Drug Design, Development and Therapy

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CLINICAL TRIAL REPORT

Impact of Sugammadex versus Neostigmine on Diaphragmatic Function and Respiratory Recovery in Morbidly Obese Patients with Moderate Neuromuscular Block: A Randomised Double-Blind Controlled Trial

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Purpose: Compared with neostigmine, sugammadex promotes faster neuromuscular recovery, but its impact on diaphragmatic function and respiratory recovery in the morbidly obese cohort, and the mechanism underlying its reduction of postoperative pulmonary complications remain unclear. This study aims to compare the effects of sugammadex and neostigmine on diaphragmatic function and respiratory recovery in morbidly obese patients after surgery, and to investigate the role of diaphragmatic function in the reduction of sugammadex-associated postoperative pulmonary complications.

Patients and Methods: For neuromuscular blockade reversal, 104 morbidly obese patients with moderate neuromuscular block (train-of-four count = 2, ratio <0.9) were randomly assigned to receive either neostigmine (50 μg kg-1+atropine 20 μg kg-1, n=51) or sugammadex (2 mg kg-1, n=53). Measurements of diaphragmatic excursion (DE) and thickening fraction (TF) were taken during deep and quiet breathing at T0 (baseline), T1 (10 min), and T2 (30 min) after extubation. The primary outcome measure was the change in deep breathing diaphragmatic excursion (ΔDE_{DB}) from baseline at T2. The secondary outcome measures included ΔDE_{QB}, ΔDE_{DB}, and ΔTF at T1; ΔDE_{QB} and ΔTF at T2; postoperative oxygenation index; number of respiratory reminders; and the frequency of postoperative pulmonary complications.

Results: At T2, the ΔDE_{DB} was smaller in the sugammadex group compared with the neostigmine group (0.05 cm vs. 0.28 cm; $P < 0.001$). At T1, the ΔDE_{QB}, ΔDE_{DB}, and ΔTF all differed significantly between groups, as did the ΔTF at T2 (all $P \leq 0.001$). The sugammadex group also demonstrated a higher oxygenation index (P=0.004) and a lower incidence of postoperative pulmonary complications (P=0.007).

Conclusion: In morbid obesity, sugammadex promotes faster diaphragmatic recovery and improves respiratory outcomes compared with neostigmine and is associated with a lower incidence of postoperative pulmonary complications.

Keywords: diaphragm, obesity, morbid, sugammadex, postoperative pulmonary complications

Introduction

As the principal muscle responsible for inspiration, the diaphragm is uniquely the core respiratory muscle that can efficiently generate negative intrathoracic pressure to drive inspiration.[1] This muscle accounts for over 60% of the volume of air displaced in a typical breath,[2] generates effective cough pressure to clear airway secretions, facilitates alveolar expansion and improves oxygenation.[3] In patients with morbid obesity, significant alterations in diaphragmatic function occur due to factors such as intra-abdominal fat accumulation, elevated intra-abdominal pressure, chronic mechanical overload, metabolic

https://doi.org/10.2147/DDDT.S577208
Received: 30 October 2025
Accepted: 23 March 2026
Published: 7 April 2026

abnormalities, and systemic inflammation.[4–6] As an integral part of the respiratory muscle ensemble, impaired diaphragmatic function due to residual neuromuscular blockade also constitutes a key risk factor hindering the complex physiological process of postoperative respiratory recovery.[7] Previous studies have reported that the incidence of postoperative pulmonary complications (PPCs) ranges from 2.6% to 7.6% in the general surgical population,[8] but it approximates 22% in patients with obesity,[9] profoundly impairing recovery and increasing healthcare costs, and the mortality rate.

The presence of residual neuromuscular blockade following surgery elevates the risk for PPCs.[10,11] Sugammadex reverses deeper levels of neuromuscular blockade more effectively than neostigmine—a pharmacological advantage consistently observed across diverse patient populations. This advantage is particularly clinically relevant in patients with morbid obesity, who face an increased risk of postoperative pulmonary complications.[12] Sugammadex promotes a faster recovery of the train-of-four (TOF) ratio to ≥0.9. However, this expedited recovery has not been directly linked to a significant decrease in PPCs.[13] Instead, the recovery of respiratory muscle function to preoperative levels may be the underlying reason for the decreased incidence of PPCs in patients with obesity. Ultrasonographic assessment of diaphragmatic excursion has been validated as a reliable and valid method for evaluating diaphragmatic function.[14] It remains unclear whether sugammadex accelerates postoperative diaphragmatic recovery, improves respiratory outcomes, and reduces PPCs in morbidly obese patients. This study therefore aimed to compare its effects with neostigmine on these measures, explore the underlying mechanisms, and provide evidence for optimizing enhanced recovery after surgery protocols after bariatric surgery.

Materials and Methods

Ethical Approval and Study Design

This prospective, randomized, single-center study was conducted in accordance with the Declaration of Helsinki at the Affiliated Hospital of Xuzhou Medical University between January and May 2025. The Institutional Review Board of the Affiliated Hospital of Xuzhou Medical University gave its approval to the study protocol (Approval No.: XYFY2024-KL575-01; Approval Date: November 19, 2024; Chairperson: Tie Xu). Prior to patient enrollment, the study was registered on https://clinicaltrials.gov (Registration No.: ChiCTR2400094886; Registration Date: December 30, 2024). Furthermore, informed consent in writing was secured from all subjects involved in the research.

Participants

The inclusion criteria comprised adult patients with a diagnosis of morbid obesity who were scheduled for elective laparoscopic bariatric surgery. To qualify for enrollment, participants were required to meet the following criteria: aged between 18 and 64 years, and possess a BMI of ≥40 kg m^{-2}, or a BMI of ≥35 kg m^{-2} accompanied by one or more obesity-related co-morbidities, such as hypertension or type 2 diabetes mellitus.[15] Exclusion criteria were: (1) known allergy to or contraindication to sugammadex, neostigmine, atropine, or ultrasound coupling gel; (2) known diaphragmatic paralysis or severe diaphragmatic dysfunction, significant pleural effusion, history of pneumonectomy, severe pulmonary dysfunction, or other significant respiratory or neurological disorders; (3) severe cardiac dysfunction (NYHA class III–IV), significant renal or hepatic impairment; (4) acute or chronic alcohol intoxication; (5) active infectious disease requiring systemic antibiotic therapy; (6) pre-existing chronic pain, chronic opioid use, psychotropic drug use, or history of drug abuse; (7) psychiatric illness or communication barriers. Withdrawal criteria for the primary analysis were: (1) conversion from laparoscopic to open surgery; (2) inability to obtain technically adequate diaphragmatic ultrasonographic images; (3) intraoperative blood loss ≥600 mL or haemoglobin level <80 g L^{-1}; (4) unplanned reintubation in the post-anaesthesia care unit (PACU); (5) postoperative admission to the ICU; (6) withdrawal of consent.

