The incidence of atelectasis was significantly lower in the sugammadex group than in the neostigmine group after RALP (18.6% vs. 39.2%, $p<0.001$). Atelectasis occurred in 94.2% (129/137) of patients on the first postoperative day and in 5.8% (8/137) of patients on the second postoperative day. However, the incidence of pneumonia was not significantly different between the sugammadex and neostigmine groups after RALP (0.0% vs. 0.4%, $p>0.999$).

In addition, duration of hospital stays, major adverse cardiac events during hospital stays, and death during hospital stays were not significantly different between the two groups before and after 1:1 propensity score matching (Table 3).

Table 3 Postoperative outcomes

Variables	Before propensity score matching			After propensity score matching		
	Neostigmine group ($n=258$)	Sugammadex group ($n=648$)	p value	Neostigmine group ($n=237$)	Sugammadex group ($n=237$)	p value
Postoperative pulmonary complications	98 (38.0)	157 (24.2)	< 0.001	93 (39.2)	44 (18.6)	< 0.001
Duration of hospital stays (days)	5.6 ± 1.7	5.8 ± 1.8	0.193	5.6 ± 1.7	5.7 ± 1.6	0.383
Major adverse cardiac events	0 (0.0)	3 (0.5)	0.562	0 (0.0)	0 (0.0)	> 0.999
Death	1 (0.4)	1 (0.2)	> 0.999	0 (0.0)	1 (0.4)	> 0.999

Continuous variables are presented as mean ± standard deviation and categorical variables as number (percent). The neostigmine group included patients receiving neostigmine as a neuromuscular blockade reversal agent. The sugammadex group included patients receiving sugammadex as a neuromuscular blockade reversal agent

Discussion

In this propensity score-matched study, we found that the overall incidence of PPCs was 28.9% in RALP and that the incidence of PPCs was significantly lower in patients receiving sugammadex than in those receiving neostigmine as a neuromuscular blockade reversal agent during RALP requiring carbon dioxide pneumoperitoneum and a steep Trendelenburg position.

RALP has gained increasing attention because it offers advantages of improved visualization of the surgical field, lower intraoperative blood loss, and shorter duration of hospital stays in comparison to open prostatectomy [1]. Therefore, RALP is more commonly performed in prostate cancer patients [1]. Previous studies have reported the incidence of PPCs as 30.9%–43.3% in patients who underwent RALP [5, 6]. Consistent with previous reports [5, 6], we found that the overall incidence of PPCs was 28.9% in our study. To optimize the surgical field, RALP requires carbon dioxide pneumoperitoneum of 15 mmHg and a steep Trendelenburg position of 45°. Therefore, the lungs and diaphragm are lifted by intraperitoneal organs, and consequently, lung compliance and functional residual capacity are reduced, and respiratory acidosis is induced [25, 26]. Furthermore, most older prostate cancer patients undergo RALP, and they typically have lower lung compliance and relatively compromised pulmonary function [4]. In the present study, the mean ages of patients were 66.0 years and 65.9 years in the sugammadex and neostigmine groups, respectively. In RALP, the relatively high incidence of PPCs could be due to surgical conditions and patient characteristics. Therefore, meticulous anesthetic and surgical management to reduce the incidence of PPCs are needed in patients undergoing RALP.

In the present study, we found that sugammadex administration was associated with a lower incidence of PPCs compared to neostigmine administration in patients who underwent RALP. Sugammadex rapidly reverses steroidal non-depolarizing neuromuscular blockers by selectively binding to these neuromuscular blockers [10, 27]. Sugammadex is neither involved with cholinergic mechanisms nor does it produce cholinergic side effects [27]. Postoperative residual neuromuscular block is associated with postoperative complications, such as upper airway obstruction, hypoxemia, atelectasis, and pneumonia [28–32]. Sugammadex is effective even in cases with profound blockades and can reduce residual neuromuscular block. However, there is still debate regarding the effect of neuromuscular blockade reversal agents on PPCs [15–18]. In line with the present study, a retrospective matched-cohort analysis revealed that sugammadex administration was associated with a significantly lower incidence of PPCs, such as pneumonia and respiratory failure, in non-cardiac surgical procedures [15]. In addition, a previous randomized study demonstrated that sugammadex administration was associated with faster reversal of moderate neuromuscular blockade and a decreased incidence of postoperative hypoxia compared with neostigmine administration in thoracic surgery with single-lung ventilation [16]. Conversely, a multicenter, prospective, observational study demonstrated no difference in the incidence of PPCs between neostigmine and sugammadex administration [17]. Another randomized controlled trial showed no differences in pulmonary functions evaluated by spirometry after major abdominal surgery between sugammadex and neostigmine administration [18]. These inconsistent results may, at least in part, be induced by different surgical conditions and patient characteristics. Our study population comprised older patients (mean ages: 66.0 years in the sugammadex group and 65.9 years in the neostigmine group), and specific surgical conditions, such as carbon dioxide pneumoperitoneum and steep Trendelenburg positioning, were needed during the intraoperative period. Therefore, in older patients undergoing RALP, sugammadex administration seems to have a beneficial effect on PPCs.

