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Respiration and the Airway

RESPIRATION AND THE AIRWAY

Succinylcholine and postoperative pulmonary complications: a retrospective cohort study using registry data from two hospital networks

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Abstract

Background: Neuromuscular blocking agents (NMBAs) with a non-depolarising mechanism of action carry the risk of postoperative residual paralysis and are associated with postoperative pulmonary complications (POPC). Owing to the shorter duration of action, the depolarising NMBA succinylcholine may be associated with less postoperative residual paralysis, and hence fewer POPC. We tested the association of succinylcholine administration during anaesthesia and POPC.
Methods: In a retrospective cohort study of registry data from two large US academic medical centres, 244 850 adult noncardiac surgical patients undergoing general anaesthesia were included. The primary outcome was POPC, defined as post-extubation haemoglobin oxygen de-saturation to <90%, or re-intubation requiring intensive care unit admission within 7 days after surgery. The association between succinylcholine and POPC and its dose-dependency were tested in a hierarchical fashion using a multivariable logistic regression model.
Results: A total of 13 206 patients (5.4%) experienced POPC. Use of succinylcholine was associated with increased risk of POPC (adjusted odds ratio [OR_{Adj}]=1.11; 95% confidence interval [CI], 1.06–1.16; $P<0.001$; adjusted risk=5.18%; 95% CI, 5.06–5.30 without and 5.69%; 95% CI, 5.53–5.85 with succinylcholine), with a dose-dependent relationship (OR_{Adj}=1.08; 95% CI, 1.05–1.11 per mg kg^{-1}; $P<0.001$). In patients receiving non-depolarising NMBAs, succinylcholine further increased the risk of POPC (ORAdj=1.08; 95% CI, 1.03–1.14; $P=0.001$). The association between succinylcholine and POPC was modified ($P=0.03$ for interaction) by the duration of surgery with higher odds of POPC in patients undergoing surgeries of <2 *vs* ≥2 h (OR_{Adj}=1.24; 95% CI, 1.15–1.33 and 1.05; 95% CI, 1.00–1.10, respectively).
Conclusions: In contrast to our prediction, succinylcholine administration was associated with an increased risk of POPC. This association was dose-dependent and magnified in surgeries of shorter duration.

Keywords: dose–response relationship; general anaesthesia; hypoxaemia; neuromuscular blocking agent; respiratory failure; succinylcholine

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Editor's key points

- Residual neuromuscular weakness has been associated with increased postoperative pulmonary complications (POPC) after general anaesthesia, which might be reduced by using short-acting neuromuscular blocking agents such as succinylcholine.
- A large two-centre retrospective cohort study was conducted to investigate the association between succinyl choline use and does with POPC.
- Of 244 850 adult noncardiac surgical patients undergoing general anaesthesia with 5.4% experiencing POPC, succinylcholine use was dose-dependently associated with increased risk of POPCs.
- Based on these findings, use of succinylcholine with general anaesthesia should follow a clear clinical indication, particularly for procedures less than 2 h.

Several hundred million patients undergo surgery annually involving general anaesthesia and mechanical ventilation.[1] In the majority of these patients, tracheal intubation is warranted, which is facilitated by administration of neuromuscular blocking agents (NMBAs).[2] There is growing evidence that use of NMBAs is associated with increased risk of adverse patient outcomes such as postoperative pulmonary complications (POPC),[3–5] which are frequent[6] and increase patient morbidity and healthcare costs.[7] Moreover, POPC are associated with an increase in postoperative mortality,[8] increasing the risk for millions of surgical patients each year.

Several studies have shown that residual neuromuscular block after tracheal extubation contributes to the increased risk of POPC after NMBA use.[9–12] However, findings from these studies were limited to non-depolarising NMBAs.[5,10–13] The depolarising NMBA succinylcholine is administered to ~20% of patients in operating rooms in the USA.[14] It is characterised by a shorter duration of action, thereby allowing more rapid recovery from neuromuscular block when administered alone.[15,16] Succinylcholine might thus reduce the risk of residual neuromuscular block and could constitute an alternative to avoid NMBA-related POPC. In the present study, we examined the association between succinylcholine and POPC.

