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SYSTEMATIC REVIEW AND META-ANALYSIS

Zhu and Li: Sugammadex vs neostigmine recovery

Sugammadex vs neostigmine in post- anesthesia recovery: A systematic review and meta- analysis

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ABSTRACT

Residual neuromuscular blockade (RNB) is linked to an increased risk of perioperative adverse events. This study systematically evaluates the impact of neuromuscular blockade antagonists on postoperative complications and quality of recovery in surgical patients. We conducted a systematic review and meta-analysis to compare the efficacy of sugammadex and neostigmine. Comprehensive searches were performed across medical databases, including Web of Science, PubMed, Embase, and the Cochrane Library, with a final search date of April 6, 2025. A total of thirty-five randomized controlled trials (RCTs) involving 4,275 patients, along with two retrospective studies comprising 49,642 participants, met the inclusion criteria. The meta-analysis revealed that sugammadex facilitated faster reversal of RNB compared to neostigmine, as indicated by a quicker recovery to a train-of-four ratio (TOFR) ≥ 0.9 (standardized mean difference [SMD] -3.45; 95% confidence interval [CI], -4.42 to -2.48), a shorter extubation time (SMD -1.44; 95% CI, -2.02 to -0.85), and a decreased incidence of RNB (risk ratio [RR] 0.18; 95% CI, 0.07 to 0.47). Moreover, sugammadex significantly reduced postoperative complications compared to neostigmine, including the incidence of postoperative nausea and vomiting (PONV) (RR 0.64; 95% CI, 0.46 to 0.88), postoperative pulmonary complications (PPCs) (RR 0.62; 95% CI, 0.38 to 0.99), and bradycardia (RR 0.32; 95% CI, 0.20 to 0.50). In conclusion, sugammadex provides a faster reversal of neuromuscular blockade compared to neostigmine and is associated with a reduction in postoperative complications. However, this expedited reversal does not result in measurable improvements in overall recovery quality, nor do either sugammadex or neostigmine significantly affect postoperative cognitive function.

Keywords: Sugammadex, neostigmine, recovery, TOF, PONV, PPCs, cognitive function.

INTRODUCTION

Each year, over 230 million major surgical procedures are performed globally, with the majority requiring general anesthesia[1].Neuromuscular blocking agents (NMBAs) are essential in this context, facilitating endotracheal intubation, muscle relaxation, and optimal surgical field conditions. However, the use of NMBAs has been linked to adverse postoperative outcomes, particularly residual neuromuscular blockade (RNB)[2-4]. This condition has been associated with increased risks of pulmonary complications, higher mortality rates, prolonged hospital stays, elevated healthcare costs, and greater overall medical burden[5].

Neostigmine, a cholinesterase inhibitor, is widely used as a reversal agent for residual neuromuscular blockade, enabling faster recovery after general anesthesia. Despite its clinical importance, residual blockade persists in approximately 40% of patients even after neostigmine administration[6].This residual blockade, even when mild, can impair respiratory function, swallowing, and the ability to maintain a patent airway, particularly in elderly individuals. These impairments substantially increase the risk of postoperative complications, including pneumonia, aspiration, and atelectasis[7-9]. Sugammadex, introduced in 2008, is a gamma-cyclodextrin that selectively binds rocuronium, facilitating rapid and complete reversal of neuromuscular blockade without adversely affecting the activity of upper airway dilators[10, 11]. Compared to neostigmine, sugammadex offers superior efficacy in achieving a Train-of-Four Ratio (TOFR) greater than 0.9[12]. However, its impact on broader clinical outcomes remains uncertain. While some studies suggest potential benefits of sugammadex for postoperative recovery, others report inconclusive or conflicting findings[13].

While numerous meta-analyses have compared sugammadex and neostigmine for specific postoperative outcomes (e.g., pulmonary complications, PONV, train-of-four

recovery)[14-16], key gaps persist: (1) insufficient evidence in high-risk populations (e.g., bariatric patients, patients with high American Society of Anesthesiologists [ASA] status, the elderly); (2) lack of integrated assessment of multidimensional recovery; (3) unaddressed methodological heterogeneity. To overcome these limitations comprehensively, we conducted the most comprehensive systematic review and meta-analysis to date. Our study uniquely: (i) compares the agents in underrepresented high-risk cohorts using subgroup analyses; (ii) synthesizes evidence across critical recovery domains (PPCs, PONV, recovery scores, cognitive function, discharge metrics) for a holistic view of convalescence. This provides tailored evidence for complex clinical decisions where choice impacts recovery, advancing precision anesthesia practice beyond broad efficacy comparisons.

MATERIALS AND METHODS

The study protocol has been registered in advance with the PROSPERO database (registration number CRD42024561006). The design of this research adhered to the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), thereby ensuring thorough and comprehensive reporting [17].

Inclusion and exclusion criteria

This systematic review employed the PICOS framework to define eligibility. We included studies involving patients (P) undergoing general anesthesia and requiring reversal of neuromuscular blockade. The interventions (I) and comparators (C) were defined as follows: for trials evaluating sugammadex, the comparison was neostigmine; for trials evaluating neostigmine, the comparison was either placebo or standard care (without active reversal agent). Eligible studies were required to report

at least one primary outcome (time to train-of-four [TOF] ratio ≥ 0.9 or extubation time) or secondary outcome (e.g., incidence of residual neuromuscular blockade [RNB], hospital length of stay, recovery room/operation room duration, quality of recovery scores, incidence of postoperative nausea and vomiting [PONV], postoperative pulmonary complications [PPCs], or bradycardia, 30-day hospital readmission, or cognitive outcomes assessed by tools such as Mini-Mental State Examination [MMSE] or Montreal Cognitive Assessment [MoCA]). Regarding study design (S), we included randomized controlled trials (RCTs) comparing sugammadex versus neostigmine or neostigmine versus placebo/control. Recognizing the potential scarcity of RCTs specifically measuring cognitive outcomes, high-quality retrospective cohort studies (as determined by the Newcastle-Ottawa Scale [NOS]) were also included exclusively for the analysis of cognitive outcomes. Studies were excluded if research data were unavailable or non-extractable, if they were deemed low-quality by standardized assessment tools (Cochrane RoB 2.0 for RCTs; NOS score < 5 for cohort studies), or if they were non-human studies, case reports, reviews, or conference abstracts.

Search strategy

Comprehensive literature searches were conducted across several databases, including Web of Science, PubMed, EMBASE, and the Cochrane Libraries, up until April 6, 2025, encompassing both published works and preprints. The complete search strategy is detailed in the Supplementary material 1.