The most common pulmonary complication in the present study was atelectasis, and its incidence was significantly lower in the sugammadex group (18.6%) than in the neostigmine group (39.2%). Reduction in diaphragm activity is associated with the postoperative development of atelectasis [33]. The use of sugammadex can improve electromyographic activity of the diaphragm and intercostal muscles, enable higher tidal volumes, and improve the ability to remove secretions [34, 35]. Therefore, sugammadex administration may be protective against the development of atelectasis.

The present study has inevitable limitations due to its retrospective study design. There may have been a possible selection bias and confounders that could influence the incidence of PPCs. In particular, the pulmonary function test was not routinely performed in RALP, which may have influenced our results. However, we included almost all possible variables and performed a propensity score-matched analysis. Therefore, we minimized the selection bias in the present study. Second, because the present study was performed at a single large center, the results should be interpreted carefully. Third, the beneficial effect of sugammadex on the reduction of PPCs in this study was almost limited to the reduction of atelectasis. Our results need to be interpreted cautiously.

Conclusion

The overall incidence of PPCs was 28.9% in RALP. The incidence of PPCs was significantly lower in patients receiving sugammadex than in those receiving neostigmine while

undergoing RALP. These results provide useful information on the appropriate selection of neuromuscular blockade reversal agents in prostate cancer patients undergoing RALP who are at a higher risk of developing PPCs because of specific surgical conditions, such as carbon dioxide pneumoperitoneum and steep Trendelenburg positioning, and generally being of advanced age.

Acknowledgements None.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest.