Methods

Adult surgical patients undergoing noncardiac surgery under general anaesthesia with tracheal intubation and planned extubation at the end of the case at Beth Israel Deaconess Medical Center (BIDMC) and Massachusetts General Hospital (MGH) in Boston, MA, USA between January 2006 and December 2017 were included in this hospital registry study. Patients with ASA physical status of 5 and 6 or with missing data for any of the confounding variables were excluded. The study was approved by the Committee on Clinical Investigations at BIDMC (#2019P000513) and the Partners Human Research Committee at MGH (#2019P003431). The requirement for informed consent was waived. This article was prepared according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (Supplementary Digital Content 1).

Exposure and outcome measures

Data were collected from hospital-governed databases comprising patient-, anaesthesia-, surgery-, and outcome-related data (Section 2 of the Supplementary Digital Content 2). The primary exposure variable was defined as the intraoperative administration of succinylcholine. The co-primary exposure was succinylcholine dose in mg kg^{-1}. The primary outcome was post-extubation desaturation (haemoglobin oxygen saturation <90%) in the operating room within 10 min after extubation, or re-intubation requiring unplanned ICU admission within 7 days after surgery, collectively named POPC.[4,17–19]

Secondary outcomes were major postoperative complications, a composite of cardiovascular (atrial fibrillation/flutter, myocardial infarction, cardiac arrest, deep venous thrombosis, pulmonary embolism, stroke), renal (acute renal failure, new-onset haemodialysis) and other major complications (bleeding, major wound disruption, pneumonia, sepsis, shock, and coma).[20]

Primary hierarchical analyses

We used an *a priori* defined hierarchical sequence for testing the primary hypotheses in order to avoid alpha inflation and limit type I error.[21,22] First, we tested the association of succinylcholine use and POPC using a multivariable logistic regression model. Conditional on a significant association between succinylcholine and POPC, we proceeded to investigate whether this association was dose-dependent using the dose of succinylcholine (mg kg^{-1}) as a continuous exposure, and dichotomised to low ($\leq$2 mg kg^{-1}) or high (>2 mg kg^{-1}) doses. Variables included in the *a priori* defined multivariable model were based on previously established prediction models for POPC.[4,19] We addressed patient-, procedure-, and anaesthesia-related covariates, and the study centre. The model further included factors associated with provider choice to administer succinylcholine, based on literature review, clinical judgement, and pharmaco-physiological plausibility (Section 2.3 of the Supplementary Digital Content 2).

Secondary analyses

We conducted a subgroup analysis to assess whether the additional administration of succinylcholine was associated with increased risk of POPC in a subgroup of patients receiving non-depolarising NMBAs. We further investigated whether duration of surgery modified the association between use of succinylcholine and POPC by including an interaction term (succinylcholine use $\times$ duration of surgery) into the primary logistic regression model. Linear combinations of the main effect and the interaction term were then applied to assess the association between the exposure and outcome across patient subgroups (duration of surgery <2 and $\geq$2 h).

We compared the risk of POPC and major postoperative complications between patients receiving only succinylcholine and patients receiving only non-depolarising NMBAs. We matched respective cases on a 1:1 basis using a caliper of 0.1, based on their propensity of receiving succinylcholine or a non-depolarising NMBA.[4,5] Effectiveness of matching was evaluated by calculating weighted conditional standardised differences of covariates after propensity score adjustment. Variables with a standardised difference >0.1 were additionally adjusted for by logistic regression analysis.[23]

The association of succinylcholine and a composite outcome consisting of postoperative pneumonia, respiratory

failure, reintubation, or pulmonary oedema within 7 postoperative days was assessed in a subgroup of patients where these data were available.[24]

We investigated the association between use of succinylcholine and delayed discharge from the PACU because of respiratory or cardiovascular complications, unplanned hospital readmission within 30 days after ambulatory surgery (adjusted for risk factors of unplanned hospital readmission[25]), postoperative noninvasive ventilation and unplanned admission to ICU within 7 days after surgery.

