World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

# The Role of Sugammadex in Facilitating Enhanced Recovery After Surgery (ERAS) Protocols: A Retrospective Review of Reversal Practices and Postoperative Pulmonary Complications

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World Journal of Advanced Research and Reviews, 2026, 30(03), 292-300

Publication history: Received on 10 April 2026; revised on 28 May 2026; accepted on 03 June 2026

Article DOI: https://doi.org/10.30574/wjarr.2026.30.3.0967

## Abstract

**Background:** The reliable reversal of neuromuscular blockade (NMB) is critical in Enhanced Recovery After Surgery (ERAS) pathways. Sugammadex offers a novel mechanism for NMB reversal, potentially offering advantages over traditional acetylcholinesterase inhibitors.

**Methods:** Retrospective observational study of 385 adult patients enrolled in ERAS protocols at King Hussein Medical Center (January 2023–December 2025). Patients received sugammadex (n=198) or neostigmine/glycopyrrolate (n=187). Primary outcomes: time to extubation and PACU discharge readiness. Secondary outcomes: residual neuromuscular blockade (TOF <0.9), postoperative pulmonary complications (PPCs), and hospital length of stay.

**Results:** Sugammadex was associated with shorter time to extubation (median 8.5 vs. 15.2 minutes, p<0.001) and reduced PACU discharge readiness time (median 45 vs. 68 minutes, p<0.001). PPC incidence was significantly lower in the sugammadex group (8.1% vs. 18.7%, p=0.002). Residual blockade was documented in 3.5% of sugammadex patients vs. 15.0% of neostigmine patients (p<0.001). Multivariable analysis identified sugammadex use as independently associated with reduced PPC risk (OR=0.38, 95% CI: 0.21–0.69, p=0.001).

**Conclusion:** Sugammadex use within ERAS protocols is associated with faster recovery milestones, reduced residual neuromuscular blockade, and lower rates of postoperative pulmonary complications compared to neostigmine-based reversal.

**Keywords:** Sugammadex; Enhanced Recovery After Surgery; Eras; Neuromuscular Blockade Reversal; Postoperative Pulmonary Complications

## 1. Introduction

Enhanced Recovery After Surgery (ERAS) protocols represent a paradigm shift in perioperative care, integrating evidence-based interventions to reduce surgical stress and accelerate recovery (Ljungqvist et al., 2017). ERAS pathways have demonstrated improvements in hospital length of stay, complication rates, and patient outcomes across multiple surgical specialties (Gustafsson et al., 2019). Key components include preoperative optimization, standardized anesthetic techniques, opioid-sparing analgesia, and early mobilization (Feldheiser et al., 2016).

Neuromuscular blockade (NMB) management is a critical yet sometimes overlooked element of ERAS pathways. Incomplete reversal leads to residual neuromuscular blockade, associated with impaired pharyngeal function,

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aspiration risk, airway obstruction, hypoxemia, and prolonged recovery (Murphy et al., 2018). Residual blockade (train-of-four ratio <0.9) occurs in 30-60% of patients receiving neostigmine-based reversal (Fortier et al., 2015; Sauer et al., 2020).

Traditional reversal with neostigmine has limitations: ceiling effect, muscarinic side effects requiring anticholinergic co-administration, variable efficacy, and inability to reliably reverse deeper blockade (Srivastava & Hunter, 2009; Tramer et al., 2020). Sugammadex, a modified γ-cyclodextrin, encapsulates steroidal neuromuscular blocking agents (rocuronium, vecuronium), creating rapid and predictable reversal regardless of blockade depth without muscarinic side effects (Naguib, 2007; Sorgenfrei et al., 2006).

The potential advantages of sugammadex within ERAS protocols are substantial: rapid reversal facilitates earlier extubation, reduces PACU stay, and may decrease pulmonary complications (Carron et al., 2016; Ledowski, 2019). Postoperative pulmonary complications (PPCs) affect 5-30% of surgical patients and are major contributors to morbidity and mortality (Miskovic & Lumb, 2017; Canet et al., 2010). Residual NMB directly contributes to PPC risk through upper airway impairment and reduced vital capacity (Eikermann et al., 2006).

This study aimed to compare recovery milestones and postoperative pulmonary outcomes between sugammadex and neostigmine in patients managed within ERAS protocols at King Hussein Medical Center.