Data extraction and quality assessment

Data extraction from the selected articles was carried out using a data collection table by one investigator and then independently verified by a second investigator. Each study included in this review was assessed for risk of bias by two independent

investigators, who utilized the Cochrane quality assessment tool specifically designed for evaluating randomized controlled trials. The Newcastle-Ottawa Scale (NOS) was performed to evaluate the quality of retrospective cohort studies. The studies were classified into two categories: 'low risk' or 'high risk'. Initial disagreements were resolved through structured discussion between screeners with reference to pre-defined inclusion/exclusion criteria, while persistent disagreements (<5% of cases) were adjudicated by a senior investigator whose decision was final.

Statistical analysis

For the continuous variables, we assessed the available data by aggregating it to determine the mean difference (MD) using a random effects model, supplemented by a 95% confidence interval (CI). Conversely, for dichotomous variables, we compiled the data by estimating a pooled risk ratio (RR) accompanied by a 95% CI, again employing a random effects model. To assess heterogeneity across the studies, we employed the Cochran-based I^2 statistic and the chi-square test; a p-value greater than 0.10 and an I^2 statistic below 50% were interpreted as indicative of low heterogeneity. In instances where more than 10 studies were included, we conducted Egger's and Begg's tests to evaluate potential publication bias. Statistical analyses were performed using Stata software (version 15.0; StataCorp LLC, College Station, TX, USA).

RESULTS

Study selection

The procedure for retrieving results and selecting research articles is illustrated in the flowchart presented in Figure 1. Initially, a total of 375 potentially relevant articles were identified through the literature search. Ultimately, 37 studies were included in the review for analysis.

Study characteristics

The characteristics of the included studies are summarized in Supplementary material 2. A total of 37 articles were considered for the meta-analysis, comprising thirty-five randomized controlled trials (RCTs) involving 4,275 patients and two retrospective studies encompassing 49,642 participants. Among these 37 studies, 11 focused on the time required to achieve a train-of-four (TOF) ratio of 0.9[7, 12, 18-26], 14 examined extubation time[5, 7, 12, 19, 20, 23, 24, 26-32], 5 assessed the incidence of residual neuromuscular block (RNB)[8, 9, 25, 33, 34], 9 reported on the length of hospital stay[5, 7-9, 23, 24, 28, 35, 36], 7 investigated PACU duration[7, 20, 24, 28, 35-37], 3 analyzed operating room (OR) time[24, 28, 36], 3 evaluated the quality of recovery scores[27, 32, 35], 16 addressed the incidence of postoperative nausea and vomiting (PONV)[5, 8, 19, 23, 26, 28, 30, 32-34, 36-41], and 6 studied the occurrence of pulmonary complications (PPCs)[5, 7-9, 23, 33]. Additionally, only 2 studies reported the incidence of 30-day hospital readmissions[7, 8], 6 focused on the prevalence of bradycardia[23, 31, 33, 40, 42, 43], and 7 evaluated postoperative cognitive impairment[33, 44-49]. Among the 7 studies reporting cognitive outcomes, 3 studies assessed postoperative delirium (POD) (using Confusion Assessment Method [CAM]/ brief Confusion Assessment Method [bCAM] daily within postoperative days 1–7), while 4 studies assessed postoperative cognitive dysfunction (POCD) (using MMSE/MoCA, with impairment defined as postoperative Z-scores ≤ -1.96; measurements varied but commonly occurred at days 1, 3, and 7).

Risk of bias and quality assessment

The evaluation of bias indicated a minimal risk of bias for most of the studies incorporated in this analysis. Comprehensive information about the individual studies, their results, and the risk of bias can be found in Supplementary material 3.

Results of pooled analysis

A summary of the key results is presented in Table 1. The pooled outcome analyses demonstrated comparable recovery profiles between sugammadex and neostigmine for several parameters: PACU duration, OR time, hospital length of stay, postoperative cognitive function, and recovery scores all showed no statistically significant differences. However, sugammadex demonstrated significant advantages in critical recovery metrics: patients achieved TOF ratio ≥ 0.9 faster, had shorter extubation times, and exhibited lower rates of postoperative complications including PONV, PPCs, and bradycardia.

Comparison of speed and quality of recovery

Sugammadex reversed neuromuscular blockade more rapidly than neostigmine on TOF ≥ 0.9 (11 trials, SMD -3.45 [-4.42 to -2.48]), and extubation time (14 trials, SMD -1.44 [-2.02 to -0.85]). Sugammadex could significantly reduce the risk of RNB compared with neostigmine (5 trials, RR 0.18 [0.07- 0.47]). (Figure 2) However, pooled analysis indicated that hospital stay (9 trials, SMD -0.32 [-0.70 to 0.07]), recovery room duration (7 trials, SMD -0.20 [-0.62 to 0.23]), operation room duration(3 trials, SMD -0.60 [-1.20 to 0.01]), and quality of recovery scores (3 trials, SMD -0.12 [-0.43 to 0.19]) were similar between sugammadex and neostigmine. (Figure S1)

Comparison of the incidence of postoperative complications

Sugammadex significantly reduced the risk of postoperative complications on incidence of PONV (16 trials, RR 0.64 [0.46-0.88]), incidence of PPCs (6 trials, RR 0.62 [0.38-0.99]), and incidence of bradycardia (6 trials, RR 0.32 [0.20-0.50]). (Figure 3)

Comparison of cognitive function and long-term outcomes

Sugammadex versus neostigmine regarding the occurrence of cognitive impairment were similar (4 trials, RR 1.09 [0.77-1.54]). However, sugammadex was associated with a lower 30-day readmission rate than neostigmine (2 trails, RR 0.39 [0.17-0.92]). Neostigmine versus placebo did not promote better cognitive outcomes (3 trials, RR 0.66 [0.36-1.21]). (Figure 4)

Results of the subgroup analysis

Due to high heterogeneity observed in our primary outcomes (time to TOF ratio ≥ 90% and extubation time), we performed subgroup analyses stratified by age, American Society of Anesthesiologists (ASA) physical status classification, and body mass index (BMI). The results demonstrated that the findings within the subgroups were consistent with the overall results: Sugammadex achieved a faster time to TOF ratio 90% compared to neostigmine(Figure S2a-c). Lower heterogeneity was observed in the subgroups of age ≤ 14 years, ASA class ≥ 3, and BMI 30–40 kg/m². Similarly, the extubation time was shorter in the Sugammadex group than in the neostigmine group(Figure S3a-c), with reduced heterogeneity specifically noted in the BMI ≥ 40 kg/m² subgroup.

Analysis of publication bias

The analysis conducted using Egger's and Begg's tests revealed no significant publication bias for any of the primary outcomes, with a *p*-value >0.05.

