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Comparison of intubating conditions with succinylcholine versus rocuronium in the prehospital setting

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Contributions: MRS conceived and designed the study and implemented the protocol changes and training. CRC, KMP, and JR supervised the process of data collection and analyzed the airway data and recordings. CM provided the statistical analysis of data. JR and KMP drafted the manuscript, and all authors substantially contributed to its revision. JR takes responsibility for the paper as a whole.

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Short Title: Succinylcholine vs. Rocuronium in Prehospital RSI

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Abstract

Objective: Rapid sequence intubation (RSI) is frequently performed by emergency medical services (EMS). We investigated the relationship between succinylcholine and rocuronium use and time until first laryngoscopy attempt, first-pass success, and Cormack-Lehane (CL) grades.

Methods: We included adult patients for whom prehospital RSI was attempted from July 2015 through June 2022 in a retrospective, observational study with pre-post analysis. Timing was verified using recorded defibrillator audio in addition to review of continuous ECG, pulse oximetry, and end-tidal carbon dioxide waveforms. Our primary exposure was neuromuscular blocking agent (NMBA) used, either rocuronium or succinylcholine. Our prespecified primary outcome was the first attempt Cormack-Lehane view. Key secondary outcomes were first laryngoscopy attempt success rate, timing from NMBA administration to first attempt, number of attempts, and hypoxemic events.

Results: Of 5,179 patients in the EMS airway registry, 1,475 adults received an NMBA while not in cardiac arrest. Cormack-Lehane grades for succinylcholine and rocuronium were similar: grade I (64%, 59% [95% CI 0.64 to 1.09]), grade II (16%, 21%), grade III (18%, 16%), grade IV (3%, 3%). The median interval from NMBA administration to start of the first attempt was 57 seconds for succinylcholine and 83 seconds for rocuronium (mean difference 28 [95% CI 20 to 36] seconds). First attempt success was 84% for succinylcholine and 83% for rocuronium.

Hypoxemic events were present in 25% of succinylcholine cases and 23% of rocuronium cases.

Conclusions: Prehospital use of either rocuronium or succinylcholine is associated with similar Cormack-Lehane grades, first-pass success rates, and rates of peri-intubation hypoxemia.

Keywords: Paralytics, Intubation, Laryngoscopy

Introduction

Background

Rapid sequence intubation (RSI) is a common advanced airway management procedure performed in the prehospital setting. RSI consists of the administration of an induction agent and neuromuscular blocking agent (NMBA), which improves laryngoscopy conditions and increases intubation success rates (1-3). Emergency medical services (EMS) practitioner proficiency in tracheal intubation varies widely, and more attempts are associated with higher rates of adverse events (4-6). Historically, succinylcholine has been the preferred NMBA due to its faster onset and shorter duration of action; but the use of rocuronium is growing (7-10).

One study evaluated intubation timing when using succinylcholine during prehospital RSI and found succinylcholine, compared to no NMBA use, reduced intubation interval from 4.1 minutes to 1.4 minutes (3). However, the details regarding time intervals when rocuronium is used in a prehospital environment remained unexplored. In addition to the known risks of hyperkalemia exacerbation, succinylcholine may exacerbate hypoxemia and be associated with higher mortality than rocuronium when used in patients with severe traumatic brain injury (11, 12). In 2017, our EMS agency began a transition from using succinylcholine as its primary NMBA to rocuronium.

At the doses used in our study (1.5 mg/kg for succinylcholine and 1.0 mg/kg for rocuronium), pharmacodynamic differences between rocuronium and succinylcholine result in rocuronium having a longer onset of action interval and an increased duration of effect (13). We were interested in determining if the proportion of reported Cormack-

Lehane grade 1 laryngeal views had decreased since the transition, which inspired the current study comparing the effects of rocuronium and succinylcholine on RSI process and conditions.