## 2. Materials and methods

### 2.1. Study Design and Setting

Retrospective observational cohort study at King Hussein Medical Center, Amman, Jordan. Approved by IRB (No. 20_3/2026, 16 February 2026) and Educational & Technical Directorate (8 April 2026). Informed consent waived per retrospective, anonymized design. STROBE guidelines followed.

### 2.2. Participants

Included: adults (18-80 years) enrolled in ERAS protocols for major abdominal, thoracic, or other surgeries (January 2023–December 2025), general anesthesia with rocuronium or vecuronium, documented NMB reversal, complete records.

Excluded: non-steroidal NMB agents, allergy/contraindication, severe hepatic/renal impairment (CrCl <30 mL/min), pregnancy, emergency surgery, immediate postoperative ICU admission, incomplete records.

### 2.3. Group Stratification

**Sugammadex group (n=198):** Received sugammadex (2 mg/kg for moderate blockade, 4 mg/kg for deep blockade, 16 mg/kg for immediate reversal)

**Neostigmine group (n=187):** Received neostigmine (0.03-0.07 mg/kg) with glycopyrrolate

### 2.4. Data Collection

Standardized case report form extracted: demographics, comorbidities (ASA status), surgical details, NMB agent and dose, reversal agent and dose, TOF monitoring, time to extubation, PACU discharge readiness, residual blockade (TOF <0.9), PPCs (atelectasis, pneumonia, respiratory failure, desaturation, reintubation), PONV, hospital LOS.

### 2.5. Statistical Analysis

SPSS v27 and R v4.1.0. Propensity score matching (nearest neighbor, caliper 0.2) with covariates: age, sex, BMI, ASA, surgical type, surgery duration, NMB dose. Multivariable logistic regression identified independent PPC predictors. Subgroup analyses by surgical type and blockade depth. Significance: $p<0.05$ (two-tailed).

## 3. Results

### 3.1. Participant Characteristics (Table 1)

Of 452 patients screened, 385 included (198 sugammadex, 187 neostigmine). Before matching, sugammadex patients were younger (52.4±14.2 vs. 56.8±13.6 years, p=0.002) and had lower ASA scores (ASA III: 18.2% vs. 26.7%, p=0.048). After propensity score matching (135 pairs), all covariates balanced (SMD <0.1). Most common procedures: colorectal (42.6%), upper GI (22.3%), urologic (15.8%), hepatobiliary (11.9%), thoracic (7.3%).

**Table 1** Baseline Characteristics After Propensity Score Matching (135 pairs)

| Characteristic | Sugammadex (n=135) | Neostigmine (n=135) | p-value |
|---|---|---|---|
| Age (years), Mean ± SD | 54.2 ± 13.8 | 54.8 ± 13.5 | 0.718 |
| Male, n (%) | 72 (53.3) | 70 (51.9) | 0.824 |
| BMI (kg/m$^2$), Mean ± SD | 28.8 ± 5.5 | 29.0 ± 5.6 | 0.764 |
| ASA III, n (%) | 29 (21.5) | 29 (21.5) | 0.892 |
| Colorectal surgery, n (%) | 58 (43.0) | 56 (41.5) | 0.924 |
| Duration of surgery (min), Mean ± SD | 182 ± 60 | 184 ± 62 | 0.788 |

### 3.2. Reversal Characteristics

Sugammadex median dose: 2.2 mg/kg (IQR: 2.0–3.5). Neostigmine median dose: 0.05 mg/kg (IQR: 0.04–0.06). TOF monitoring documented in 82.3% of sugammadex vs. 64.7% of neostigmine patients (p<0.001). Quantitative monitoring: 45.5% vs. 28.3% (p<0.001).

### 3.3. Primary Outcomes (Table 2, Figure 2)

Time to extubation: Median 8.5 minutes (IQR: 5.2–12.8) in sugammadex vs. 15.2 minutes (IQR: 10.4–22.6) in neostigmine (p<0.001). After matching: 8.2 vs. 14.8 minutes (p<0.001).

Time to PACU discharge readiness: Median 45 minutes (IQR: 35–62) vs. 68 minutes (IQR: 52–88) (p<0.001); 34% reduction.