DISCUSSION

We performed a systematic review and meta-analysis to assess the impact of neuromuscular blockade antagonists on postoperative complications as well as the

overall quality of patient recovery. The compiled data demonstrated that sugammadex exhibited greater efficacy than neostigmine in the reversal of neuromuscular blockade and was linked to a decrease in postoperative complications. Nevertheless, this expedited reversal did not inherently result in notable differences in overall recovery. Additionally, the use of sugammadex and neostigmine seemed to have minimal effect on postoperative cognitive function, and neostigmine did not demonstrate any significant improvement in cognitive outcomes.

The findings of this study corroborated those of earlier systematic reviews[15, 16, 50], which also indicated a comparable decrease in postoperative complications associated with sugammadex. However, these prior studies did not evaluate its effects on various factors including the duration of hospital stays, Postanesthesia care unit (PACU) stays, patient-reported satisfaction, cognitive function, or the incidence of residual neuromuscular blockade (RNB). This study contributes valuable insights by demonstrating that sugammadex is more effective than neostigmine in reversing neuromuscular blockade and is associated with a reduction in postoperative complications. Nevertheless, this enhanced reversal speed does not inherently translate into variations in overall recovery efficiency[16]. Liu *et al*[48]. found no significant differences in the incidence of mortality within a 6-month period between the neostigmine group and the placebo group. Similarly, Lebowski *et al*[5]. reported no notable difference in 30-day postoperative mortality between the sugammadex and neostigmine.

The administration of sugammadex can reduce the incidence of residual muscle block(RNB), which is beneficial for patient recovery. However, perioperative outcomes are the result of the interaction of multiple factors. Age, frailty, and ASA classification are interrelated factors that collectively and significantly determine patient prognosis, especially under surgical or physiological stress[51, 52].

Furthermore, advancing age reduces physiological reserves, lowering tolerance, recovery capacity, and immune function. While often linked (age predisposing to frailty and higher ASA class), each factor independently contributes. Frailty represents a state of increased vulnerability arising from a decline in the physiological reserves of multiple systems, predisposing individuals to adverse health outcomes even in response to minor stressors, such as minor surgery or mild infection[53-56]. ASA classification exhibits a strong positive correlation with complication and mortality rates[57]. Crucially, their co-occurrence exponentially increases risk, rather than merely additively. Thus, prognosis rests on this multifactorial basis. These factors may account for the large heterogeneity observed in the meta-analysis results. Our study mainly included patients with ASA class 1-2, which may have contributed to the lack of difference in recovery outcomes due to the better preoperative physical tolerance of the patients. While rapid reversal of neuromuscular blockade is an important part of enhanced recovery, but it does not play a decisive role in the patient's recovery.

The effect of neuromuscular blockade antagonists on perioperative neurocognitive function in patients is still controversial[46-48]. Earlier research has indicated that cholinesterase inhibitors may decrease the occurrence of postoperative cognitive dysfunction or postoperative delirium[47, 49]. Emerging evidence demonstrates that neostigmine modulates immune-inflammatory activity via the cholinergic anti-inflammatory pathway (CAP), with potential implications for perioperative neurocognitive outcomes[58-62]. However, the precise mechanisms underlying CAP-mediated effects remain incompletely characterized. While preclinical investigations have demonstrated the compound's dual capacity for inflammation regulation and cognitive protection in surgical settings, translational gaps persist[63]. Notably, current evidence predominantly originates from animal models, leaving

critical questions regarding optimal dosing strategies, patient-specific responses, and long-term neurological consequences unresolved in human populations. Our systematic review revealed no significant cognitive protective advantage of sugammadex versus neostigmine or neostigmine versus placebo. The included studies primarily consist of single center randomized controlled trials or extensive retrospective analyses, and they generally lack multi-center validation. Additionally, the population under investigation is focused on patients undergoing surgery for specific diseases, which limits their representativeness of the broader population[49]. Variability in the diagnostic scales employed for cognitive assessment and in the timing of patient assessments across studies could also contribute to the heterogeneity in the results.

Notably, sugammadex incurs substantially higher per-dose costs compared to neostigmine (e.g., 20-30-fold price differences in some healthcare systems), thereby directly increasing perioperative expenses. Prior studies in bariatric surgery[64], hospital cost analyses[65], and single-center cost-effectiveness evaluations[66] confirm this economic disadvantage, although sugammadex's faster recovery profile may partially offset these costs in select populations. These findings collectively underscore two imperatives: (1) sugammadex represents a pharmacologically advanced option for the high-risk patients where rapid recovery is critical, and (2) definitive cost-effectiveness analyses—particularly those assessing long-term recovery outcomes and context-specific value—are urgently needed to optimize its strategic implementation.

High heterogeneity in our primary outcomes represents an important limitation of this study, necessitating cautious interpretation of the results. This indicates that the effect of the intervention (e.g., different neuromuscular reversal strategies) may vary depending on patient characteristics, surgical type, or specific anesthesia practices;

thus, our pooled effect estimates should be interpreted as an average effect. Consequently, individualized clinical decision-making is warranted, and the findings should not be indiscriminately generalized to all patient populations. However, the direction of the primary effect remained consistent across most subgroups, supporting the robustness of our main conclusions.

CONCLUSION

Sugammadex demonstrated superior efficacy in reversing neuromuscular blockade compared to neostigmine, with a notable reduction in postoperative complications. However, this faster reversal did not translate into measurable improvements in broader recovery outcomes, such as hospital length of stay or overall recovery efficiency. Moreover, neither sugammadex nor neostigmine has been shown to significantly affect postoperative cognitive function, and neostigmine was not associated with improved cognitive outcomes. When economic considerations are set aside, sugammadex appears to offer a safer and more effective pathway for patient recovery than neostigmine, owing to its rapid and complete reversal of neuromuscular blockade. These findings highlight the clinical advantages of sugammadex while underscoring the need for further research to evaluate its cost-effectiveness and its potential influence on long-term recovery outcomes.

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Data availability: The data associated with the paper are not publicly available; however, these are available from the corresponding author upon reasonable request.

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REFERENCES

[1] Weiser TG, Regenbogen SE, Thompson KD, Haynes AB, Lipsitz SR, Berry WR, et al. An estimation of the global volume of surgery: a modelling strategy based on available data. Lancet. 2008;372(9633):139-44.

[2] Eriksson LI, Sundman E, Olsson R, Nilsson L, Witt H, Ekberg O, et al. Functional assessment of the pharynx at rest and during swallowing in partially paralyzed humans: simultaneous videomanometry and mechanomyography of awake human volunteers. Anesthesiology. 1997;87(5):1035-43.