Importance

Due to its slower onset of action compared to succinylcholine, adequate neuromuscular relaxation after rocuronium administration with standard doses of 0.6 to 1.2 mg/kg may require up to 90 seconds, making timing crucial in optimizing intubating conditions. To our knowledge, our prehospital study is the first to examine objective and verifiable data revealing the precise time intervals between drug administration and initiation of the intubation attempt.

Goals of this Investigation

We investigated if the time intervals between succinylcholine or rocuronium administration and the start of the first laryngoscopy attempt influenced laryngeal exposure and first-pass tracheal intubation success in the prehospital environment. We hypothesized that when rocuronium was used, paramedics would attempt intubation prematurely, prior to adequate muscle relaxation, resulting in worse Cormack-Lehane laryngeal views.

Methods

Study Design and Setting

We performed a retrospective, observational study with pre-post analysis after a policy change using a rigorously maintained prehospital airway registry. The University of Washington Institutional Review Board reviewed and approved our study.

Seattle Medic One is the city of Seattle's sole advanced life support provider within a two-tiered EMS response system (14). All paramedics participate in at least ten tracheal intubations annually and complete periodic intubation training sessions. If they

are unable to obtain ten prehospital intubations, paramedics perform tracheal intubations in the hospital operating room to maintain proficiency. Paramedic students at the University of Washington Michael K. Copass Paramedic Training Program participate in field intubations between December and June each year under paramedic supervision. In recent years, paramedic students average 21 intubations in the operating room and 9 in the field during their training program. Direct laryngoscopy is performed using Macintosh or Miller blades (Heine, Germany). Video laryngoscopy was introduced in a limited manner beginning in summer of 2021 (PatCen Healthcare, Bellevue, WA).

Selection of Participants

All patients who received a tracheal intubation attempt in the prehospital setting between July 1st, 2015, and June 30th, 2022, were eligible for inclusion. The following cases were then excluded: intubation cases with first attempt during cardiac arrest, NMBA administered during cardiac arrest, no NMBA administered prior to first attempt, patients less than 18 years old, both rocuronium and succinylcholine were given prior to intubation, use of video laryngoscopy, and cases with missing waveform or audio data. Cases excluded due to missing data were compared to demographics of included populations to examine possible exclusion bias (Supplementary Table 1).

Interventions

The primary exposure was neuromuscular blocking agent used, either rocuronium or succinylcholine. Prior to 2017, rocuronium use was limited to patients with a perceived contraindication to succinylcholine use. From January 2017 through June 2019, paramedics were encouraged to use rocuronium as the preferred NMBA. In July 2019, succinylcholine was removed from the paramedic units (Supplementary Figure 1). Recommended doses for NMBAs were 1.5 mg/kg for succinylcholine and 1.0 mg/kg for rocuronium. Dosing weight was estimated by paramedics or obtained from

family members.

Measurements

An ongoing registry of all attempts at advanced airway management by Seattle Medic One paramedics is maintained by the University of Washington Section of EMS. The registry is hosted in REDCap and includes patient demographics, indications for intubation, pre-intubation vital signs, medications administered, patient position, preoxygenation performed, tools used by the operator, additional details related to each attempt, and the final airway outcome (15). Cormack-Lehane grade is a required field, and since April 28, 2017, paramedics see an example image of the different laryngeal views while completing the registry data form. Paramedics typically complete the REDCap form within a day of the procedure. When they are involved, paramedic students complete the form with the assistance of the paramedic. The corresponding LIFEPAK 15 defibrillator data are uploaded to post-event CODESTAT review software, which provides a complete view of the patient's ECG, capnogram (ETCO₂), and pulse oximetry (SpO₂) waveforms along with an audio recording of the case (Stryker, Kalamazoo, MI). A trained team of abstractors reviews the audio and waveform data, adding annotations to capture the timing of medication administration, intubation attempts, and intubation completion.