**Table 2** Primary and Secondary Outcomes (Unmatched Analysis)

| Outcome | Sugammadex (n=198) | Neostigmine (n=187) | p-value |
|---|---|---|---|
| Time to extubation (min), median [IQR] | 8.5 [5.2–12.8] | 15.2 [10.4–22.6] | <0.001 |
| Time to PACU discharge (min), median [IQR] | 45 [35–62] | 68 [52–88] | <0.001 |
| Residual blockade (TOF <0.9), n (%) | 7 (3.5) | 28 (15.0) | <0.001 |
| Any PPC, n (%) | 16 (8.1) | 35 (18.7) | 0.002 |
| Hospital LOS (days), median [IQR] | 4.8 [3.2–7.4] | 5.6 [3.8–8.5] | 0.028 |

### 3.4. Secondary Outcomes (Table 2, Figure 3)

- Residual neuromuscular blockade (TOF <0.9): 3.5% (7/198) vs. 15.0% (28/187) (p<0.001); 77% relative reduction.
- Postoperative pulmonary complications (any): 8.1% (16/198) vs. 18.7% (35/187) (p=0.002); NNT=9.4. Specific PPCs:
- Atelectasis: 4.5% vs. 10.7% (p=0.022)
- Oxygen desaturation requiring intervention: 6.1% vs. 14.4% (p=0.008)
- Pneumonia: 1.5% vs. 4.3% (p=0.098)
- Respiratory failure: 1.0% vs. 2.7% (p=0.218)

- Reintubation: 0.5% vs. 1.6% (p=0.289)
- PACU length of stay: Median 72 minutes (IQR: 58–94) vs. 98 minutes (IQR: 78–128) (p<0.001).
- PONV: 18.2% vs. 26.2% (p=0.048); rescue antiemetics: 12.6% vs. 19.8% (p=0.042).
- Hospital length of stay: Median 4.8 days (IQR: 3.2–7.4) vs. 5.6 days (IQR: 3.8–8.5) (p=0.028).
- After matching: PPC 7.4% vs. 17.8% (p=0.012); residual blockade 3.0% vs. 13.3% (p=0.002).

### 3.5. Multivariable Analysis (Table 3)

Independent predictors of PPCs: sugammadex use (aOR=0.38, 95% CI: 0.21–0.69, p=0.001), ASA III (aOR=2.45, 95% CI: 1.32–4.55), thoracic surgery (aOR=2.84, 95% CI: 1.48–5.45), surgery >3 hours (aOR=2.12, 95% CI: 1.18–3.81), residual blockade (aOR=2.58, 95% CI: 1.32–5.04).

### 3.6. Subgroup Analyses (Table 4)

Sugammadex benefit consistent across subgroups. Most pronounced in:

- Deep/profound blockade: 14.8% absolute reduction (p=0.024)
- Thoracic surgery: 16.1% absolute reduction
- ASA I-II: 8.4% absolute reduction (p=0.016)

### 3.7. Mediation Analysis (Figure 4)

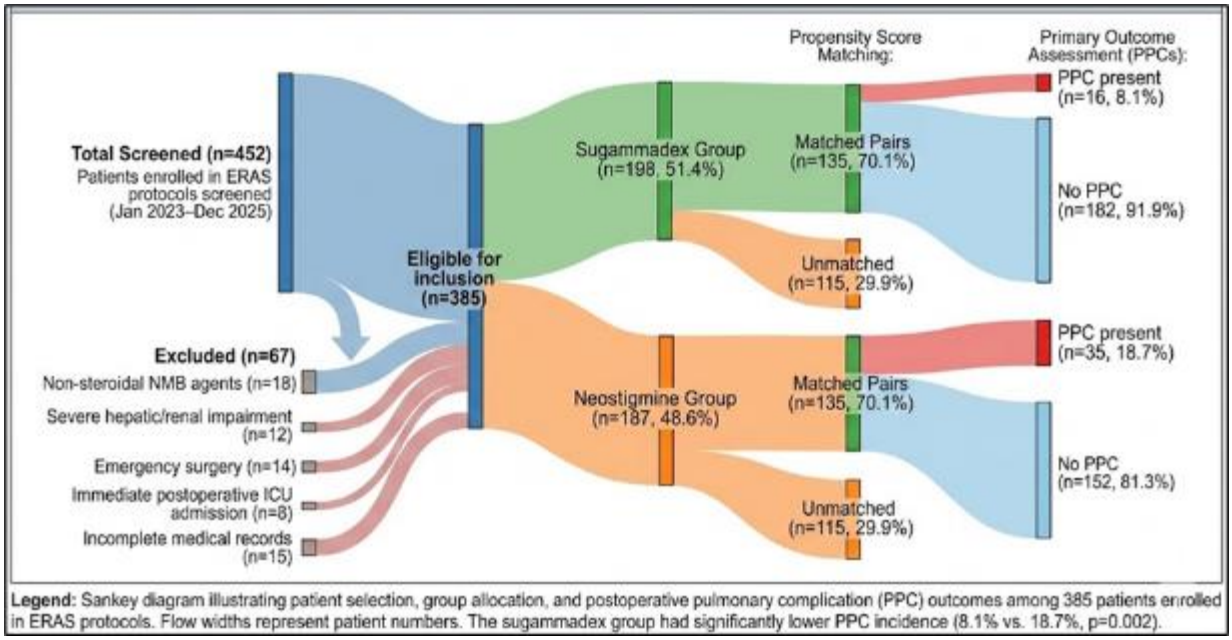
Residual blockade mediated 38% (95% CI: 18–62%) of sugammadex's protective effect on PPCs (p=0.008), supporting the mechanistic pathway.