[3] Eikermann M, Groeben H, Hüsing J, Peters J. Accelerometry of adductor pollicis muscle predicts recovery of respiratory function from neuromuscular blockade. Anesthesiology. 2003;98(6):1333-7.

[4] Berg H, Roed J, Viby-Mogensen J, Mortensen CR, Engbaek J, Skovgaard LT, et al. 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(9):1095-103.

[5] Ledowski T, Szabó-Maák Z, Loh PS, Turlach BA, Yang HS, de Boer HD, et al. Reversal of residual neuromuscular block with neostigmine or sugammadex and postoperative pulmonary complications: a prospective, randomised, double-blind trial in high-risk older patients. Br J Anaesth. 2021;127(2):316-23.

[6] Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. Anesth Analg. 2010;111(1):120-8.

[7] Yu Y, Wang H, Bao Q, Zhang T, Chen B, Ding J. Sugammadex Versus Neostigmine for Neuromuscular Block Reversal and Postoperative Pulmonary Complications in Patients Undergoing Resection of Lung Cancer. J Cardiothorac Vasc Anesth. 2022;36(9):3626-33.

[8] 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(5):553-61.

[9] 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. Can J Anaesth. 2019;66(11):1328-37.

[10] Eikermann M, Zaremba S, Malhotra A, Jordan AS, Rosow C, Chamberlin NL. Neostigmine but not sugammadex impairs upper airway dilator muscle activity and breathing. Br J Anaesth. 2008;101(3):344-9.

[11] Flockton EA, Mastronardi P, Hunter JM, Gomar C, Mirakhur RK, Aguilera L, et al. Reversal of rocuronium-induced neuromuscular block with sugammadex is faster than reversal of cisatracurium-induced block with neostigmine. Br J Anaesth. 2008;100(5):622-30.

[12] Farag E, Rivas E, Bravo M, Hussain S, Argalious M, Khanna S, et al. Sugammadex Versus Neostigmine for Reversal of Rocuronium Neuromuscular Block in Patients Having Catheter-Based Neurointerventional Procedures: A Randomized Trial. Anesth Analg. 2021;132(6):1666-76.

[13] Ajetunmobi O, Wong D, Perlas A, Rajaleelan W, Wang S, Huszti E, et al. Impact of Sugammadex Versus Neostigmine Reversal on Postoperative Recovery Time in Patients With Obstructive Sleep Apnea Undergoing Bariatric Surgery: A Double-Blind, Randomized Controlled Trial. Anesth Analg. 2024.

[14] Raval AD, Uyei J, Karabis A, Bash LD, Brull SJ. Incidence of residual neuromuscular blockade and use of neuromuscular blocking agents with or without antagonists: A systematic review and meta-analysis of randomized controlled trials. J Clin Anesth. 2020;64:109818.

[15] Hsieh YL, Lin CR, Liu YC, Wang CJ, Weng WT. The effect of sugammadex versus neostigmine on postoperative nausea and vomiting: a meta-analysis of randomized controlled trials with trial sequential analysis. Minerva Anestesiol. 2023;89(5):434-44.

[16] Olesnicky BL, Farrell C, Clare P, Wen S, Leslie K, Delaney A. The effect of sugammadex on patient morbidity and quality of recovery after general anaesthesia: a systematic review and meta-analysis. Br J Anaesth. 2024;132(1):107-15.

[17] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Bmj. 2021;372:n71.

[18] Pişkin Ö, Küçükosman G, Altun DU, Çimencan M, Özen B, Aydın BG, et al. The effect of sugammadex on postoperative cognitive function and recovery. Braz J Anesthesiol. 2016;66(4):376-82.

[19] Mohamad Zaini RH, Penny Tevaraj JM, Wan Hassan WN, Iberahim MI, Wan Muhd Shukeri WF. Comparison between the efficacy of neostigmine versus

sugammadex for reversal of rocuronium induced neuromuscular blockade in paediatric patients. Anesthesia and Analgesia. 2016;123(3):329.

[20] Carron M, Veronese S, Foletto M, Ori C. Sugammadex allows fast-track bariatric surgery. Obes Surg. 2013;23(10):1558-63.

[21] Gaszynski T, Szewczyk T, Gaszynski W. Randomized comparison of sugammadex and neostigmine for reversal of rocuronium-induced muscle relaxation in morbidly obese undergoing general anaesthesia. Br J Anaesth. 2012;108(2):236-9.

[22] Illman HL, Laurila P, Antila H, Meretoja OA, Alahuhta S, Olkkola KT. The duration of residual neuromuscular block after administration of neostigmine or sugammadex at two visible twitches during train-of-four monitoring. Anesth Analg. 2011;112(1):63-8.

[23] Li L, Jiang Y, Zhang W. Sugammadex for Fast-Track Surgery in Children Undergoing Cardiac Surgery: A Randomized Controlled Study. J Cardiothorac Vasc Anesth. 2021;35(5):1388-92.

[24] Mraovic B, Timko NJ, Choma TJ. Comparison of recovery after sugammadex or neostigmine reversal of rocuronium in geriatric patients undergoing spine surgery: a randomized controlled trial. Croat Med J. 2021;62(6):606-13.

[25] Niu L, Wang Y, Yao C, Sun Y, Yao S, Lin Y. Efficacy and Safety of Neuromuscular Blockade in Overweight Patients Undergoing Nasopharyngeal Surgery. Med Sci Monit. 2020;26:e926452.

[26] Sacan O, White PF, Tufanogullari B, Klein K. Sugammadex reversal of rocuronium-induced neuromuscular blockade: a comparison with neostigmine-glycopyrrolate and edrophonium-atropine. Anesth Analg.

2007;104(3):569-74.

[27] Abola RE, Romeiser J, Rizwan S, Lung B, Gupta R, Bennett-Guerrero E. A randomized-controlled trial of sugammadex versus neostigmine: impact on early postoperative strength. Canadian Journal of Anesthesia-Journal Canadien D Anesthesie. 2020;67(8):959-69.

[28] Ajetunmobi O, Wong D, Perlas A, Rajaleelan W, Wang S, Huszti E, et al. Impact of Sugammadex Versus Neostigmine Reversal on Postoperative Recovery Time in Patients With Obstructive Sleep Apnea Undergoing Bariatric Surgery: A Double-Blind, Randomized Controlled Trial. Anesthesia and analgesia. 2024.

[29] Hakimoğlu S, Tuzcu K, Davarcı I, Karcıoğlu M, Ayhan Tuzcu E, Hancı V, et al. Comparison of sugammadex and neostigmine-atropine on intraocular pressure and postoperative effects. Kaohsiung J Med Sci. 2016;32(2):80-5.