Outcomes

The primary outcome was the first laryngoscopy attempt Cormack-Lehane grade, which was self-reported by the intubating paramedic and confirmed, when possible, via audio recording verbalizations (16). Secondary outcomes included first – laryngoscopy tracheal intubation success rate, interval from NMBA administration to initiation of the first laryngoscopy attempt, total number of intubation attempts, and hypoxemia, defined as one or more oxygen saturation readings <90% during the

interval from initiation of the first attempt through two minutes after successful tracheal intubation. First and subsequent intubation attempts were defined as the laryngoscope blade passing the teeth.

Analysis

Point estimates and 95% confidence intervals (95% CI) were reported when appropriate. We calculated the difference and 95% CI in proportions with Cormack-Lehane grade 1 view in both NMBA groups. We used logistic regression to examine the association of NMBA used and Cormack-Lehane grade 1 view while adjusting for patient age, sex, patient cohort (post cardiac arrest resuscitation is reference category, 2=trauma, 3=other), paramedic versus paramedic student operating the laryngoscope, and interval from NMBA administration to initiation of the first laryngoscopy attempt. We used a similar logistic regression adjusting for age, sex, patient cohort (post cardiac arrest resuscitation is reference category, 2=trauma, 3=other), paramedic versus paramedic student holding the laryngoscope, interval from NMBA administration to initiation of the first laryngoscopy attempt, grade 1 view, and use of a bougie to examine the association between type of NMBA and success at first pass as well as hypoxemia. We report odds ratios (OR) and 95% CIs. Stata (version 17.0; StataCorp, College Station, TX) was used for statistical analysis.

Results

Characteristics of the Study Subjects

During the study period, 5,179 patient encounters involved an intubation attempt by a paramedic or paramedic student. After exclusion criteria, 329 (22%) were included in the succinylcholine cohort, and 1,146 (78%) were included in the rocuronium cohort (Figure 1). Males accounted for the majority of both the succinylcholine (64.7%) and rocuronium (63.4%) groups (Table 1). Paramedic students performed the first attempt in

a third of each group. The mean pre-intubation NMBA dosing was 155 mg for succinylcholine and 86 mg for rocuronium.

Main Results

Cormack-Lehane grades for succinylcholine and rocuronium were similar: grade I (64%, 59%), grade II (16%, 21%), grade III (18%, 16%), grade IV (3%, 3%) (Figure 2). For the difference in proportions for grade 1 views, the 95% CI included 0 (-0.01 to 0.11) (Table 2). Logistic regression analysis indicated no association between the use of rocuronium and grade 1 view (adjusted OR 0.84, 95% CI 0.64 to 1.09) (Figure 4).

Median interval and interquartile range (IQR) from NMBA to first attempt was 57 seconds (IQR 40-85) for succinylcholine and 83 seconds (IQR 57-121) for rocuronium (median difference 26) (Figure 3). Median interval from NMBA to tracheal intubation was 132 seconds (IQR 99-184) for succinylcholine and 162 seconds (IQR 128-232) for rocuronium (median difference 30).

A bougie was used during the first attempt in 62% and 94%, respectively, for succinylcholine and rocuronium. First attempt success was 84% with succinylcholine and 83% with rocuronium. Logistic regression analysis indicated no association between the use of rocuronium and first-pass success (adjusted OR 0.85, 95% CI 0.57 to 1.27). The final airways for each period were (succinylcholine, rocuronium): tracheal intubation (99.7%, 97.5%), iGel (0.6%, 2.3%), cricothyrotomy (0%, 0.1%), and bag valve mask (0%, 0.2%).

Hypoxemia was noted in 25% and 23% of the total succinylcholine and rocuronium groups, respectively. When stratified by Cormack-Lehane grade, the incidence of hypoxemia for succinylcholine and rocuronium were similar: grade 1 (20% and 22%), grade 2 (28% and 26%), grade 3 (53% and 40%), and grade 4 (60% and 57%). The 95% CI for the difference in proportions for grade 3 included 0 (-0.02 to

0.28). For grade 4, only 10 subjects received succinylcholine. The incidence of hypoxemia for two or more attempts was 59% for succinylcholine compared to 45% for rocuronium. The 95% CI for the difference between the proportions included 0 (95% CI -0.02 to 0.30).