Randomisation and Blinding

Participants were equally allocated to either the neostigmine group or the sugammadex group using computer-generated random numbers. Sequentially numbered, opaque, sealed envelopes were used to assure allocation concealment. Study drugs were prepared by staff not involved in clinical care or assessment in identical syringes labelled only with randomisation codes. Patients, anaesthesiologists, and assessing staff remained blinded.

Anaesthesia Methods

A standardized anaesthetic protocol was used. Monitoring included ECG, SpO_2, end-tidal carbon dioxide, temperature, and invasive arterial pressure via radial catheter. Anaesthetic depth was assessed with bispectral index (BIS). Neuromuscular function was monitored using a piezoelectric neuromuscular monitor (GE Datex-Ohmeda E-NMT-00) with TOF stimulation (2 Hz, 0.2 ms, 60 mA) every 20s. Electrodes were positioned over the ulnar nerve with the sensor on the thumb. After calibration to a stable baseline TOF, the monitor continuously recorded TOF ratio and TOF count throughout surgery.

Drug doses were calculated using ideal body weight (IBW) or corrected body weight (CBW), defined as: IBW = Height (cm) – 100 (male) or 105 (female); CBW = IBW + 0.4 × (actual body weight – IBW). No premedication was given. After 3–5 min preoxygenation, anaesthesia was induced with etomidate 0.3 mg kg^{-1} IBW, sufentanil 0.5 μg kg^{-1} IBW, remifentanil 1 μg kg^{-1} IBW, and rocuronium 0.9 mg kg^{-1} IBW.

Propofol (2–5 mg kg^{-1} h^{-1} IBW) and remifentanil (0.1–0.3 μg kg^{-1} min^{-1} IBW) were continuously infused to maintain anaesthesia, and sevoflurane (1–2%) was breathed. Infusions were titrated to maintain BIS 40–60. Haemodynamics were kept within 20% of baseline using vasopressors/fluids as needed. Neuromuscular blockade was maintained at TOF count 0 and post-tetanic count 1–3; rocuronium 0.2 mg kg^{-1} IBW was given if TOF count ≥2. Intraperitoneal pressure was maintained at 14 mmHg. Thirty minutes before the procedure ended, sevoflurane was terminated, and no further rocuronium was administered. Propofol ended after abdominal manipulation, remifentanil at skin closure. Postoperative nausea and vomiting prophylaxis included dexamethasone 5 mg and tropisetron 2 mg; preventive analgesia was provided with intravenous flurbiprofen axetil 50 mg.

Intervention

Following surgery, patients received neuromuscular blockade reversal based on CBW when the TOF count reached 2: the neostigmine group was given 0.05 mg kg^{-1} along with 20 μg kg^{-1} of atropine, while the sugammadex group was given 2 mg kg^{-1} of sugammadex.[16] Extubation occurred after TOF ratio ≥0.9 and meeting standard clinical criteria for extubation. Patients were transferred to the PACU, and TOF monitoring was discontinued post-extubation. Transfer to the ward followed haemodynamic stability. Analgesia (oxycodone/flurbiprofen axetil) targeted a visual analogue scale (VAS) score ≤4; patients with severe PONV received intravenous metoclopramide 10 mg.

Ultrasonographic Measurements

Diaphragmatic function was assessed by a single trained anaesthesiologist blinded to group allocation using a Wilson Navis ultrasound system at three timepoints: before the administration of neuromuscular blocking agents (T0), 10 min (T1), and 30 min (T2) after extubation. Patients were positioned semi-recumbent (head elevated 45°). Diaphragmatic excursion (DE) was measured using a low-frequency convex probe (1–5 MHz) placed in the right subcostal midclavicular line. After identifying the diaphragm via the liver window, excursion was recorded during quiet (DE_{QB}) and deep breathing (DE_{DB}) using M-mode (scan speed 25 mm s^{-1}). Diaphragmatic thickening fraction (TF) was assessed with a high-frequency linear probe (4–15 MHz) placed over the right apposition zone (8th–9th intercostal space, midaxillary line), visualizing the three-layer structure (pleura-diaphragm-peritoneum). Thickness was measured at end-inspiration (TI) and end-expiration (TE) during deep breathing; TF was calculated as: [(TI – TE)/TE] × 100%. The average of three respiratory cycles was recorded for both DE and TF (Figure 1). Pain intensity assessed by visual analogue scores (VAS) and presence of PONV (yes/no) were also recorded at each timepoint.

Data Collection

The arterial oxygenation index (PaO_2/FiO_2) was calculated from blood gas analysis performed at T0 and T2 while patients were breathing room air. The time to TOF ratio of 0.9 after reversal agent administration was recorded. PACU data included: number of SpO_2<90% episodes; breathing prompts (triggered by SpO_2 drop>10 s or reduced chest movement); and PACU stay duration. We also collected the incidence of PPCs within 24 hours. PPCs were defined as the occurrence of any of the following: (1) respiratory failure (defined as PaO_2 < 60 mmHg on room air, PaO_2/FiO_2 ratio < 300 mmHg, or SpO_2 < 90% requiring supplemental oxygen); (2) pleural effusion; (3) atelectasis; (4) pneumothorax; (5) bronchospasm; (6) aspiration