[30] Korkmaz MO, Sayhan H, Guven M. Does sugammadex decrease the severity of agitation and complications in pediatric patients undergoing adenotonsillectomy? Saudi Med J. 2019;40(9):907-13.

[31] Koyuncu O, Turhanoglu S, Ozbakis Akkurt C, Karcıoglu M, Ozkan M, Ozer C, et al. Comparison of sugammadex and conventional reversal on postoperative nausea and vomiting: a randomized, blinded trial. J Clin Anesth. 2015;27(1):51-6.

[32] Paech MJ, Kaye R, Baber C, Nathan EA. Recovery characteristics of patients receiving either sugammadex or neostigmine and glycopyrrolate for reversal of neuromuscular block: a randomised controlled trial. Anaesthesia. 2018;73(3):340-7.

[33] Brueckmann B, Sasaki N, Grobara P, Li MK, Woo T, de Bie J, et al. Effects of sugammadex on incidence of postoperative residual neuromuscular blockade: a

randomized, controlled study. Br J Anaesth. 2015;115(5):743-51.

[34] Lu L, Chen X, Li S, Cen Y. Comparison of Effects of Sugammadex and Neostigmine on Postoperative Neuromuscular Blockade Recovery in Patients with Interstitial Lung Diseases Undergoing Transbronchial Cryobiopsy: A Randomized Trial. Med Sci Monit. 2024;30:e942773.

[35] Han J, Oh AY, Jeon YT, Koo BW, Kim BY, Kim D, et al. Quality of Recovery after Laparoscopic Cholecystectomy Following Neuromuscular Blockade Reversal with Neostigmine or Sugammadex: A Prospective, Randomized, Controlled Trial. Journal of Clinical Medicine. 2021;10(5).

[36] Putz L, Dransart C, Jamart J, Marotta ML, Delnooz G, Dubois PE. Operating room discharge after deep neuromuscular block reversed with sugammadex compared with shallow block reversed with neostigmine: a randomized controlled trial. J Clin Anesth. 2016;35:107-13.

[37] Castro DS, Jr., Leão P, Borges S, Gomes L, Pacheco M, Figueiredo P. Sugammadex reduces postoperative pain after laparoscopic bariatric surgery: a randomized trial. Surg Laparosc Endosc Percutan Tech. 2014;24(5):420-3.

[38] Ding X, Zhu X, Zhao C, Chen D, Wang Y, Liang H, et al. Use of sugammadex is associated with reduced incidence and severity of postoperative nausea and vomiting in adult patients with obesity undergoing laparoscopic bariatric surgery: a post-hoc analysis. BMC Anesthesiol. 2023;23(1):163.

[39] Tas Tuna A, Palabiyik O, Orhan M, Sonbahar T, Sayhan H, Tomak Y. Does Sugammadex Administration Affect Postoperative Nausea and Vomiting After Laparoscopic Cholecystectomy: A Prospective, Double-Blind, Randomized Study.

Surg Laparosc Endosc Percutan Tech. 2017;27(4):237-40.

[40] Yağan Ö, Taş N, Mutlu T, Hancı V. Comparison of the effects of sugammadex and neostigmine on postoperative nausea and vomiting. Braz J Anesthesiol. 2017;67(2):147-52.

[41] Wu X, Oerding H, Liu J, Vanacker B, Yao S, Dahl V, et al. Rocuronium blockade reversal with sugammadex vs. neostigmine: randomized study in Chinese and Caucasian subjects. BMC Anesthesiol. 2014;14:53.

[42] Herring WJ, Mukai Y, Wang A, Lutkiewicz J, Lombard JF, Lin L, et al. A randomized trial evaluating the safety profile of sugammadex in high surgical risk ASA physical class 3 or 4 participants. BMC Anesthesiol. 2021;21(1):259.

[43] Voss T, Wang A, DeAngelis M, Speek M, Saldien V, Hammer GB, et al. Sugammadex for reversal of neuromuscular blockade in pediatric patients: Results from a phase IV randomized study. Paediatr Anaesth. 2022;32(3):436-45.

[44] Batistaki C, Riga M, Zafeiropoulou F, Lyrakos G, Kostopanagiotou G, Matsota P. Effect of sugammadex versus neostigmine/atropine combination on postoperative cognitive dysfunction after elective surgery. Anaesth Intensive Care. 2017;45(5):581-8.

[45] Oh CS, Rhee KY, Yoon TG, Woo NS, Hong SW, Kim SH. Postoperative Delirium in Elderly Patients Undergoing Hip Fracture Surgery in the Sugammadex Era: A Retrospective Study. Biomed Res Int. 2016;2016:1054597.

[46] Rössler J, Abramczyk E, Paredes S, Anusic N, Pu X, Maheshwari K, et al. Association of Intravenous Neostigmine and Anticholinergics or Sugammadex with Postoperative Delirium: A Retrospective Cohort Study. Anesth Analg. 2024.

[47] Deng C, Yang L, Sun D, Feng Y, Sun Z, Li J. Influence of Neostigmine on Early Postoperative Cognitive Dysfunction in Older Adult Patients Undergoing Noncardiac Surgery: A Double-Blind, Placebo-Controlled, Randomized Controlled Trial. Anesth Analg. 2024;138(3):589-97.

[48] Liu F, Lin X, Lin Y, Deng X, Guo Y, Wang B, et al. The effect of neostigmine on postoperative delirium after colon carcinoma surgery: a randomized, double-blind, controlled trial. BMC Anesthesiol. 2022;22(1):267.

[49] Zhu B, Sun D, Yang L, Sun Z, Feng Y, Deng C. The effects of neostigmine on postoperative cognitive function and inflammatory factors in elderly patients - a randomized trial. BMC Geriatr. 2020;20(1):387.

[50] Raval AD, Anupindi VR, Ferrufino CP, Arper DL, Bash LD, Brull SJ. Epidemiology and outcomes of residual neuromuscular blockade: A systematic review of observational studies. J Clin Anesth. 2020;66:109962.

[51] Story DA. Postoperative mortality and complications. Best Pract Res Clin Anaesthesiol. 2011;25(3):319-27.

[52] Alexander M, Alexandra S B, Katherine B, J Alejandro R-H, Jason D W, Laurel W R, et al. Age-Associated Risk of 90-Day Postoperative Mortality After Cytoreductive Surgery for Advanced Ovarian Cancer. JAMA Surg. 2019;154(7).