Limitations

As with all before and after observational studies, the likely presence of unmeasured confounding is a limitation; and we cannot equate our study findings to causation. We also acknowledge other specific limitations of our study. First, Cormack-Lehane grades are self-reported by the paramedics and not independently verifiable, exposing a potential for recall bias. Starting April 28, 2017, a graphic depicting Cormack-Lehane grades was added to the REDCap form in an attempt to reduce reporting bias about the distinctions between each grade. Though not independently verifiable, the distribution of reported views in our registry was similar to direct laryngoscopy views reported in an anesthesiologist-staffed helicopter EMS program (17). Second, weight-based dosing may be inaccurate due to errors in weight estimation and is not verified independently. Thus, only total administered doses were reported (18). Third, the airway registry does not include race information which may be influential when determining hypoxemia via pulse oximeters which may be less accurate in patients with more pigmentation (19, 20). Fourth, 625 cases were missing waveform and/or audio data due to technology issues and were excluded. The patient and pre-intubation attempt airway characteristics of this excluded group, however, did not differ from the included population (Supplementary Table 1). Finally, the continuous quality improvement efforts of the Seattle Medic One program focusing on prehospital airway management, including recommending increased bougie and iGel use, and evolving choice of etomidate and ketamine sedative administration have biased

the results of this study (21).

While the magnitude of this bias is unknown, we believe our choice of the primary outcome as the reported Cormack-Lehane grade may reduce the potential impact of some of these other changes. For example, the increased bougie use in the rocuronium cohort may have influenced the secondary outcome of first-pass success rate; however, this should not have a large effect on Cormack-Lehane grade. Similarly, other quality improvement efforts and procedural changes such as increasing post-intubation sedation, improved pre-intubation oxygenation, and increased iGel use should have minimal effect on reported Cormack-Lehane grades.

These limitations should be considered in light of the strengths of this analysis. Data elements were recorded within hours of the event to minimize recall bias. Many elements were independently verified using audio and ET CO_2 waveform recordings. Time points were determined using audio recordings rather than electronic health record documentation. Finally, more than 1,400 patients were included, representing a broad base of patient types.

Discussion

In an EMS system with paramedics who consistently perform tracheal intubations, an RSI protocol using rocuronium at a dose of 1.0 mg/kg elicits similar laryngeal views as succinylcholine. A potential driver of the laryngeal views was a longer time from rocuronium administration to beginning the first laryngoscopy attempt due to the slower onset of rocuronium. The median time of 83 seconds closely aligned with a previous randomized trial comparing rocuronium and succinylcholine in an intensive care unit (ICU) environment (22). Though limited by potential confounding factors such as variable bougie use and medication regimen, our study adds support to other work, which showed no difference in first-pass success and similar Cormack-

Lehane grades in the emergency department when rocuronium was dosed higher than 0.9 mg/kg (23-25).

In the United States, succinylcholine is the most commonly used NMBA during RSI procedures in the prehospital setting (26). While a recent Cochrane review meta-analysis concluded succinylcholine superior in creating “excellent” intubating conditions based on the Goldberg scale, our study found no statistically significant difference in Cormack-Lehane grades or first-pass success (27). Possible explanations for this difference could be the setting of the studies and differences in dosing. When rocuronium was dosed between 0.9 to 1.2 mg/kg such as in our study, the Cochrane review found no difference compared to succinylcholine. The Cochrane review primarily included studies from the operating room, with only a few studies from the emergency department, and none from a prehospital environment. The prehospital setting provides its own unique environmental challenges that may not be translatable from hospital-based environments (28). A prehospital study in the United Kingdom comparing RSI protocols of etomidate and succinylcholine versus fentanyl, ketamine, and rocuronium found Cormack-Lehane views and first-pass success were significantly better in the rocuronium group (29).