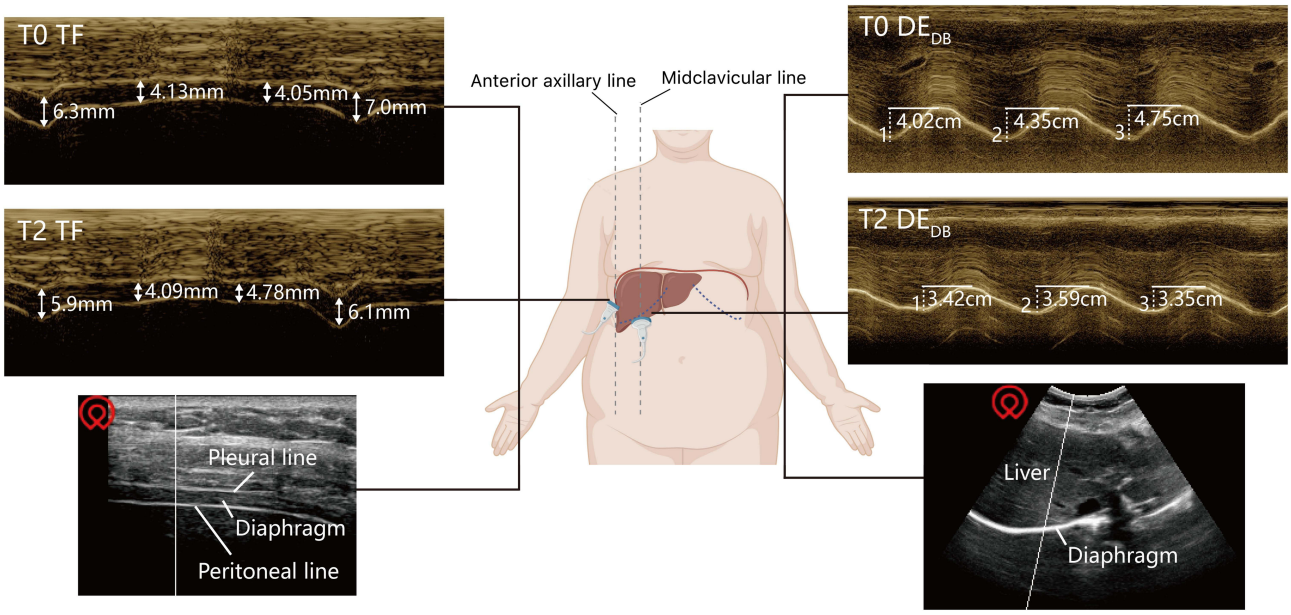

Figure 1 Schematic diagram illustrating the measurement of diaphragmatic thickening fraction (TF) and diaphragmatic excursion during deep breathing (DE_{DB}), performed before induction of anaesthesia (T0) and 30 minutes after extubation (T2).

pneumonia; (7) pneumonia, assessed according to the diagnostic criteria established in previous literature[17–19] and the EPCO classification.[20]

Outcomes

Demographic and intraoperative data were recorded. We analyzed the changes in all diaphragmatic function parameters from preoperative baseline to each postoperative time point. The primary outcome was ΔDE_{DB} at T2. Secondary outcomes comprised: (1) ΔDE_{QB} and ΔTF at T2; (2) ΔDE_{DB}, ΔDE_{QB}, and ΔTF at T1; (3) time to TOF ratio of 0.9; (4) PaO_2/FiO_2 at T2; (5) number of SpO_2<90% episodes in PACU; (6) number of breathing prompts in PACU; (7) PACU stay duration; (8) 24-hour PPCs incidence.

Statistical Analysis

Data were analyzed using SPSS (version 29.0) and GraphPad Prism (version 9.0.0 for Mac OS). A two-sided $P < 0.05$ was considered significant. Normally distributed data are compared with the independent samples *t*-test; non-normal data are compared with the Mann–Whitney *U*-test (Hodges-Lehmann median difference [MD] and 95% CI reported). A Generalized Estimating Equations (GEE) model (continuous outcome, exchangeable working correlation) was used, in which we first tested the group-time interaction, followed by Bonferroni-adjusted comparisons if significant. Categorical data are presented as n (%) and analysed with the χ^2-test (Relative Risk (RR) and 95% CI reported). Bonferroni correction was applied to two secondary outcome families: diaphragmatic recovery (5 tests) and respiratory recovery (6 tests). Mediation analysis (PROCESS Macro, Model 4) assessed whether ΔDE_{DB} at T2 mediated the effect of sugammadex on PPCs, with adjustment for potential clinical confounders, using bootstrapping (5000 samples) with effects reported as log-odds and 95% Boot CI. ROC (Receiver Operating Characteristic) analysis evaluated ΔDE_{DB}'s predictive value for hypoxaemia (defined as PaO_2/FiO_2 ≤300 mmHg on room air), reporting AUC (95% CI) and the optimal cut-off via Youden's index.

Sample Size Calculations

As no prior data existed for ΔDE_{DB} comparing sugammadex and neostigmine in morbid obesity, the sample size was determined using data obtained from our preliminary investigations conducted prior to this trial. The mean±SD ΔDE_{DB} for sugammadex vs neostigmine were 0.018±0.47 cm vs 0.34±0.42 cm. Using PASS 15.0 (90% power, α=0.05), 42 patients per group were required. With a 20% dropout rate, 106 patients were needed.

Results

Of 140 patients assessed for eligibility, 34 were excluded, leaving 106 for analysis (Figure 2). Two patients (neostigmine group) were excluded due to inadequate ultrasonographic images. Between groups, patient characteristics were similar (Tables 1 and 2).

Primary Outcome

The sugammadex group showed a significantly smaller ΔDE_{DB} at T2 than the neostigmine group (median [IQR]: 0.05 [0 to 0.11]cm vs. 0.28 [0.05 to 0.9]cm; MD, 0.19; 95% CI, 0.08 to 0.29; $P<0.001$) (Table 3).