Exploratory analysis

We identified a subset of patients undergoing general surgery who had received continuous infusion of succinylcholine. In an exploratory analysis in a sub-cohort of general surgical patients, we calculated the risk of POPC depending on type of administration of succinylcholine (bolus or continuous infusion) by including a categorical variable as primary exposure in the logistic regression model. Finally, we compared the risk of POPC in patients undergoing upper *vs* lower abdominal surgery and receiving both succinylcholine plus a non-depolarising NMBA.

Sensitivity analyses

We performed sensitivity analyses to assess the robustness of our primary findings (detailed in Sections 4 and 5 of the Supplementary Digital Content 2): (1) we conducted propensity score matching comparing patients receiving or not receiving succinylcholine; we excluded (2) patients receiving continuous infusion of succinylcholine; (3) emergency cases and surgeries because of ileus; (4) patients receiving a laryngeal mask airway; and (5) patients with doses of succinylcholine >1.5 mg kg^{-1} body weight from the primary analysis; (6) we further explored whether the association between succinylcholine use and POPC was modified by patient emergency status (7) or study site through interaction term analysis; (8) we used reintubation within 7 days after surgery as the sole outcome; (9) we adjusted for non-depolarising NMBA dose (ED_{95}); (10) we included only the last case of patients who underwent multiple surgeries over the study period; (11) we conducted the primary analyses in a subgroup of patients undergoing upper and lower abdominal surgery; and (12) we addressed bias arising from missing covariates through multiple imputation with chained equations.

Statistical analyses

Analyses were predefined in a statistical analysis plan, which was approved by all authors (Supplementary Digital Content 3). The linearity assumption was tested for all continuous variables before inclusion into the logistic regression model. In case of non-linearity, variables were divided into equally sized quintiles or clinically meaningful categories. An initial sample size estimation was performed (Section 3 of the Supplementary Digital Content 2) and statistical significance was assumed at $P<0.05$. All statistical analyses were performed using Stata (version 15; StataCorp LLC, College Station, TX, USA).

Results

Of 274 803 adult surgical patients included in our study, the final study cohort comprised 244 850 patient cases after exclusion of ineligible cases and those with missing confounder variable information. Figure 1 and Table 1 show study flow and patient and perioperative characteristics, respectively.

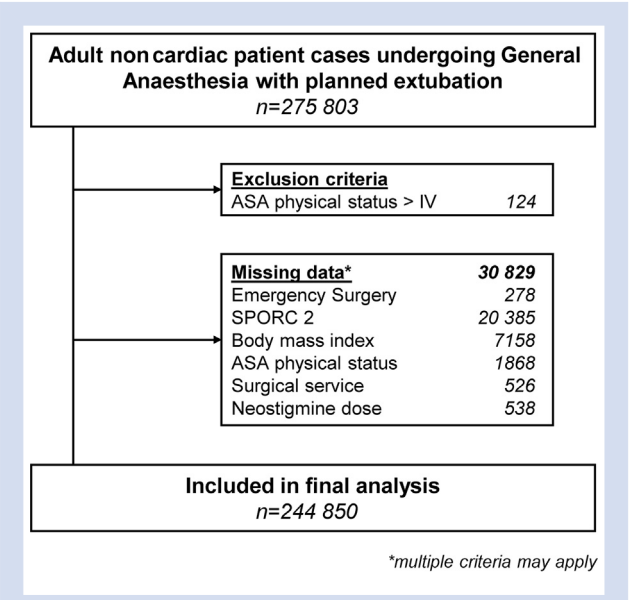

Fig 1. Study flowchart. SPORC 2, Score for the Prediction of Respiratory Complications.