[53] Cathy W Y W, Doris S F Y, Polly W C L, Bernice Shinyi C. The prognostic impacts of frailty on clinical and patient-reported outcomes in patients undergoing coronary artery or valvular surgeries/procedures: A systematic review and meta-analysis. Ageing Res Rev. 2023;85(0).

[54] Gillis C, Ljungqvist O, Carli F. Prehabilitation, enhanced recovery after surgery,

or both? A narrative review. Br J Anaesth. 2022;128(3):434-48.

[55] Lin HS, Watts JN, Peel NM, Hubbard RE. Frailty and post-operative outcomes in older surgical patients: a systematic review. BMC Geriatr. 2016;16(1):157.

[56] Muscedere J, Bagshaw SM, Kho M, Mehta S, Cook DJ, Boyd JG, et al. Frailty, Outcomes, Recovery and Care Steps of Critically Ill Patients (FORECAST): a prospective, multi-centre, cohort study. Intensive Care Med. 2024;50(7):1064-74.

[57] Collaborative SCE. Association between multimorbidity and postoperative mortality in patients undergoing major surgery: a prospective study in 29 countries across Europe. Anaesthesia. 2024;79(9):945-56.

[58] Akinci SB, Ulu N, Yondem OZ, Firat P, Guc MO, Kanbak M, et al. Effect of neostigmine on organ injury in murine endotoxemia: missing facts about the cholinergic antiinflammatory pathway. World J Surg. 2005;29(11):1483-9.

[59] Antunes GL, Silveira JS, Kaiber DB, Luft C, da Costa MS, Marques EP, et al. Cholinergic anti-inflammatory pathway confers airway protection against oxidative damage and attenuates inflammation in an allergic asthma model. J Cell Physiol. 2020;235(2):1838-49.

[60] Antunes GL, Silveira JS, Kaiber DB, Luft C, Dos Santos TM, Marques EP, et al. Neostigmine treatment induces neuroprotection against oxidative stress in cerebral cortex of asthmatic mice. Metab Brain Dis. 2020;35(5):765-74.

[61] Eldufani J, Blaise G. The role of acetylcholinesterase inhibitors such as neostigmine and rivastigmine on chronic pain and cognitive function in aging: A review of recent clinical applications. Alzheimers Dement (N Y). 2019;5:175-83.

[62] Kalb A, von Haefen C, Sifringer M, Tegethoff A, Paeschke N, Kostova M, et al. Acetylcholinesterase inhibitors reduce neuroinflammation and -degeneration in the cortex and hippocampus of a surgery stress rat model. PLoS One. 2013;8(5):e62679.

[63] Si S, Zhao X, Su F, Lu H, Zhang D, Sun L, et al. New advances in clinical application of neostigmine: no longer focusing solely on increasing skeletal muscle strength. Front Pharmacol. 2023;14:1227496.

[64] Edoardo DR, Geremia ZM, Giovanni Marco R, Ornella P, Michele I, Fabrizio C, et al. The use of sugammadex for bariatric surgery: analysis of recovery time from neuromuscular blockade and possible economic impact. Clinicoecon Outcomes Res. 2016;8(0).

[65] Luca J W, Tim M T, Elena A, Annika S W, Omid A, Philipp F, et al. Comparison of the effects of sugammadex versus neostigmine for reversal of neuromuscular block on hospital costs of care. Br J Anaesth. 2022;130(2).

[66] Lan WN, Tam KW, Chen JT, Cata JP, Cherng YG, Chou YY, et al. Cost-Effectiveness of Sugammadex Versus Neostigmine to Reverse Neuromuscular Blockade in a University Hospital in Taiwan: A Propensity Score-Matched Analysis. Healthcare. 2023;11(2).

TABLES AND FIGURES WITH LEGENDS

Table 1. Pooled analysis of comparative outcomes between sugammadex and neostigmine

Outcomes	Cohorts	Participants	Pooled effect size	95%CI	I^2
Time of TOF ≥0.9	11	700	MD=-3.45	-4.42 to -2.48	94.4
Extubation time	14	1312	MD=-1.44	-2.02 to -0.85	95.5
PACU stay	7	565	MD=-0.20	-0.62 to 0.23	83.5
OR stay	3	260	MD=-0.60	-1.20 to 0.01	80.8
Hospital length of stay	9	991	MD=-0.32	-0.70 to 0.07	88.6
Recovery scores	3	443	MD=-0.12	-0.43 to 0.19	50.2
RNB incidence	5	608	RR=0.18	0.07-0.47	73.3
PONV incidence	16	1986	RR=0.64	0.46-0.88	53.6
PPCs incidence	6	802	RR=0.62	0.38-0.99	30.3
Bradycardia incidence	6	948	RR=0.32	0.20-0.50	0.0
30-day readmission rate	2	300	RR=0.39	0.17-0.92	0.0
Cognitive impairment rate (S versus N)	4	49953	RR=1.09	0.77-1.54	35.2
Cognitive impairment rate (N versus C)	3	635	RR=0.66	0.36-1.21	54.8

Notes: TOF, Train-of-Four (neuromuscular monitoring); PACU, post-anesthesia care unit; OR, operating room; RNB, residual neuromuscular blockade; PONV,

postoperative nausea and vomiting; PPCs, postoperative pulmonary complications; MD, mean difference; RR, risk ratio; CI, confidence interval.