Compared with the neostigmine group, the sugammadex group experienced a considerably decreased incidence of PPCs (7.5% vs 27.5%; RR = 0.216, 95% CI: 0.066 to 0.709; $P=0.007$). The distribution of PPC subtypes was as follows: in the neostigmine group, a total of 14 events occurred, including respiratory failure in 7 cases (13.7%), atelectasis in 6 cases (11.7%), and pleural effusion in 1 case (1.9%); in the sugammadex group, a total of 4 events occurred, including atelectasis in 3 cases (5.6%) and respiratory failure in 1 case (1.9%). Due to the limited number of events in each subtype, between-group statistical comparisons were not performed. An exploratory path analysis, adjusted for BMI, surgery duration, total rocuronium dose, OSAS, and Diabetes, was conducted to assess the potential role of diaphragmatic function (ΔDE_{DB} at T2). ΔDE_{DB} at T2 remained significantly lower in the sugammadex group ($\beta = -0.350$, $P<0.001$). However, its association with PPCs risk was not significant ($\beta = 0.875$, $P=0.177$). Consequently, the indirect effect of sugammadex on PPCs through ΔDE_{DB} at T2 was not statistically significant ($\beta = -0.306$, 95% Bootstrap CI: −1.098 to 0.159). The direct protective effect of sugammadex on PPCs remained significant after adjustment ($\beta = -2.128$, $P=0.0079$).

Secondary Outcomes

Postoperative Diaphragmatic Function Recovery

At T1, the sugammadex group showed significantly smaller changes from baseline in ΔDE_{DB} (MD, 0.63; 95% CI, 0.4 to 0.92), ΔDE_{QB} (MD, 0.18; 95% CI, 0.08 to 0.3), and ΔTF (MD, 0.042; 95% CI, 0.036 to 0.048) compared with the neostigmine group (all Bonferroni-corrected $P\leq0.001$). At T2, the ΔTF remained significantly smaller in the sugammadex group (MD, 0.039; 95% CI, 0.035 to 0.042; Bonferroni-corrected $P<0.001$), while the difference in ΔDE_{QB} between groups was not statistically significant (MD, 0.08; 95% CI, 0 to 0.2; Bonferroni-corrected $P=0.051$) (Table 3).

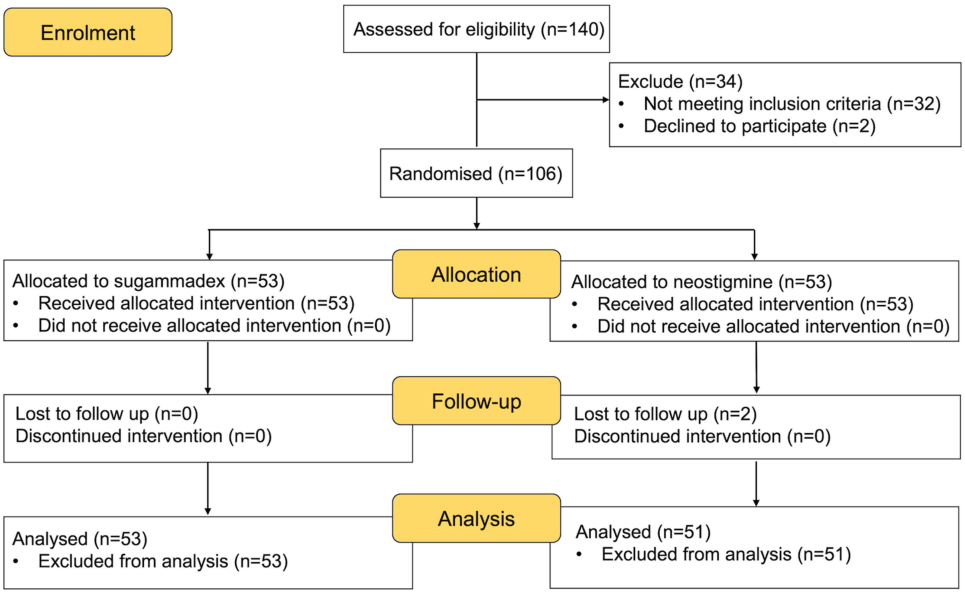

Figure 2 Study flow diagram.

https://doi.org/10.2147/DDDT.S577208

Table 1 Baseline Characteristics of Patients Receiving Sugammadex or Neostigmine for Bariatric Surgery

	Sugammadex (n=53)	Neostigmine (n=51)
Age, yr	34.25 (7.37)	33.4 (6.4)
Female sex, n (%)	38 (72)	36 (71)
ASA (II/III)	33/20	38/13
BMI, kg m^{-2}	39 (35–45.5)	37 (35–40)
Smoking History	21 (39.6)	16 (31.4)
History of Previous Surgery	13 (24.5)	12 (23.5)
Comorbidities		
Hypertension	27 (50.9)	21 (41.2)
Type 2 Diabetes Mellitus	22 (42.3)	27 (52.9)
OSAS	8 (15.1)	7 (13.7)
Preoperative Pulmonary Function		
FEV_1/FVC	85.1 (81–87.5)	86 (82–88)
PEF, l s^{-1}	7.2 (1.59)	7.62 (1.43)
Preoperative PaO_2/FiO_2, mmHg	399 (44.1)	387.69 (47.2)
Preoperative Diaphragmatic Ultrasonography		
DE_{QB}, cm	1.84 (0.52)	1.86 (0.55)
DE_{DB}, cm	3.6 (2.35–4.54)	3.7 (2.54–5.31)
TF, %	52.61 (5.52)	52.87 (7.27)

Notes: Values are mean (SD), number (proportion) or median (IQR [range]).
Abbreviations: OSAS, obstructive sleep apnoea syndrome; FEV_1/FVC, forced expiratory volume in 1 second/forced vital capacity ratio; PEF, peak expiratory flow; PaO_2/FiO_2, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen; DE_{QB}, diaphragmatic excursion during quiet breathing; DE_{DB}, diaphragmatic excursion during deep breathing; TF, diaphragmatic thickening fraction.