Primary analyses

Succinylcholine was administered to 93 034 (38.0%) patients. The median succinylcholine dose was 1.22 mg kg^{-1} (interquartile range, 1.03–1.46), the mean dose was 1.30 (SD 0.52) mg kg^{-1}, and 3557 (1.5%) patients received >2 mg kg^{-1} succinylcholine. A total of 13 206 patients (5.4%) suffered a POPC. After adjustment for potential confounding factors, administration of succinylcholine was associated with an increased risk of POPC (adjusted odds ratio [OR_{Adj}]=1.11; 95% confidence interval [CI], 1.06–1.16; $P<0.001$, adjusted risk 5.18%; 95% CI, 5.06–5.30 without and 5.69%; 95% CI, 5.53–5.85 with succinylcholin(e adjusted risk difference=0.51%; 95% CI, 0.30–0.73). Adjusted ORs for each of four possible combinations of succinylcholine and nondepolarising NMBA are depicted in Table 2.

The association between succinylcholine and increased risk of POPC was dose-dependent (OR_{Adj} per mg kg^{-1} succinylcholine=1.08; 95% CI, 1.05–1.11; $P<0.001$). Compared with no succinylcholine, succinylcholine doses >2 mg kg^{-1} were associated with a greater increase in risk of POPC than doses ≤2 mg kg^{-1} (OR_{Adj}=1.62; 95% CI, 1.41–1.86 and 1.09; 95% CI, 1.05–1.14, respectively).

Secondary analyses

In a subgroup of 170 700 patients receiving nondepolarising NMBAs, succinylcholine was associated with increased risk of POPC (Table 2).

The association between succinylcholine and POPC was further modified by duration of surgery ($P=0.027$ for interaction): administration of succinylcholine was associated with an increased risk of POPC in surgeries <2 h, but not in surgeries >2 h (Fig 2).

Table 1 Patient cohort characteristics. IQR, inter-quartile range; COPD, chronic obstructive pulmonary disease; NMBA, neuromuscular blocking agent; SD, standard deviation