A recent non-inferiority study that evaluated both NMBAs in the prehospital setting using a rocuronium dose of 1.2 mg/kg found rocuronium failed to demonstrate non-inferiority to succinylcholine (30). The authors noted that while fasciculations often indicate the effects of succinylcholine to the intubating physicians, it is possible those in the rocuronium arm were intubated before the recommended 60 second delay. Another study reporting the interval from NMBA administration to intubation attempt, a randomized controlled trial in the ICU, found no difference in intubating conditions or first-pass success (84% with succinylcholine, 83% with rocuronium) (22).

In addition to intubating conditions, safety is a crucial consideration when comparing rocuronium and succinylcholine. Hypersensitivity to rocuronium is the only absolute contraindication, and anaphylactic reactions to rocuronium are rare (<1 per 1,000,000) (31). Succinylcholine has several known contraindications and cautions, primarily related to risk of precipitating life-threatening hyperkalemia. Some contraindications, including history of malignant hyperthermia, skeletal myopathies, or an upper motor neuron lesion may be difficult to ascertain in the prehospital setting (32). Reversal agents exist for non-depolarizing neuromuscular blocking agents like rocuronium, limiting the downside risk of prolonged duration of action (33-35). Longer-acting NMBAs carry a risk of an increased incidence of awareness with paralysis, which has been demonstrated in the emergency department and ICU (36).

Conclusion

In conclusion, in our EMS system, the use of either rocuronium or succinylcholine is associated with similar Cormack-Lehane grades, first-pass success rates, number of attempts, and rates of peri-intubation hypoxemia. Further investigation into the adverse effects, outcomes, and awareness with paralysis of patients receiving prehospital rocuronium is warranted.

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Disclosure Statement

The authors report there are no competing interests to declare.

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Table Captions

Table 1. Pre-NMBA conditions.

	All		Succinylcholine		Rocuronium	
TOTAL	1475	#####	329	22.3%	1146	77.7%
Demographics						
Age, mean \pm SD	51.7	\pm 20.2	49.5	\pm 19.7	52.4	\pm 20.2
Male sex	937	63.5%	213	64.7%	726	63.4%
Patient Cohort						
Coma post cardiac arrest	87	5.9%	19	5.8%	68	5.9%
Trauma	419	28.4%	109	33.1%	310	27.1%
Other	970	65.8%	202	61.4%	768	67.0%
Initial Patient Condition						
Pre-intubation GCS \pm SD	6.4	\pm 4.3	6.5	\pm 4.4	6.4	\pm 4.2
Respiratory rate \pm SD	18.8	\pm 12.5	18.6	\pm 12.5	18.8	\pm 12.5
Pre-Intubation Sedation						
Etomidate	1203	81.6%	313	95.1%	890	77.7%
Ketamine	248	16.8%	7	2.1%	241	21.0%
Midazolam	111	7.5%	31	9.4%	80	7.0%
Opiates	38	2.6%	5	1.5%	33	2.9%
None	23	1.6%	9	2.7%	14	1.2%
NMBA Dosing						
Mean dose (mg) \pm SD	-	-	154.8	\pm 23.8	86.3	\pm 20.8
Pre-oxygenation						
Yes	1441	97.7%	305	92.7%	1136	99.1%
Bougie with First Attempt						
Yes	1284	87.1%	205	62.3%	1079	94.2%
First Attempt Operator						
Paramedic	983	66.6%	229	69.6%	754	65.8%

Paramedic Student	493	33.4%	101	30.7%	392	34.2%
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Table 2. Post-NMBA conditions and outcomes.