References

1. Novara G, Ficarra V, Rosen RC, Artibani W, Costello A, Eastham JA, Graefen M, Guazzoni G, Shariat SF, Stolzenburg JU, Van Poppel H, Zattoni F, Montorsi F, Mottrie A, Wilson TG. Systematic review and meta-analysis of perioperative outcomes and complications after robot-assisted radical prostatectomy. Eur Urol. 2012;62:431–52.
2. Ilic D, Evans SM, Allan CA, Jung JH, Murphy D, Frydenberg M. Laparoscopic and robot-assisted vs open radical prostatectomy for the treatment of localized prostate cancer: a Cochrane systematic review. BJU Int. 2018;121:845–53.
3. Kilic OF, Börgers A, Köhne W, Musch M, Kröpfl D, Groeben H. Effects of steep Trendelenburg position for robotic-assisted prostatectomies on intra- and extrathoracic airways in patients with or without chronic obstructive pulmonary disease. Br J Anaesth. 2015;114:70–6.
4. Pienta KJ, Esper PS. Risk factors for prostate cancer. Ann Intern Med. 1993;118:793–803.
5. Yu J, Park JY, Kim DH, Kim S, Hwang JH, Seo H, Kim YK. Incidence and risk factors of pulmonary complications after robot-assisted laparoscopic prostatectomy: a retrospective observational analysis of 2208 patients at a large single center. J Clin Med. 2019;8.
6. Choi E-S, Oh A-Y, In C-B, Ryu J-H, Jeon Y-T, Kim H-G. Effects of recruitment manoeuvre on perioperative pulmonary complications in patients undergoing robotic assisted radical prostatectomy: a randomised single-blinded trial. PloS one. 2017;12:e0183311.
7. Purdy R, Bevan DR, Donati F, Lichtor JL. Early reversal of rapacuronium with neostigmine. Anesthesiology. 1999;91:51–7.
8. Sasaki N, Meyer MJ, Malviya SA, Stanislaus AB, MacDonald T, Doran ME, Igumenshcheva A, Hoang AH, Eikermann M. Effects of neostigmine reversal of nondepolarizing neuromuscular blocking agents on postoperative respiratory outcomes: a prospective study. Anesthesiology. 2014;121:959–68.
9. Stair C, Fernandez-Bustamante A. Sugammadex, the first selective relaxant binding agent for neuromuscular block reversal. Drugs Today (Barc). 2012;48:405–13.
10. Gijsenbergh F, Ramael S, Houwing N, van Iersel T. First human exposure of Org 25969, a novel agent to reverse the action of rocuronium bromide. Anesthesiology. 2005;103:695–703.
11. Brueckmann B, Sasaki N, Grobara P, Li MK, Woo T, de Bie J, Maktabi M, Lee J, Kwo J, Pino R, Sabouri AS, McGovern F, Staehr-Rye AK, Eikermann M. Effects of sugammadex on incidence of postoperative residual neuromuscular blockade: a randomized, controlled study. Br J Anaesth. 2015;115:743–51.
12. Geldner G, Niskanen M, Laurila P, Mizikov V, Hubler M, Beck G, Rietbergen H, Nicolayenko E. A randomised controlled trial comparing sugammadex and neostigmine at different depths of neuromuscular blockade in patients undergoing laparoscopic surgery. Anaesthesia. 2012;67:991–8.
13. Flockton EA, Mastronardi P, Hunter JM, Gomar C, Mirakhur RK, Aguilera L, Giunta FG, Meistelman C, Prins ME. Reversal of rocuronium-induced neuromuscular block with sugammadex is faster than reversal of cisatracurium-induced block with neostigmine. Br J Anaesth. 2008;100:622–30.
14. Kopman AF. Sugammadex: a revolutionary approach to neuromuscular antagonism. Anesthesiology. 2006;104:631–3.
15. Kheterpal S, Vaughn MT, Dubovoy TZ, Shah NJ, Bash LD, Colquhoun DA, Shanks AM, Mathis MR, Soto RG, Bardia A, Bartels K, McCormick PJ, Schonberger RB, Saager L. Sugammadex versus neostigmine for reversal of neuromuscular blockade and postoperative pulmonary complications (STRONGER): a multicenter matched cohort analysis. Anesthesiology. 2020;132:1371–81.
16. Moon TS, Reznik S, Pak T, Jan K, Pruszynski J, Kim A, Smith KM, Lu R, Chen J, Gasanova I, Fox PE, Ogunnaike B. Sugammadex versus neostigmine for reversal of rocuronium-induced neuromuscular blockade: a randomized, double-blinded study of thoracic surgical patients evaluating hypoxic episodes in the early postoperative period. J Clin Anesth. 2020;64:109804.
17. Kirmeier E, Eriksson LI, Lewald H, Jonsson Fagerlund M, Hoeft A, Hollmann M, Meistelman C, Hunter JM, Ulm K, Blobner M. Post-anaesthesia pulmonary complications after use of muscle relaxants (POPULAR): a multicentre, prospective observational study. Lancet Respir Med. 2019;7:129–40.
18. Alday E, Muñoz M, Planas A, Mata E, Alvarez C. Effects of neuromuscular block reversal with sugammadex versus neostigmine on postoperative respiratory outcomes after major abdominal surgery: a randomized-controlled trial. Canadian J Anesthesia. 2019;66:1328–37.
19. Kim SC, Song C, Kim W, Kang T, Park J, Jeong IG, Lee S, Cho YM, Ahn H. Factors determining functional outcomes after radical prostatectomy: robot-assisted versus retropubic. Eur Urol. 2011;60:413–9.
20. Jeong IG, Yoo S, Lee C, Kim M, You D, Song C, Park S, Hong JH, Ahn H, Kim CS. Obesity as a risk factor for unfavorable disease in men with low risk prostate cancer and its relationship with anatomical location of tumor. J Urol. 2017;198:71–8.
21. D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, Broderick GA, Tomaszewski JE, Renshaw AA, Kaplan I, Beard CJ, Wein A. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA. 1998;280:969–74.
22. Abbott TEF, Fowler AJ, Pelosi P, Gama de Abreu M, Moller AM, Canet J, Creagh-Brown B, Mythen M, Gin T, Lalu MM, Futier E, Grocott MP, Schultz MJ, Pearse RM, St EPCG. A systematic review and consensus definitions for standardised end-points in perioperative medicine: pulmonary complications. Br J Anaesth. 2018;120:1066–79.
23. Jammer I, Wickboldt N, Sander M, Smith A, Schultz MJ, Pelosi P, Leva B, Rhodes A, Hoeft A, Walder B, Chew MS, Pearse RM. European Society of Anaesthesiology (ESA) and the European Society of Intensive Care Medicine (ESICM); European Society of Anaesthesiology; European Society of Intensive Care Medicine. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures. Eur J Anaesthesiol. 2015;32:88–105.
24. Kristensen SD, Knuuti J, Saraste A, Anker S, Botker HE, Hert SD, Ford I, Gonzalez-Juanatey JR, Gorenek B, Heyndrickx GR,