	Patient not receiving succinylcholine (*n*=151 816)	Patient receiving succinylcholine (*n*=93 034)	P-value
Patient characteristics			
Age, mean (SD, range) (yr)	54.0 (16.6, 18–104)	54.1 (16.2, 18–102)	0.44
Male sex	67 088 (44.2)	40 070 (43.1)	<0.001
BMI, mean (SD, range) (kg m^{-2})	27.6 (6.0, 15.0–79.7)	29.9 (7.9, 15.0–80.0)	<0.001
American Society of Anesthesiologists physical status			<0.001
1	20 163 (13.3)	8888 (9.6)	
2	86 152 (56.7)	48 785 (52.4)	
3	42 913 (28.3)	33 027 (35.5)	
4	2588 (1.7)	2334 (2.5)	
Study site I	83 443 (55.0)	39 503 (42.5)	<0.001
Study site II	68 373 (56.1)	53 531 (43.9)	<0.001
Type of admission			<0.001
Ambulatory	55 867 (36.8)	29 987 (32.2)	
Same-day admission	71 542 (47.1)	44 770 (48.1)	
Inpatient	24 407 (16.1)	18 277 (19.6)	
Emergency surgery	3152 (2.1)	7408 (8.0)	<0.001
Patient comorbidities			
Charlson comorbidity index, median (IQR)	1 (0–3)	1 (0–3)	<0.001
Renal disease	10 880 (7.2)	6448 (6.9)	0.027
Congestive heart failure	9685 (6.4)	6094 (6.6)	0.095
Liver disease	12 046 (7.9)	10 638 (11.4)	<0.001
Haemiplegia	3207 (2.1)	1073 (1.2)	<0.001
Diabetes mellitus	19 999 (13.2)	17 120 (18.4)	<0.001
History of smoking	27 262 (18.0)	14 059 (15.1)	<0.001
COPD	9888 (6.5)	6427 (6.9)	<0.001
Asthma	9335 (6.1)	7945 (8.5)	<0.001
Lower respiratory infections	3656 (2.4)	2330 (2.5)	0.13
Upper respiratory infections	698 (0.5)	474 (0.5)	0.084
History of sleep apnoea	4950 (3.3)	5090 (5.5)	<0.001
Valvular heart disease	13 375 (8.8)	7602 (8.2)	<0.001
Hypertension	59 294 (39.1)	40 976 (44.0)	<0.001
Coronary artery disease	15 593 (10.3)	10 162 (10.9)	<0.001
Anaemia	21 559 (14.2)	14 864 (16.0)	<0.001
Gastro-oesophageal reflux disease	19 014 (12.5)	18 345 (19.7)	<0.001
Axial hernia	2160 (1.4)	3132 (3.4)	<0.001
Gastrectomy	73 (<1)	167 (0.2)	<0.001
Myasthenia gravis	218 (0.1)	114 (0.1)	<0.001
Other neuromuscular disorders	1011 (0.7)	598 (0.6)	<0.001
Intraoperative factors			
Duration of surgery, mean (SD) (min)	164 (109)	154 (103)	<0.001
Work relative value units, median (IQR)	13.4 (7.5–20.8)	12.3 (7.4–18.5)	<0.001
Minutes of mean arterial pressure below 55 mm Hg, median (IQR)	0 (0–2)	0 (0–2)	<0.001
Age-adjusted mean alveolar concentration of inhalation anaesthetics, mean (SD)	0.92 (0.32)	0.91 (0.32)	<0.001
Vasopressor dose, median (IQR) (mg norepinephrine equivalents)	0.01 (0.00–0.13)	0.01 (0.00, 0.10)	0.26
Total opioid dose, median (IQR) (mg oral morphine equivalents)	50.5 (28.4–79.5)	54.5 (35.2–79.5)	<0.001
Crystalloid and colloid infusion, median (IQR) (ml)	1800 (1000–2800)	2000 (1000–3250)	<0.001
Units of packed red blood cells, median (IQR)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.79
Use of non-depolarising NMBA	112 467 (74.1)	58 233 (62.6)	<0.001
Use of succinylcholine	0 (0.0)	93 034 (100.0)	<0.001
Non-depolarising NMBA, median (IQR) (ED_{95})	2.26 (0.00–3.48)	1.16 (0.00–2.25)	<0.001
Succinylcholine dose, median (IQR) (mg kg^{-1})	0.00 (0.00–0.00)	1.22 (1.03–1.46)	<0.001
Neostigmine dose, median (IQR) (mg kg^{-1})	0.03 (0.00–0.04)	0.02 (0.00–0.04)	<0.001
Additional regional anaesthesia	17 384 (11.5)	6969 (7.5)	<0.001
Ileus as primary reason for surgery	3091 (2.0)	3616 (3.9)	<0.001
Surgical service			<0.001
Acute care surgery	3638 (2.4)	4728 (5.1)	
Colorectal surgery	1686 (1.1)	833 (0.9)	
Ear, nose, and throat surgery	2365 (1.6)	2514 (2.7)	
General surgery	21 988 (14.5)	20 518 (22.1)	
Gynaecology surgery	16 727 (11.0)	8140 (8.7)	
Neurosurgery	11 401 (7.5)	4678 (5.0)	
Oncology	2227 (1.5)	1384 (1.5)	

Continued

Table 1 Continued

	Patient not receiving succinylcholine (*n*=151 816)	Patient receiving succinylcholine (*n*=93 034)	P-value
Oral/maxillofacial surgery	1810 (1.2)	801 (0.9)	
Orthopaedic surgery	35 212 (23.2)	18 206 (19.6)	
Otolaryngology	786 (0.5)	177 (0.2)	
Plastic surgery	10 486 (6.9)	5303 (5.7)	
Surgical oncology	3760 (2.5)	4018 (4.3)	
Thoracic surgery	9506 (6.3)	5349 (5.7)	
Urology	14 031 (9.2)	6551 (7.0)	
Vascular surgery	6253 (4.1)	3340 (3.6)	
Other	9940 (6.5)	6494 (4.3)	

Table 2 Risk of postoperative pulmonary complications (POPC) in patients receiving four possible combinations of succinylcholine and non-depolarising neuromuscular blocking agents (NMBAs) compared with patients receiving no NMBA (baseline). The added risk of POPC with administration of succinylcholine in patients receiving nondepolarising NMBA is shown in the bottom row. OR_{adj}, adjusted odds ratio; 95% CI, 95% confidence interval