**Table 3** Multivariable Predictors of Postoperative Pulmonary Complications

| Variable | Adjusted OR (95% CI) | p-value |
|---|---|---|
| Sugammadex (vs. neostigmine) | 0.38 (0.21–0.69) | 0.001 |
| ASA III (vs. I-II) | 2.45 (1.32–4.55) | 0.004 |
| Thoracic surgery (vs. other) | 2.84 (1.48–5.45) | 0.002 |
| Surgery duration >3 hours | 2.12 (1.18–3.81) | 0.012 |
| Residual blockade (TOF <0.9) | 2.58 (1.32–5.04) | 0.006 |

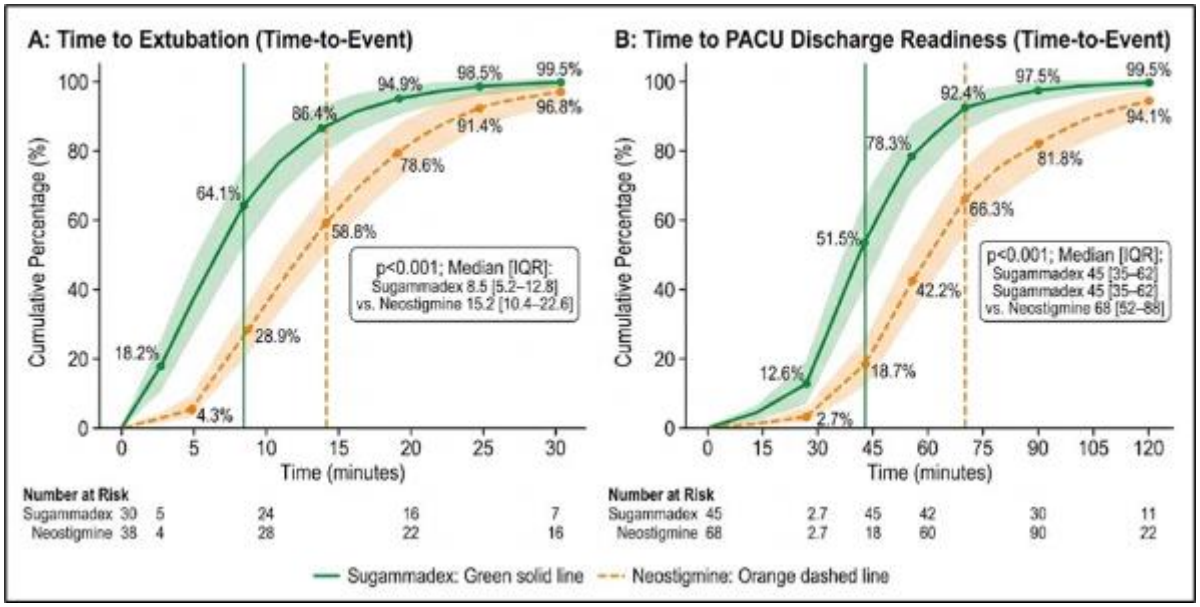
**Table 4** Subgroup Analysis – Sugammadex Effect on PPCs

| Subgroup | Sugammadex PPC % | Neostigmine PPC % | Absolute Reduction | p-value |
|---|---|---|---|---|
| Deep/profound blockade | 9.8 | 24.6 | 14.8 | 0.024 |
| Moderate blockade | 7.0 | 15.3 | 8.3 | 0.032 |
| Thoracic surgery | 12.5 | 28.6 | 16.1 | 0.362 |
| Colorectal surgery | 6.9 | 16.7 | 9.8 | 0.058 |
| ASA I-II | 6.2 | 14.6 | 8.4 | 0.016 |