	All		Succinylcholine		Rocuronium	
TOTAL	1475	#####	329	22.3%	1146	77.7%
First Attempt CL Grade						
Grade I	884	59.9%	210	63.8%	674	58.8%
Grade II	293	19.9%	51	15.5%	242	21.1%
Grade III	246	16.7%	58	17.6%	188	16.4%
Grade IV	49	3.3%	11	3.3%	38	3.3%
Unknown	4	0.3%	0	0.0%	4	0.3%
Number of Attempts						
1	1227	83.2%	276	83.9%	951	83.0%
2	176	11.9%	39	11.9%	137	12.0%
3+	73	4.9%	15	4.6%	58	5.1%
Hypoxemia						
Yes	348	23.6%	83	25.2%	265	23.1%
No	936	63.5%	204	62.0%	732	63.9%
Missing Pulse Ox Data	192	13.0%	43	13.1%	149	13.0%
Final Airway						
Endotracheal Intubation	1445	98.0%	328	99.7%	1117	97.5%
iGel	28	1.9%	2	0.6%	26	2.3%
Cricothyrotomy	1	0.1%	0	0.0%	1	0.1%
Bag Valve Mask	2	0.1%	0	0.0%	2	0.2%
Post-Intubation Sedation						
Midazolam	1233	83.6%	285	86.6%	948	82.7%
Ketamine	8	0.5%	3	0.9%	5	0.4%
Opiates	916	62.1%	86	26.1%	830	72.4%
None	202	13.7%	40	12.2%	162	14.1%
Post-Intubation NMBA						
Succinylcholine	3	0.2%	3	0.9%	0	0.0%
Rocuronium	31	2.1%	27	8.2%	4	0.3%

Figure Captions

Figure 1. Flow diagram for generation of study population. *NMBA: neuromuscular blocking agent. ROC: rocuronium. SUX: succinylcholine.*

Figure 2. Cormack-Lehane view by neuromuscular blocking agent and condition.

Figure 3. Intervals from neuromuscular blocking agent to first attempt and tracheal intubation.

Figure 4. Time intervals by NMBA and Cormack-Lehane views for NMBA to both first attempt and tracheal intubation. *NMBA: neuromuscular blocking agent.*