Group	*n* (%)	OR_{adj} for POPC (95% CI)	*P*-value
No NMBA	39 349 (16.1)	1.00 (baseline)	–
Only succinylcholine	34 801 (14.2)	1.29 (1.14–1.45)	<0.001
Only nodepolarising NMBA	112 467 (45.9)	1.19 (1.06–1.34)	0.004
Succinylcholine and non-depolarising NMBA	58 233 (23.8)	1.29 (1.14–1.46)	<0.001
Succinylcholine in patients receiving ND-NMBA	58 233/170 700 (34.1)	1.08 (1.03–1.14)	0.001

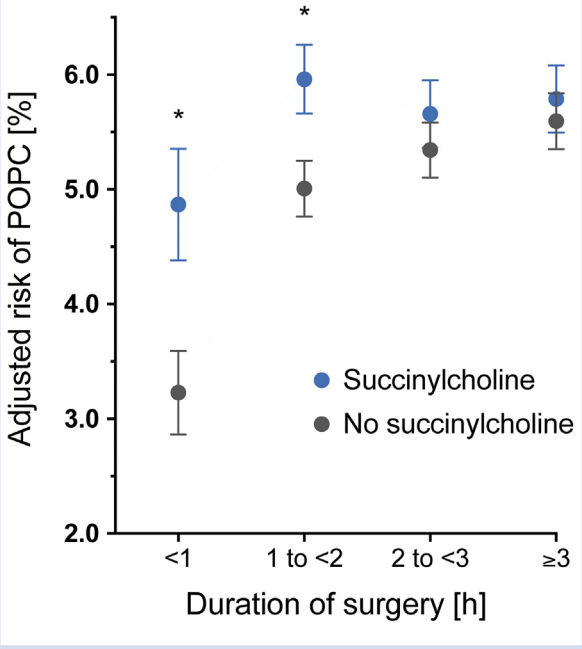

Fig 2. Adjusted risk of postoperative pulmonary complications (POPC) by duration of surgery in patients receiving succinylcholine (blue) and in patients not receiving succinylcholine (grey). Risk estimates with corresponding 95% confidence intervals for POPC with and without the use of succinylcholine at different durations of surgery. Marginal risk estimates were calculated based on the primary model used in the logistic regression analysis, conditional on the statistically significant interaction between succinylcholine and duration of surgery. *P<0.001 compared with no succinylcholine.

After propensity score matching of 59 242 patients (29 621 patients receiving only succinylcholine and 29 621 receiving only non-depolarising NMBA), the two groups were comparable across confounding variables based on patient characteristics and perioperative factors (standardised differences <0.1; Section 2 of the Supplementary Digital Content 2). There were no statistically significant differences in the risk of POPC (OR_{Adj}=1.07; 95% CI, 0.99–1.15; *P*=0.09, adjusted risk difference [ARD_{Adj}]=0.31%; 95% CI, −0.05 to 0.67) or in the risk of major complications between the two groups (OR_{Adj}=0.98; 95% CI, 0.90–1.07; *P*=0.63, ARD_{Adj}=−0.08%; 95% CI, −0.39 to 0.24).

In 122 946 patients where these data were available, succinylcholine was associated with increased risk of postoperative pneumonia, respiratory failure, reintubation, or pulmonary oedema within 7 postoperative days (OR_{Adj}=1.13; 95% CI, 1.07–1.20; *P*<0.001), reflecting findings from the primary analysis.

Succinylcholine was further associated with increased risk of delayed discharge from the PACU because of respiratory or cardiovascular complications (99 526 patients, OR_{Adj}=1.07; 95% CI, 1.02–1.12; *P*=0.006), and unplanned hospital readmission within 30 days after ambulatory surgery (85 815 patients, OR_{Adj}=1.41; 95% CI, 1.29–1.54; *P*<0.001).