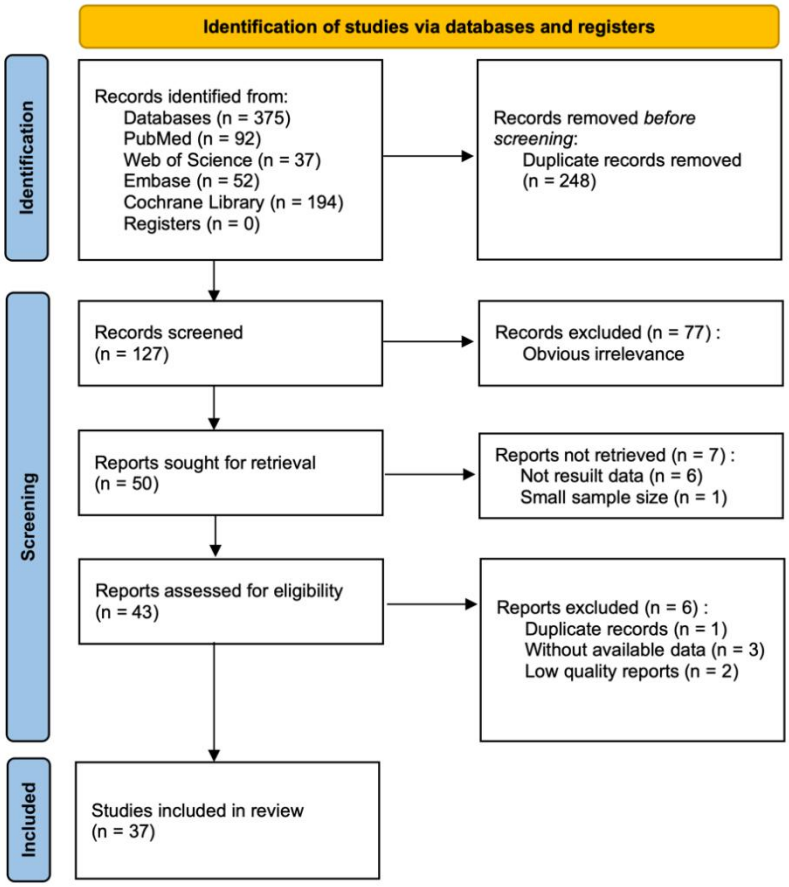

Figure 1. Flowchart illustrating the study selection process

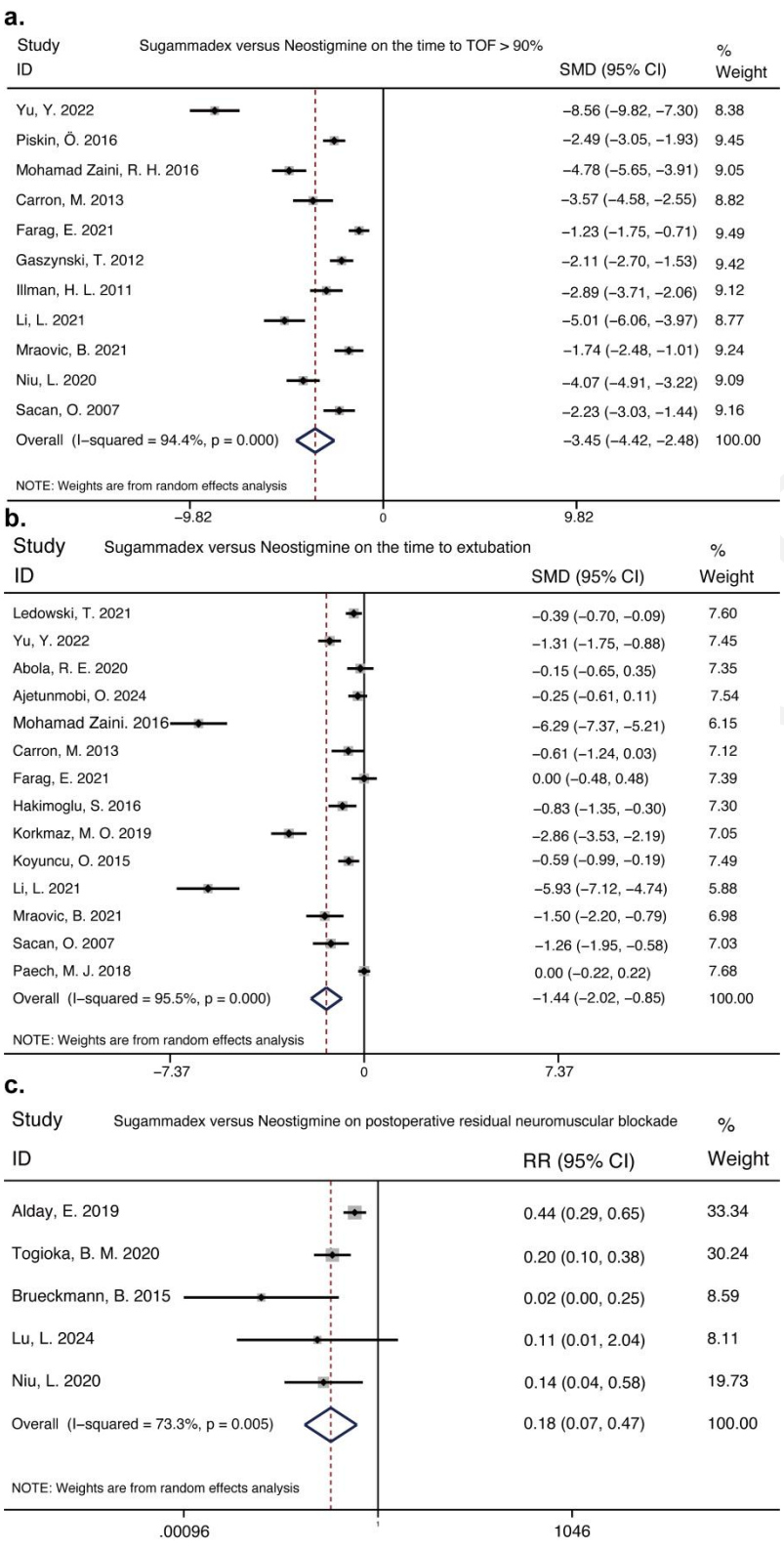

Figure 2. Comparative assessment of recovery speed between sugammadex and neostigmine, evaluated through Train- of- Four (TOF) ratios and extubation times.