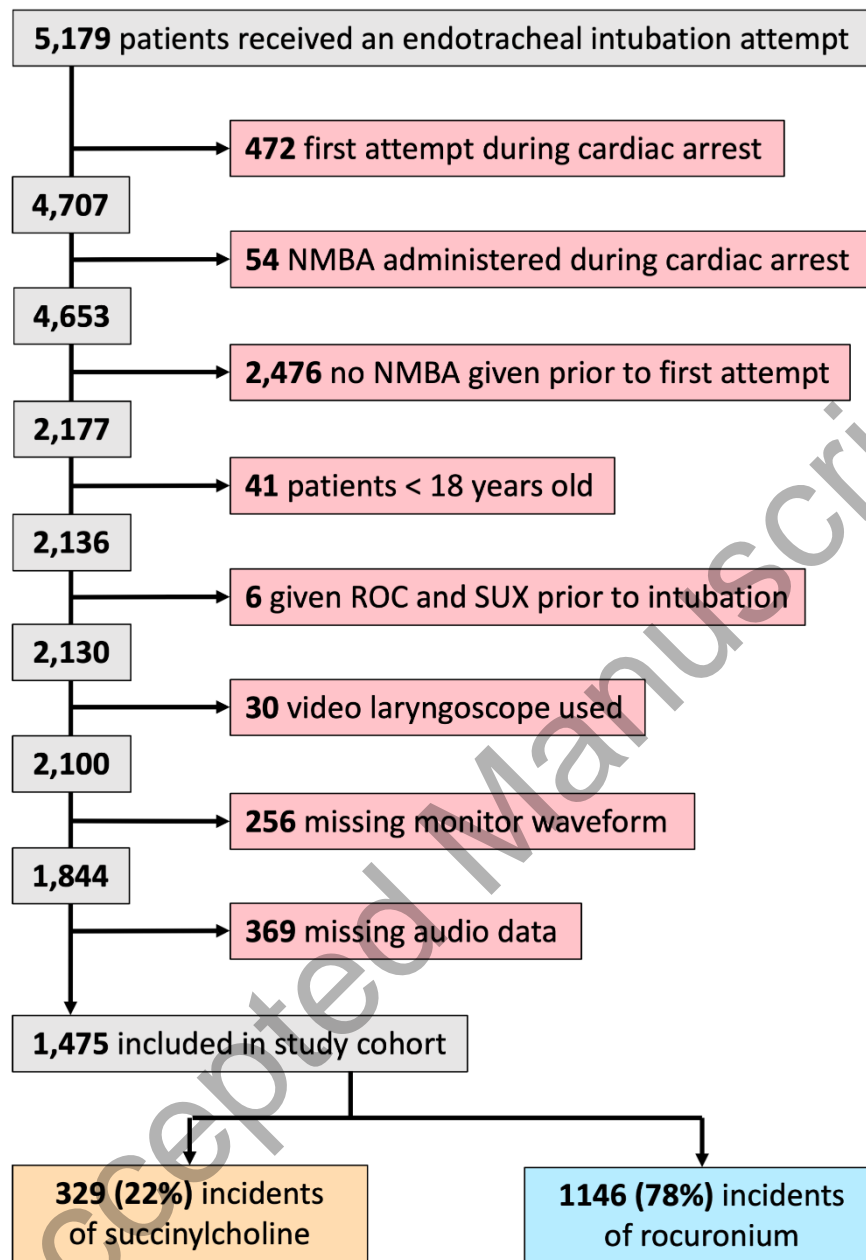
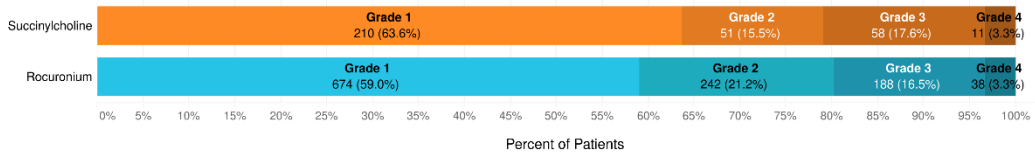
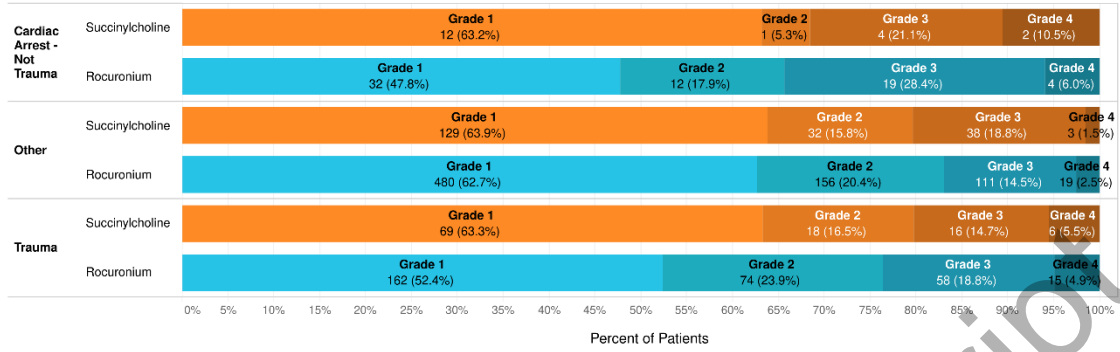


Figure 1. Flow diagram for generation of study population. *NMBA*: neuromuscular blocking agent. *ROC*: rocuronium. *SUX*: succinylcholine.

Cormack-Lehane View by Neuromuscular Blocking Agent



Cormack-Lehane View by Neuromuscular Blocking Agent and Condition



Cormack-Lehane grade view was missing in four cases.

Figure 2. Cormack-Lehane view by neuromuscular blocking agent and condition.