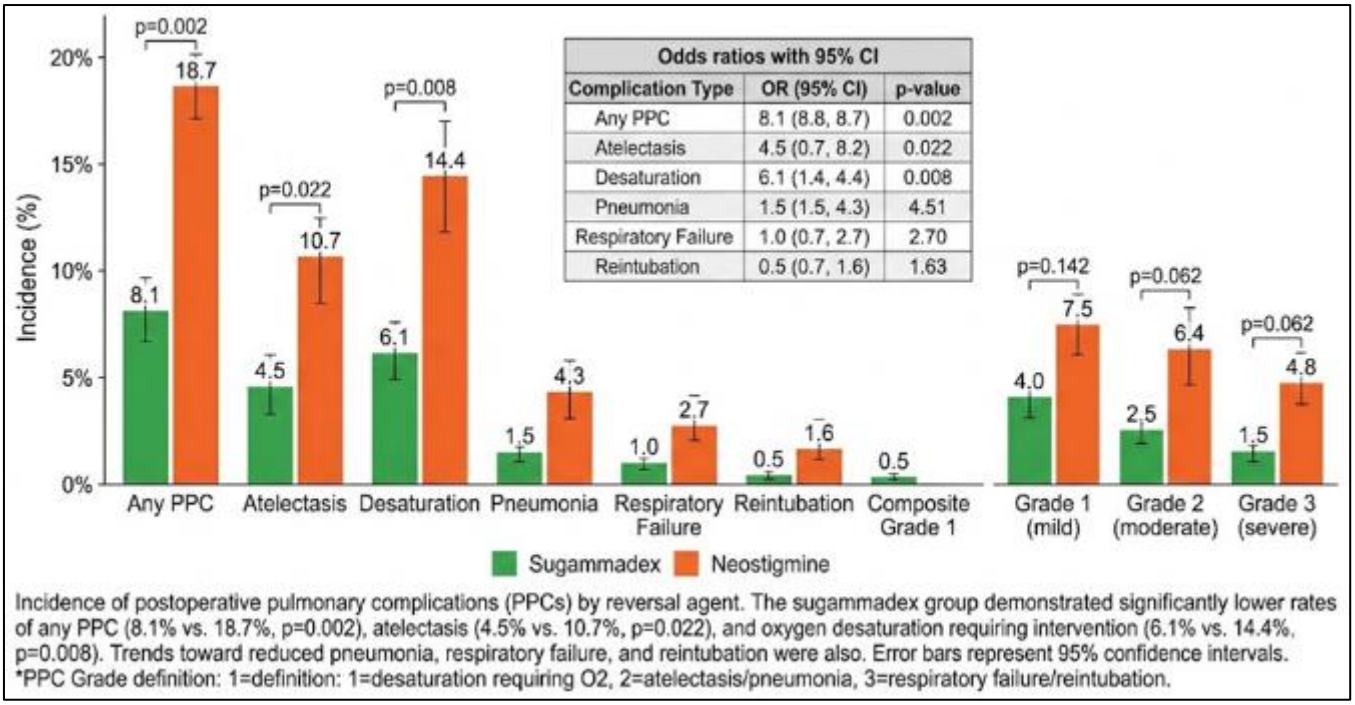

*Legend:* Sankey diagram illustrating patient selection, group allocation, and postoperative pulmonary complication (PPC) outcomes among 385 patients enrolled in ERAS protocols. Flow widths represent patient numbers. The sugammadex group had significantly lower PPC incidence (8.1% vs. 18.7%, p=0.002).