Table 2 Perioperative Characteristics of Patients Receiving Sugammadex or Neostigmine for Bariatric Surgery

	Sugammadex (n=53)	Neostigmine (n=51)
Type of Surgery		
LSG	14 (26.4)	16 (31.4)
LRYGB	39 (73.6)	35 (68.6)
Duration of Pneumoperitoneum, h	2.2 (1.8–2.8)	2.2 (1.8–2.6)
Duration of Trendelenburg Position, h	2.2 (1.8–2.8)	2.2 (1.9–2.6)
Duration of Surgery, h	2.4 (1.9–2.9)	2.4 (1.9–2.7)
Intraoperative Respiratory Mechanics		
PaO_2/FiO_2, mmHg	356 (252–404.5)	350 (320–380)
$P_{ET}CO_2$, mmHg	37 (34–39)	36 (36–40)
DP, cmH_2O	20.36 (3.54)	20.89 (3.15)
Cdyn, mL.cmH_2O^{-1}	40.13 (2.9)	39.8 (2.61)
Cstat, mL.cmH_2O^{-1}	48 (46–49)	47 (46–48)
Total Drug Consumption		
Rocuronium, mg	100 (77.5–110)	95 (80–100)
Remifentanil, mg	3 (2.3–3.55)	3 (2.5–3)
Propofol, mg	350 (270–400)	350 (300–400)

Notes: Values are mean (SD), number (proportion) or median (IQR [range]). DP = plateau pressure (Pplat) - positive end-expiratory pressure (PEEP); Dynamic Lung Compliance (Cdyn): Cdyn = tidal volume (V_T)/[peak airway pressure (Ppeak) - positive end-expiratory pressure (PEEP)]; Static Lung Compliance (Cstat): Cstat = tidal volume (V_T)/[plateau pressure (Pplat) - positive end-expiratory pressure (PEEP)].
Abbreviations: LSG, Laparoscopic Sleeve Gastrectomy; LRYGB, Laparoscopic Roux-en-Y Gastric Bypass; PaO_2/FiO_2, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen; $P_{ET}CO_2$, end-tidal carbon dioxide partial pressure; DP, Driving Pressure.

Table 3 Primary and Secondary Outcomes in Patients Receiving Sugammadex or Neostigmine for Bariatric Surgery

	Sugammadex (n=53)	Neostigmine (n=51)	*P* -value
Primary Outcome			
T2ΔDE$_{DB}$, cm	0.05 (0–0.11)	0.28 (0.05–0.9)	<0.001
Secondary Outcomes			
Postoperative Diaphragmatic Function Recovery			
T1ΔDE$_{DB}$, cm	0.71 (0.53)	1.39 (0.72)	<0.001[a]
T1ΔDE$_{QB}$, cm	0.32 (0.2–0.495)	0.49 (0.34–0.8)	0.001[a]
T1ΔTF, %	8.77 (0.96)	12.98 (1.59)	<0.001[a]
T2ΔDE$_{QB}$, cm	0.1 (0.005–0.275)	0.2 (0.05–0.42)	0.051[a]
T2ΔTF, %	4.90 (0.75)	8.75 (0.88)	<0.001[a]
Postoperative Respiratory Recovery			
Time to train-of-four ratio ≥0.9, min	5 (3–7)	7 (5–9)	<0.001[b]
PaO_2/FiO_2 at T2	369.26 (47.55)	337.59 (61.33)	0.004[b]
Incidence of PPCs, %	4 (7.5)	14 (27.5)	0.007[b]
Number of episodes with SpO_2 <90%	1 (0–3)	2 (0–5)	0.285[b]
Number of deep breathing encouragements	2 (0.5–3)	3 (1–5)	0.012[b]
Duration of PACU stay, min	50 (40–60)	60 (40–60)	0.066[b]
VAS pain score at T1	4 (1–6)	4 (2–6)	0.898
VAS pain score at T2	3 (2–6)	3 (2–4)	0.418

Notes: Values are expressed as mean ± SD, median (interquartile range [IQR]), and frequency (%). The Bonferroni-corrected *P*-values for the two families of secondary endpoints—postoperative diaphragmatic function recovery and postoperative respiratory recovery—are represented by "a" and "b", respectively. Both a and b can be directly compared with 0.05.

Abbreviations: T1, 10 min after extubation; T2, 30 min after extubation; ΔDE$_{DB}$, the change in diaphragmatic excursion during deep breathing from preoperative baseline; ΔDE$_{QB}$, the change in diaphragmatic excursion quiet breathing from preoperative baseline; ΔTF, the change in diaphragmatic thickening fraction from preoperative baseline; PaO_2/FiO_2, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen; PPCs, postoperative pulmonary complications; PACU, post-anaesthesia care unit; VAS, visual analogue scores.

GEE analysis, adjusted for BMI and baseline (T0) diaphragmatic function, showed different temporal trends in diaphragmatic recovery between groups (Figure 3). Significant group-by-time interactions occurred for DE$_{DB}$ (P<0.001), DE$_{QB}$ (P=0.004), and TF (P=0.004). In both groups, values at T1 and T2 differed significantly from those at T0 (all P<0.001). The sugammadex group had higher DE$_{DB}$ and TF at T1 and T2 (all P<0.001), and higher DE$_{QB}$ at T1