Hoeft A, Huber K, Iung B, Kjeldsen KP, Longrois D, Luscher TF, Pierard L, Pocock S, Price S, Roffi M, Sirnes PA, Sousa-Uva M, Voudris V, Funck-Brentano C. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J. 2014;35:2383–431.

25. Awad H, Walker CM, Shaikh M, Dimitrova GT, Abaza R, O'Hara J. Anesthetic considerations for robotic prostatectomy: a review of the literature. J Clin Anesth. 2012;24:494–504.
26. Fitzgerald SD, Andrus CH, Baudendistel LJ, Dahms TE, Kaminski DL. Hypercarbia during carbon dioxide pneumoperitoneum. Am J Surg. 1992;163:186–90.
27. Nicholson WT, Sprung J, Jankowski CJ. Sugammadex: a novel agent for the reversal of neuromuscular blockade. Pharmacotherapy. 2007;27:1181–8.
28. Bulka CM, Terekhov MA, Martin BJ, Dmochowski RR, Hayes RM, Ehrenfeld JM. Nondepolarizing neuromuscular blocking agents, reversal, and risk of postoperative pneumonia. Anesthesiology. 2016;125:647–55.
29. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. Anesth Analg. 2008;107:130–7.
30. Murphy GS, Szokol JW, Franklin M, Marymont JH, Avram MJ, Vender JS. Postanesthesia care unit recovery times and neuromuscular blocking drugs: a prospective study of orthopedic surgical patients randomized to receive pancuronium or rocuronium. Anesth Analg. 2004;98:193–200.
31. Martinez-Ubieto J, Ortega-Lucea S, Pascual-Bellosta A, Arazo-Iglesias I, Gil-Bona J, Jimenez-Bernardó T, Muñoz-Rodriguez L. Prospective study of residual neuromuscular block and postoperative respiratory complications in patients reversed with neostigmine versus sugammadex. Minerva Anestesiol. 2016;82:735–42.
32. Berg H, Roed J, Viby-Mogensen J, Mortensen CR, Engbaek J, Skovgaard LT, Krintel JJ. Residual neuromuscular block is a risk factor for postoperative pulmonary complications: a prospective, randomised, and blinded study of postoperative pulmonary complications after atracurium, vecuronium and pancuronium. Acta Anaesthesiol Scand. 1997;41:1095–103.
33. Karayiannakis AJ, Makri GG, Mantzioka A, Karousos D, Karatzas G. Postoperative pulmonary function after laparoscopic and open cholecystectomy. Br J Anaesth. 1996;77:448–52.
34. Cammu G, Schepens T, De Neve N, Wildemeersch D, Foubert L, Jorens PG. Diaphragmatic and intercostal electromyographic activity during neostigmine, sugammadex and neostigmine-sugammadex-enhanced recovery after neuromuscular blockade: a randomised controlled volunteer study. Eur J Anaesthesiol. 2017;34:8–15.
35. Togioka BM, Yanez D, Aziz MF, Higgins JR, Tekkali P, Treggiari MM. Randomised controlled trial of sugammadex or neostigmine for reversal of neuromuscular block on the incidence of pulmonary complications in older adults undergoing prolonged surgery. Br J Anaesth. 2020;124:553–61.