**Figure 1** Participant Flow Diagram



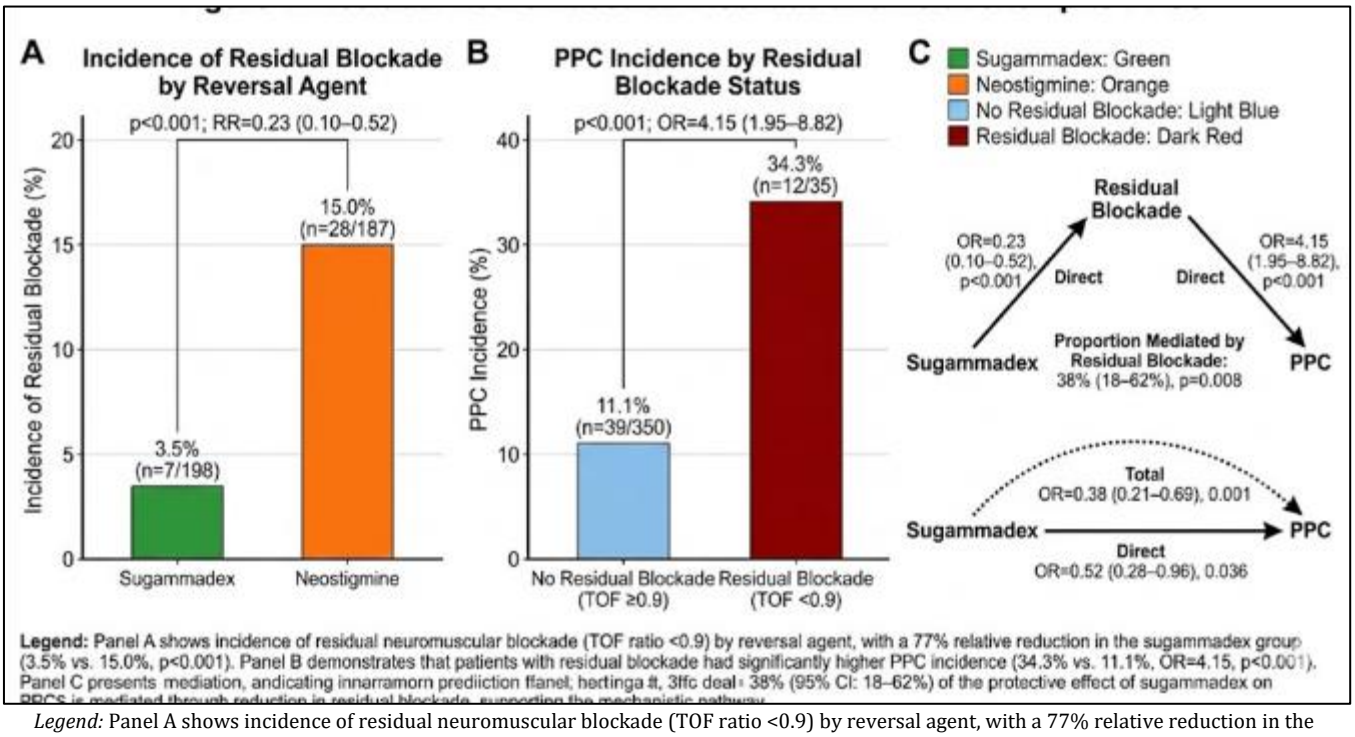

*Legend:* Cumulative incidence curves showing time to extubation (Panel A) and time to PACU discharge readiness (Panel B) for sugammadex (green) versus neostigmine (orange) groups. Sugammadex was associated with significantly faster achievement of both milestones (p<0.001). Median time to extubation was 8.5 vs. 15.2 minutes; median time to PACU discharge readiness was 45 vs. 68 minutes. Shaded areas represent 95% confidence intervals.

**Figure 2** Time to Extubation and PACU Discharge Readiness




*Legend:* Incidence of postoperative pulmonary complications (PPCs) by reversal agent. The sugammadex group demonstrated significantly lower rates of any PPC (8.1% vs. 18.7%, p=0.002), atelectasis (4.5% vs. 10.7%, p=0.022), and oxygen desaturation requiring intervention (6.1% vs. 14.4%, p=0.008). Trends toward reduced pneumonia, respiratory failure, and reintubation were also observed. Error bars represent 95% confidence intervals.