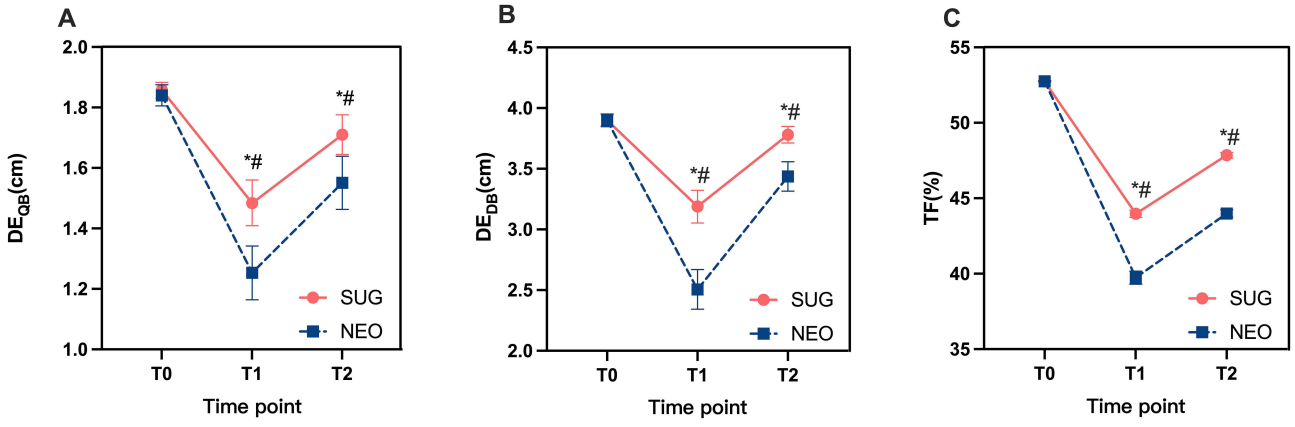

Figure 3 Diaphragmatic function parameters between the two patient groups at each time point. (**A**) Comparison of diaphragmatic excursion during quiet breathing (DE$_{QB}$) between patient groups at each time point; (**B**) Comparison of diaphragmatic excursion during deep breathing (DE$_{DB}$) between patient groups at each time point; (**C**) Comparison of diaphragmatic thickening fraction (TF) between patient groups at each time point. T0: before induction; T1: 10 min after extubation; T2: 30 min after extubation; *P < 0.05 (sugammadex group vs Neostigmine group at the respective time point). #: P < 0.001 (each time point within a group vs baseline (T0)).

https://doi.org/10.2147/DDDT.S577208

(P<0.001) and T2 (P=0.006) than the neostigmine group. Each 1 kg m^{-2} increase in BMI was associated with a 0.02 cm reduction in DE_{DB} (β =−0.02; 95% CI: −0.027 to −0.013; P<0.001), but no associations were seen between BMI and DE_{QB} (P=0.073) or TF (P=0.696).

Postoperative Respiratory Recovery

The sugammadex group had a shorter time to TOF ratio≥0.9 (median[IQR]: 5[3 to 7]min vs 7[5 to 9]min; MD, 2 min; 95% CI, 1 to 3 min; Bonferroni-corrected P<0.001), higher PaO_2/FiO_2 at T2 (Bonferroni-corrected P=0.004), and fewer deep breathing prompts (Bonferroni-corrected P=0.012) than the neostigmine group. There were no discernible variations in the quantity of SpO_2<90% occurrences, (Bonferroni-corrected P=0.285), PACU stay duration (Bonferroni-corrected P=0.066). VAS pain ratings showed no discernible variations at T1 or T2 in either group, additionally, no episodes of PONV were recorded in either group at these time points (Table 3).

ROC analysis showed that ΔDE_{DB} at T2 had moderate predictive value for postoperative hypoxemia (defined as PaO_2/FiO_2 ≤300 mmHg; AUC=0.7854; 95% CI: 0.6515 to 0.9193; P<0.001) (Supplementary Figure 1). At the optimal cutoff of 0.215 cm, sensitivity was 86.7%, specificity 75.3% (Youden's index = 0.62), Positive Predictive Value 40%, and Negative Predictive Value 97.1%, indicating high sensitivity and Negative Predictive Value but limited Positive Predictive Value. The predictive performance of ΔDE_{DB} at T2 (AUC = 0.7854) was superior to that of ΔDE_{DB} at T1 (AUC = 0.6981), ΔDE_{QB} at T1 (AUC = 0.7509), and ΔDE_{QB} at T2 (AUC = 0.7577).

Discussion

Significantly less time was required to attain a TOF ratio of 0.9 in the sugammadex group compared to the neostigmine group. This finding is unsurprising and consistent with previous studies.[16] Our results further demonstrate that the sugammadex cohort maintained a statistically significant advantage in diaphragmatic contractile function throughout the 30-minute post-extubation period relative to the neostigmine group. The changes from baseline in DE_{DB}, DE_{QB}, and TF at T1, and in DE_{DB} and TF at T2, were all significantly smaller in the sugammadex group, indicating more rapid and complete functional recovery. Although the effect size estimated from the pilot data was overestimated, the prespecified sample size successfully detected a statistically significant between-group difference in the primary outcome, confirming the adequacy of the sample size calculation for the present study. Although the between-group difference in ΔDE_{DB} at T2 was modest (0.19 cm), its occurrence during the immediate post-extubation period reflects a meaningful acceleration in early neuromuscular recovery, which may carry potential clinical implications for morbidly obese patients with limited respiratory reserve. GEE analysis revealed differing temporal trends in ΔDE_{DB} between the two groups. These differences stem from the distinct mechanisms of each reversal agent: neostigmine, an acetylcholinesterase inhibitor, increases acetylcholine to competitively antagonize neuromuscular blocking agents (NMBAs), but in morbid obesity, adipose tissue may sequester and later release NMBAs, potentially leading to recurarization[21] and inadequate neostigmine concentrations. In contrast, sugammadex forms specific complexes with aminosteroid NMBAs (eg, rocuronium), inactivating and promoting their renal excretion,[22] thereby lowering plasma concentrations and restoring neuromuscular function more rapidly and completely. These results confirm that sugammadex facilitates quicker diaphragmatic recovery in morbid obesity, promoting early spontaneous breathing and aiding in the prevention of postoperative residual neuromuscular blockade.

A notable finding was the significant between-group difference in ΔDE_{DB} at T2, but not in ΔDE_{QB}. This is physiologically explained by the fact that quiet breathing requires only about 8% of the maximal transdiaphragmatic pressure generated during a deep inspiration.[23,24] By 30 minutes post-extubation, neuromuscular recovery in both groups was sufficient for quiet breathing, potentially masked in morbidly obese patients by compensatory chest breathing and accessory muscle use. Deep breathing, requiring maximal diaphragmatic contraction, is a more robust strength test. The superior DE_{DB} recovery, higher oxygenation index, and lower 24-hour PPCs incidence (7.5% vs 27.5%) with sugammadex all indicate enhanced respiratory recovery.

The exploratory path analysis, conducted with adjustment for key perioperative confounders, did not yield a statistically significant indirect effect of sugammadex on PPCs through diaphragmatic function. This suggests that the clinical advantage of sugammadex in reducing PPCs is likely mediated through mechanisms beyond a singular improvement in early diaphragmatic recovery. This finding aligns with the established view that postoperative pulmonary complications are more strongly

linked to impaired coordination of upper airway and pharyngeal muscles rather than isolated diaphragmatic dysfunction.[7] Therefore, the superior efficacy of sugammadex may stem from its ability to ensure more complete and rapid recovery of global neuromuscular function, thereby enhancing the integrity of the entire respiratory system and airway protective reflexes.