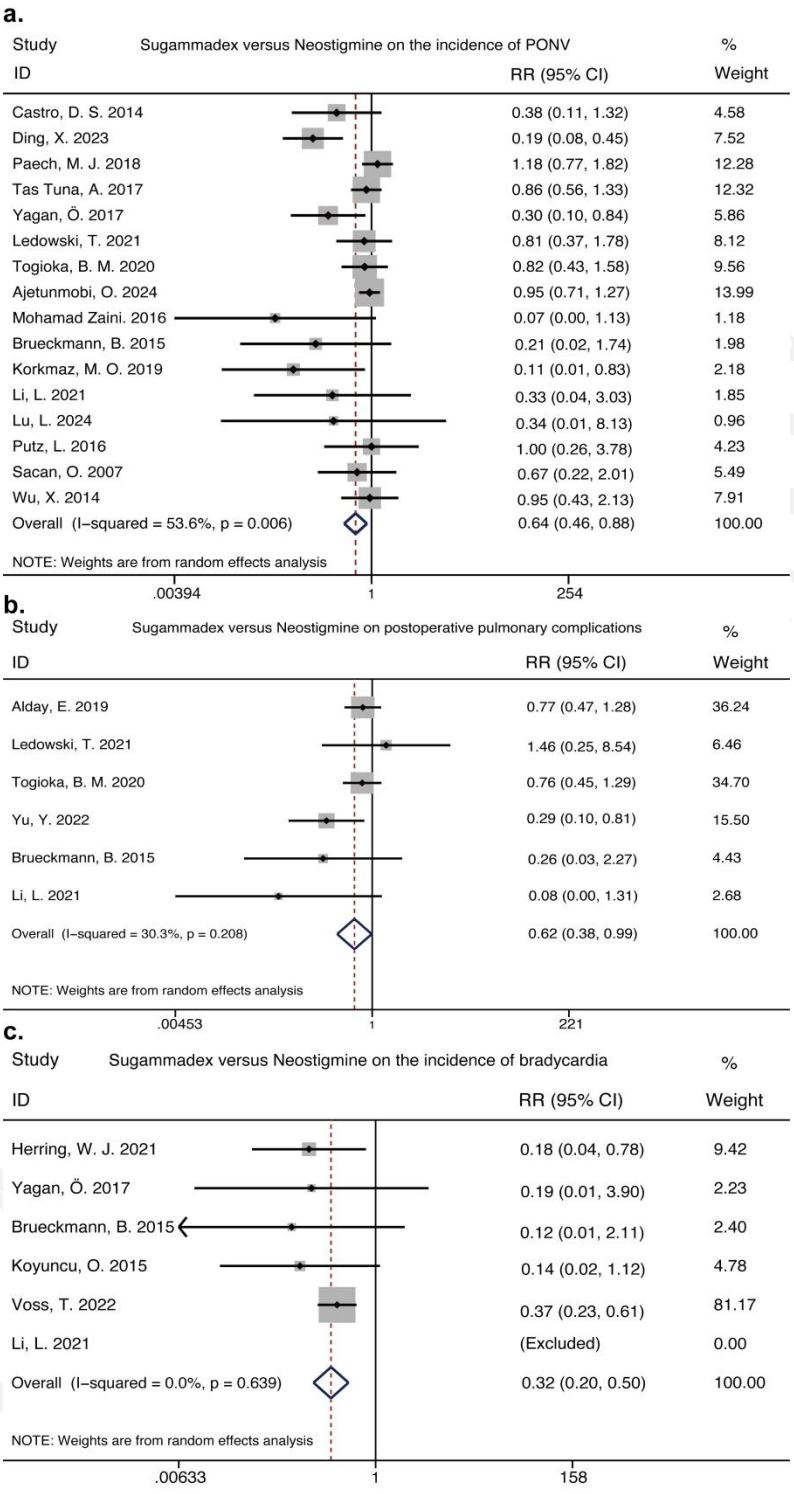

Figure 3. Comparative incidence of postoperative complications between sugammadex and neostigmine. A study reporting zero events in both arms was omitted from the analysis.

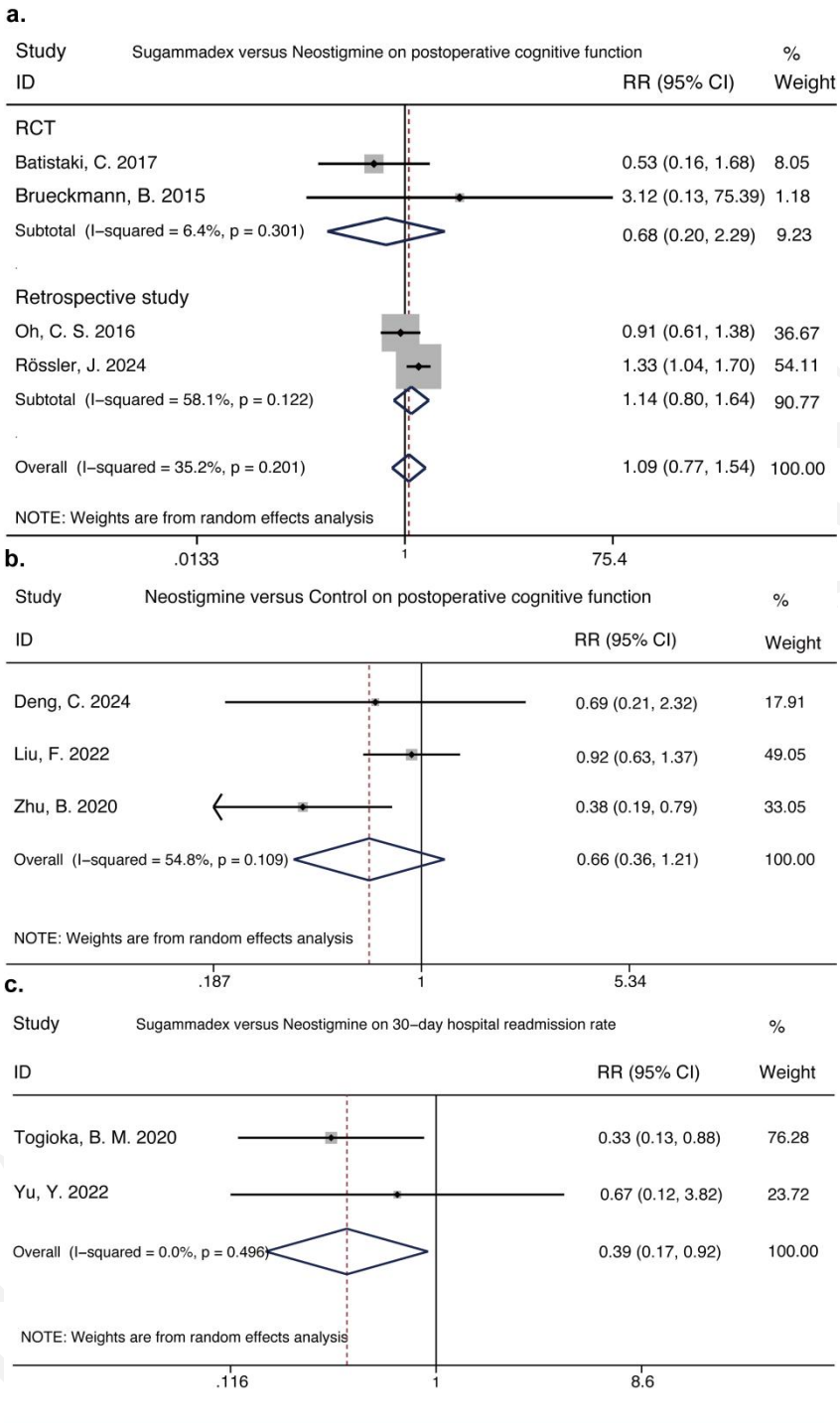

Figure 4. Comparison of sugammadex and neostigmine regarding postoperative cognitive function and long-term recovery outcomes, illustrating their respective impacts on cognitive performance and extended health indicators.

SUPPLEMENTAL DATA

Supplemental data are available at the following link:

https://www.bjbms.org/ojs/index.php/bjbms/article/view/12689/3972