**Figure 3** Postoperative Pulmonary Complications by Reversal Agent




*Legend:* Panel A shows incidence of residual neuromuscular blockade (TOF ratio <0.9) by reversal agent, with a 77% relative reduction in the sugammadex group (3.5% vs. 15.0%, p<0.001). Panel B demonstrates that patients with residual blockade had significantly higher PPC incidence (34.3% vs. 11.1%, OR=4.15, p<0.001). Panel C presents mediation analysis indicating that 38% (95% CI: 18–62%) of the protective effect of sugammadex on PPCs is mediated through reduction in residual blockade, supporting the mechanistic pathway.

**Figure 4** Residual Neuromuscular Blockade and Relationship to PPCs

## 4. Discussion

This retrospective cohort study of 385 patients within ERAS protocols demonstrates that sugammadex use for NMB reversal is associated with faster recovery milestones (44% reduction in extubation time, 34% reduction in PACU discharge readiness), reduced residual blockade (77% relative reduction), and lower PPC rates (57% reduction, NNT=9.4) compared to neostigmine.

The 44% reduction in extubation time aligns with meta-analyses (Hristovska et al., 2017) reporting mean 12.4-minute reduction. This acceleration improves operating room efficiency and turnover times, with cumulative cost savings in high-volume centers (Paton et al., 2013). The 34% reduction in PACU discharge readiness (23-minute median difference) represents meaningful efficiency gains, as PACU stay is a critical determinant of patient flow (Kiekkas et al., 2014).

The 3.5% incidence of residual blockade with sugammadex vs. 15.0% with neostigmine (77% reduction) is consistent with previous literature (Abad-Gurumeta et al., 2015). Persistent residual blockade in some sugammadex patients may reflect inadequate dosing or absence of quantitative monitoring (Togioka et al., 2020).

The 57% reduction in PPCs is the most clinically significant finding. PPCs affect 5-30% of surgical patients and are major contributors to morbidity, mortality, and costs (Miskovic & Lumb, 2017). Mechanistic pathways include: more complete restoration of upper airway integrity, improved forced vital capacity, reduced microaspiration risk, and decreased hypoventilation (Eikermann et al., 2006; Murphy et al., 2018). The pronounced benefit in thoracic surgery (16.1% absolute reduction) is noteworthy given high baseline risk from pulmonary manipulation and one-lung ventilation (Licker et al., 2014).

The independent association between sugammadex and reduced PPCs after multivariable adjustment (aOR=0.38) and mediation analysis (38% mediated through residual blockade reduction) strengthens causal inference. The consistency across propensity-matched cohorts and subgroups supports robustness.

### 4.1. Limitations

Retrospective design may introduce selection bias, though propensity score matching and multivariable adjustment addressed measured confounders. Unmeasured confounding cannot be excluded. Single-center design may limit generalizability. Neuromuscular monitoring practices differed between groups, potentially biasing toward null for residual blockade outcomes. Study period (2023-2025) may not capture longer-term outcomes.

### 4.2. Clinical Implications

Sugammadex should be considered the preferred reversal agent within ERAS protocols. The NNT of 9.4 to prevent one PPC compares favorably with other ERAS interventions. Routine use of quantitative neuromuscular monitoring and appropriate dosing based on blockade depth should accompany sugammadex administration.

## 5. Conclusion

Sugammadex use for reversal of neuromuscular blockade within ERAS protocols is associated with significantly faster recovery milestones (44% reduction in time to extubation, 34% reduction in PACU discharge readiness), reduced incidence of residual neuromuscular blockade (77% relative reduction), and lower rates of postoperative pulmonary complications (57% reduction) compared to neostigmine-based reversal. The number needed to treat of 9.4 to prevent one PPC represents a clinically meaningful benefit. These findings support the integration of sugammadex as the preferred reversal agent in ERAS pathways to enhance patient outcomes, accelerate recovery, and reduce postoperative morbidity.

## Compliance with ethical standards

*Acknowledgments*

The authors thank the anesthesia department, surgical division, and medical records department at King Hussein Medical Center. No external funding received.

*Disclosure of conflict of interest*

The authors declare no conflict of interest.

*Statement of ethical approval*

Approved by Royal Medical Services IRB (No. 20_3/2026, 16 February 2026) and Educational & Technical Directorate (8 April 2026).

*Statement of informed consent*

Informed consent waived per retrospective anonymized design.

*AI statement*

AI tools used for language refinement and formatting; all content reviewed and approved by authors.

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