Although extubation was carried out after TOF ratio ≥0.9 in both groups, diaphragmatic function had not fully returned to baseline by the end of observation. This aligns with reports that respiratory muscle strength may remain impaired even at TOF ratio=1, possibly due to persistent neuromuscular transmission deficits.[25] In morbid obesity, intra-abdominal fat accumulation and laparoscopic surgery-related pneumoperitoneum induced increased intra-abdominal pressure may mechanically compromise diaphragmatic function. Additionally, adipose-derived pro-inflammatory cytokines (eg, TNF-α[26]) might impair diaphragmatic mitochondrial function and oxidative phosphorylation,[27] limiting its capacity for deep breathing and contributing to prolonged diaphragmatic function recovery.

Although prior studies indicate sugammadex enhances immediate post-extubation diaphragmatic recovery compared with neostigmine,[13,14] the immediate post-extubation period is often complicated by cardiovascular instability (eg, hypertension, tachycardia), patient movement, and retained secretions, which can impair patient cooperation and the reliability of ultrasound measurements for diaphragmatic indices. Allowing 10 minutes post-extubation improves patient adaptation to spontaneous breathing and compliance with deep inspiration commands, increasing the accuracy of measurements at 10 min post-extubation (T1).

Morbidly obese patients have reduced oxygen reserves. Diaphragmatic dysfunction often precedes oxygen desaturation. Ultrasonographic diaphragmatic excursion is a non-invasive, safe,[28] and easily operable bedside tool offering real-time assessment, avoiding delays from difficult blood gas sampling (eg, challenging vascular access in obese patients). Monitoring ΔDE_{DB} is clinically valuable post-bariatric surgery. ROC analysis showed that ΔDE_{DB} at T2 has high sensitivity (86.7%) for predicting postoperative hypoxaemia. A ΔDE_{DB}<0.215 cm at 30 min post-extubation may prompt early intervention (eg, non-invasive ventilation) to prevent hypoxaemia-related complications. However, this finding is derived from a single-center exploratory study with a limited sample size and may be subject to overfitting. External validation in larger, multicenter cohorts is warranted before this threshold can be considered for clinical application.

This study employed acceleromyography combined with kinemyographic signal processing for neuromuscular monitoring. While this method is commonly used clinically, its underlying principle differs from electromyography, which measures the compound muscle action potential more directly. It is noteworthy that kinemyography may overestimate the TOF ratio.[29] This might explain why the recovery time in the neostigmine group in our study (median 7 minutes, IQR 5–9) was shorter than that reported in some previous studies.[25,30]

This study has several limitations. First, although ultrasonographic measurements were standardized, this technique remains partially dependent on patient effort; variability in inspiratory depth due to inconsistent patient cooperation may therefore introduce measurement bias. Furthermore, despite the use of a single trained and blinded operator to ensure consistency, intra-observer variability and potential subconscious bias cannot be entirely excluded. Second, PPCs were assessed only within the first 24 hours postoperatively, a window that may fail to capture delayed-onset complications (eg, pneumonia or respiratory failure occurring 48–72 hours after surgery). This limitation could lead to an underestimation of the overall incidence of PPCs. Third, the findings are based on a specific cohort of patients aged 18–55 years undergoing laparoscopic bariatric surgery, which limits the generalizability of our results to other surgical procedures (eg, open bariatric surgery, thoracic surgery) or age groups (eg, elderly patients, adolescents). Regarding future directions, the use of electromyography, which offers higher precision, may be considered to monitor the depth of neuromuscular blockade. Additionally, this study did not include a cost-effectiveness analysis. Although sugammadex has a higher acquisition cost than neostigmine, determining whether its clinical benefits translate into overall healthcare cost savings warrants further investigation.

Conclusion

In conclusion, in morbidly obese patients with moderate neuromuscular block (TOF count of 2), sugammadex facilitates more rapid recovery of diaphragmatic and respiratory function than neostigmine, with benefits for at least 30 minutes after extubation. Future studies should examine the long-term effects of sugammadex on diaphragmatic function and compare

both agents under guideline-recommended minimal block (TOF ratio ≥ 0.4) using electromyography (EMG)-based monitoring for more precise and valid assessment.

Data Sharing Statement

All data will be shared from the corresponding author (Guanglei Wang).

Acknowledgments

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Funding

No funding was received.

Disclosure

All authors declare no competing interests.