There was no association between succinylcholine and need for postoperative noninvasive ventilation (OR_{Adj}=1.06; 95% CI, 0.89–1.26; *P*=0.54) or unplanned admission to the intensive care unit within 7 days after surgery (OR_{Adj}=1.02; 95% CI, 0.95–1.09; *P*=0.62).

Exploratory analysis

In 1274 patient patients who received a continuous infusion of succinylcholine (median dose of 3.9 mg kg^{-1}; inter-quartile range, 3.3–4.8) of 42 506 patients undergoing general surgery, there was a greater numerical increase in the odds of POPC than a bolus dose when both were compared with no

succinylcholine (OR_{Adj}=1.90; 95% CI, 1.33–2.72; P<0.001 and 1.17; 95% CI, 1.04–1.31; P=0.008, respectively; adjusted risks=6.90%; 95% CI, 4.77–9.02 and 4.43%; 95%, CI 4.14–4.72, respectively). In 18 281 patients undergoing upper or lower abdominal surgery and receiving both succinylcholine plus a non-depolarising NMBA, there was a trend towards increased risk of POPC in patients undergoing lower *vs* upper abdominal surgery OR_{Adj}=1.15; 95% CI, 0.99–1.34; P=0.08); however, this did not reach statistical significance.

Sensitivity analyses

The results of the primary analysis remained robust throughout sensitivity analyses a (Sections 4 and 5 of the Supplementary Digital Content 2). In a propensity score-matched analysis including 97 638 patients, findings from the primary analysis were confirmed. Imputation of missing data resulted in the addition of 30 799 patients to the analysis with robust results. After exclusion of 65 414 patients with a laryngeal mask airway or 16 168 emergency procedures and patients with ileus, or 19 709 patients who received >1.5 mg kg^{-1} succinylcholine and in a sub-cohort of 44 855 patients undergoing lower or upper abdominal surgery, the association between succinylcholine and POPC remained robust. The association between succinylcholine and POPC was not modified by emergency status or study site (P=0.40 and P=0.65 for interaction, respectively).

Discussion

Administration of succinylcholine during general anaesthesia was associated with increased risk of POPC; this effect was dose-dependent and magnified when higher doses were administered. Succinylcholine compared with nondepolarising NMBA did not decrease the risk of POPC, and added additional risk when administered in patients who also received a non-depolarising NMBA. Succinylcholine was also associated with increased risk of hospital readmission within 30 days after ambulatory surgery.

Recent studies reported that use of NMBAs was associated with increased risk of POPC[3,4,12,26]; however, those findings were limited to non-depolarising NMBAs. A small RCT trial involving 100 cardiac surgery patients reported no difference in POPC between the depolarising succinylcholine and non-depolarising NMBAs.[14] While confirming this finding in a propensity-matched analysis, our study offers explanation by showing that succinylcholine is also associated with an increased risk of POPC. We found that 14.2% of all patients received succinylcholine as the only NMBA. Although this is much higher than in a previous European study (2.4%),[3] it reflects practice in the USA, where succinylcholine is administered to 20% of all patients having surgery.[27]

Increased vulnerability to POPC in patients who receive an NMBA has been linked to residual paralysis after extubation,[3,13,28] which causes dysfunction of the diaphragm and upper airways, increasing vulnerability to airway obstruction, hypoxaemia, and misdirected swallowing.[29–31] Our finding of an increased risk of POPC after succinylcholine in shorter surgeries and with higher doses supports the assumption of a case-effect relation. There is wide variability in the time to recovery from succinylcholine-induced neuromuscular block; this is significant for low doses (0.8 mg kg^{-1}),[32] and probably even more so for higher doses of succinylcholine.[33,34] Low butyrylcholinesterase activity affects succinylcholine elimination and can be inherited[35,36] or acquired[35,37] and is often undiagnosed.[37] Even small degrees of residual paralysis predispose to POPC,[3,9] and are difficult to diagnose given the absence of twitch fade during depolarising neuromuscular block.