References

1. Sieck GC, Fogarty MJ. Diaphragm muscle: a pump that can not fail. *Physiol Rev*. 2025;105(4):2589–2656. doi:10.1152/physrev.00043.2024
2. Nguyen-Huu T, Molgó J, Servent D, Duvaldestin P. Resistance to D-tubocurarine of the rat diaphragm as compared to a limb muscle: influence of quantal transmitter release and nicotinic acetylcholine receptors. *Anesthesiology*. 2009;110(5):1011–1015. doi:10.1097/ALN.0b013e31819faeaa
3. Fu X, Wang Z, Wang L, et al. Increased diaphragm echodensity correlates with postoperative pulmonary complications in patients after major abdominal surgery: a prospective observational study. *BMC Pulm Med*. 2022;22(1):400. doi:10.1186/s12890-022-02194-6
4. Sood A. Altered resting and exercise respiratory physiology in obesity. *Clin Chest Med*. 2009;30(3):445–vii. doi:10.1016/j.ccm.2009.05.003
5. Buras ED, Converso-Baran K, Davis CS, et al. Fibro-adipogenic remodeling of the diaphragm in obesity-associated respiratory dysfunction. *Diabetes*. 2019;68(1):45–56. doi:10.2337/db18-0209
6. Rodrigues GC, Rocha NN, Maia LA, et al. Impact of experimental obesity on diaphragm structure, function, and bioenergetics. *J Appl Physiol*. 2020;129(5):1062–1074. doi:10.1152/japplphysiol.00262.2020
7. Fuchs-Buder T, Schmartz D. Neuromuskuläre Restblockade [Residual neuromuscular blockade]. *Anaesthesist*. 2017;66(6):465–476. doi:10.1007/s00101-017-0325-1
8. Carron M, Tamburini E, Iepparielloo G, Linassi F. Reversal of neuromuscular block with sugammadex compared with neostigmine and postoperative pulmonary complications in obese patients: meta-analysis and trial sequential analysis. *Br J Anaesth*. 2023;130(6):e461–e463. doi:10.1016/j.bja.2023.03.003
9. Bluth T, Serpa Neto A, Schultz MJ, et al; Writing Committee for the PROBESE Collaborative Group of the PROtective VEntilation Network (PROVEnet) for the Clinical Trial Network of the European Society of Anaesthesiology. Effect of intraoperative high positive end-expiratory pressure (PEEP) with recruitment maneuvers vs low PEEP on postoperative pulmonary complications in obese patients: a randomized clinical trial. *JAMA*. 2019;321(23):2292–2305. doi:10.1001/jama.2019.7505
10. Mazzinari G, Díaz-Cambronero O, Garutti I, Errando CL, Ferrando C; iPROVE-OLV investigators. Impact of neuromuscular block monitoring and reversal on postoperative pulmonary complications in thoracic surgery: a Bayesian analysis of the iPROVE-OLV trial. *Br J Anaesth*. 2025;135(5):1428–1440. doi:10.1016/j.bja.2024.11.041
11. Cammu G. Residual neuromuscular blockade and postoperative pulmonary complications: what does the recent evidence demonstrate? *Curr Anesthesiol Rep*. 2020;10(2):131–136. doi:10.1007/s40140-020-00388-4
12. Kheterpal S, Vaughn MT, Dubovoy TZ, et al. Sugammadex versus neostigmine for reversal of neuromuscular blockade and postoperative pulmonary complications (STRONGER): a multicenter matched cohort analysis. *Anesthesiology*. 2020;132(6):1371–1381. doi:10.1097/ALN.0000000000003256
13. Kirmeier E, Eriksson LI, Lewald H, et al; POPULAR Contributors. Post-anaesthesia pulmonary complications after use of muscle relaxants (POPULAR): a multicentre, prospective observational study. *Lancet Respir Med*. 2019;7(2):129–140. doi:10.1016/S2213-2600(18)30294-7
14. Cappellini I, Ostento D, Loriga B, Tofani L, De Gaudio AR, Adembri C. Comparison of neostigmine vs. sugammadex for recovery of muscle function after neuromuscular block by means of diaphragm ultrasonography in microlaryngeal surgery: a randomised controlled trial. *Eur J Anaesthesiol*. 2020;37(1):44–51. doi:10.1097/EJA.0000000000001055
15. Koskinas KC, Van Craenenbroeck EM, Antoniades C, et al. Obesity and cardiovascular disease: an ESC clinical consensus statement. *Eur J Prev Cardiol*. 2025;32(3):184–220. doi:10.1093/eurjpc/zwae279
16. 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):236–239. doi:10.1093/bja/aer330
17. Miskovic A, Lumb AB. Postoperative pulmonary complications. *Br J Anaesth*. 2017;118(3):317–334. doi:10.1093/bja/aex002
18. Qaseem A, Snow V, Fitterman N, et al. Clinical efficacy assessment subcommittee of the American college of physicians: risk assessment for and strategies to reduce perioperative pulmonary complications for patients undergoing noncardiothoracic surgery: a guideline from the American college of physicians. *Ann Intern Med*. 2006;144(8):575–580. doi:10.7326/0003-4819-144-8-200604180-00008
19. Smetana GW. Postoperative pulmonary complications: an update on risk assessment and reduction. *Cleve Clin J Med*. 2009;76(10 suppl 4):S60–S65. doi:10.3949/ccjm.76.s4.10

20. Jammer I, Wickboldt N, Sander M, et al. 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(2):88–105. doi:10.1097/EJA.0000000000000118
21. Ekinci O, Gulmez D, Subasi F, Ozgultekin A, Demiroluk O. Neostigmine versus sugammadex on post-operative recovery following bariatric surgery. *North Clin Istanb*. 2022;9(4):311–316. doi:10.14744/nci.2021.94715
22. Chandrasekhar K, Togioka BM, Jeffers JL. Sugammadex. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2023.
23. Fogarty MJ, Mantilla CB, Sieck GC. Breathing: motor control of diaphragm muscle. *Physiology*. 2018;33(2):113–126. doi:10.1152/physiol.00002.2018
24. Sieck GC. Physiological effects of diaphragm muscle denervation and disuse. *Clin Chest Med*. 1994;15(4):641–659. doi:10.1016/S0272-5231(21)00958-8
25. Huang C, Wang X, Gao S, et al. Sugammadex versus neostigmine for recovery of respiratory muscle strength measured by ultrasonography in the postextubation period: a randomized controlled trial. *Anesth Analg*. 2023;136(3):559–568. doi:10.1213/ANE.0000000000006219
26. Tzanavari T, Giannogonas P, Karalis KP. TNF-alpha and obesity. *Curr Dir Autoimmun*. 2010;11:145–156.
27. Davizon-Castillo P, McMahon B, Aguila S, et al. TNF-α-driven inflammation and mitochondrial dysfunction define the platelet hyperreactivity of aging. *Blood*. 2019;134(9):727–740. doi:10.1182/blood.2019000200
28. Lang J, Liu Y, Zhang Y, Huang Y, Yi J. Peri-operative diaphragm ultrasound as a new method of recognizing post-operative residual curarization. *BMC Anesthesiol*. 2022;22(1):25. doi:10.1186/s12871-022-01565-0
29. Hemmerling TM, Donati F. The M-NMT mechanosensor cannot be considered as a reliable clinical neuromuscular monitor in daily anesthesia practice. *Anesth Analg*. 2002;95(6):1826–1827. doi:10.1097/00000539-200212000-00086
30. Sun Y, Sun S, Chen R, et al. Diaphragm ultrasonography as a monitor in assessing antagonistic effect of sugammadex on rocuronium in patients with Child-Pugh grades A and B. *Front Med Lausanne*. 2024;11:1370021. doi:10.3389/fmed.2024.1370021