Clinical implications

Dose-dependent increases in the risk of POPC in patients who receive succinylcholine support the view that use of succinylcholine should follow a clear clinical indication. A recent study suggested that succinylcholine may be superior to rocuronium when given for rapid sequence induction.[38] However, our data show that in patients who receive nondepolarising NMBAs, even a single additional dose of succinylcholine increases the risk of POPC. Thus, use of succinylcholine for intubation needs to be considered based on a careful risk–benefit analysis. If clinicians use succinylcholine, recovery of twitch height should be measured quantitatively; however, recovery from depolarising neuromuscular block cannot be quantified using the train-of-four ratio (no fade of contraction).[39] Quantification of twitch height depression requires a control value taken before injection of succinylcholine. There are commercially available devices that can be used for measurement of twitch height depression in the operating theatre. Our data show that the risk of POPC after succinylcholine is elevated in patients undergoing procedures of <2 h duration and with hospital re-admission after ambulatory surgery. This is relevant because clinicians often use succinylcholine for short procedures and for ambulatory surgery to achieve rapid recovery of spontaneous breathing, without confirmation of full recovery of muscle strength before extubation.[40] Previous evidence suggests that reversal of nondepolarising NMBAs with neostigmine may also be associated with increased risk of residual neuromuscular block, POPCs and hospital readmission compared with reversal with sugammadex.[12,41–43]

We observed that high doses 1.5 mg kg^{-1} were administered to 19 709 out of 93 034 (21.2%) patients receiving succinylcholine, and 3557 (3.8%) patients received doses >2 mg kg^{-1}. Also, 1274 patients were treated with a continuous infusion of succinylcholine. Our data show that use of high-dose succinylcholine >2 mg kg^{-1} further increased the risk of POPC (OR_{Adj}=1.62 and 1.90 compared with no succinylcholine, respectively). Based on these data, we discourage use of succinylcholine infusions.

Succinylcholine administration was associated with increased risk of delayed discharge from the PACU for reasons related to respiratory or cardiovascular complications, and with increased risk of unplanned admission to the hospital within 30 days after ambulatory surgery. These observations agree with a previous study reporting a dose-dependent increased risk of unplanned hospital readmission for respiratory complications with administration of non-depolarising NMBAs.[5] Avoidance of non-depolarising NMBAs and succinylcholine in ambulatory surgery patients might therefore improve patient care through reducing delayed discharge from the PACU and unplanned readmission to the hospital, which also contributes to increased hospital costs.[44]

Limitations

Our study is limited by its observational nature and certain limitations of the design. Use of routinely collected billing

codes and administrative and clinical data entails the risk of unaccounted confounding and bias, and unmeasured factors that influence provider choice with regard to succinylcholine might have contributed to our findings. We accounted for this through extensive confounder control and a series of sensitivity analyses such as additional propensity score matching, exclusion of patients with ileus and emergency surgeries, and imputation of missing data.

Conclusions

Succinylcholine use was associated with an increased risk of pulmonary complications after surgery under general anaesthesia. Based on our data, high doses and continuous infusions of succinylcholine should be avoided to minimise risk of POPC, particularly in patients undergoing procedures shorter than 2 h.

Authors' contributions

Study concept and design: MSS, MH, ME, PS, TTH, PK
Data collection: MSS, MH, ME, PS, SDG
Data analysis: MSS, MH, ME, SDG, FCA, TTH
Interpretation of data: MSS, MH, ME, PS, SDG, FCA, TTH, PK
Drafting of the manuscript: MSS, MH, ME, MP, PK
Critical revision of the manuscript: all authors
All authors approved of the final manuscript version to be published and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declarations of interest

MSS, MH, PS, SDG, MP, FCA and TTH declare that they have no conflicts of interest. ME is an associate editor of the *British Journal of Anaesthesia*. He has received funding for investigator-initiated trials not related to this manuscript from MERCK Inc., and is holding a patent for acyclic curcubiturils, a new agents to reverse NMBA. PK has been consulting for Baxter GmbH Germany, Air Liquide Medical GmbH Germany, and TEVA Ratiopharm Germany, and received lecture fees and travelling expenses from these companies. He is an associate editor of *BMC Anesthesiology*.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.05.059.

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