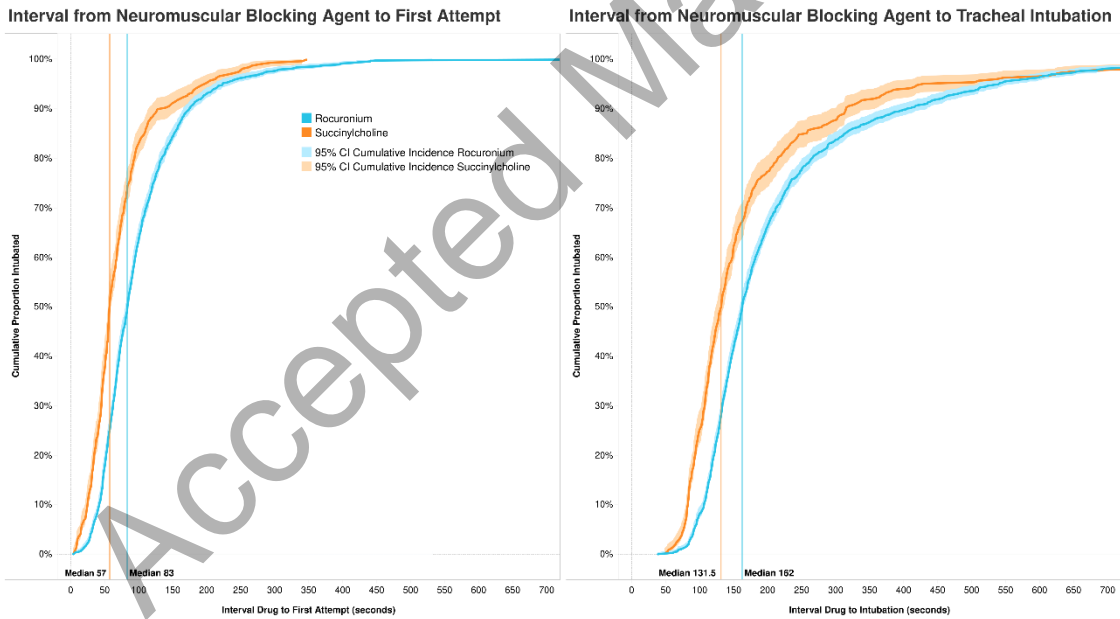
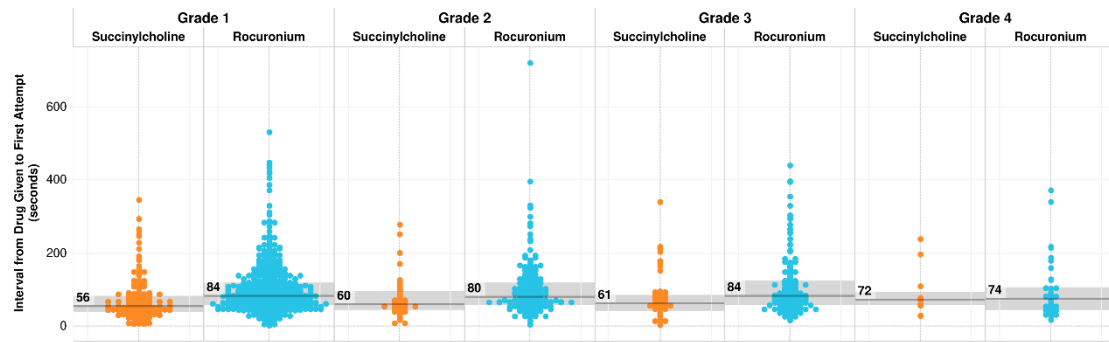


Figure 3. Intervals from neuromuscular blocking agent to first attempt and tracheal intubation.

Cormack-Lehane Grade on First Attempt by Interval from Drug Administration



Cormack-Lehane Grade on First Attempt by Interval to Tracheal Intubation

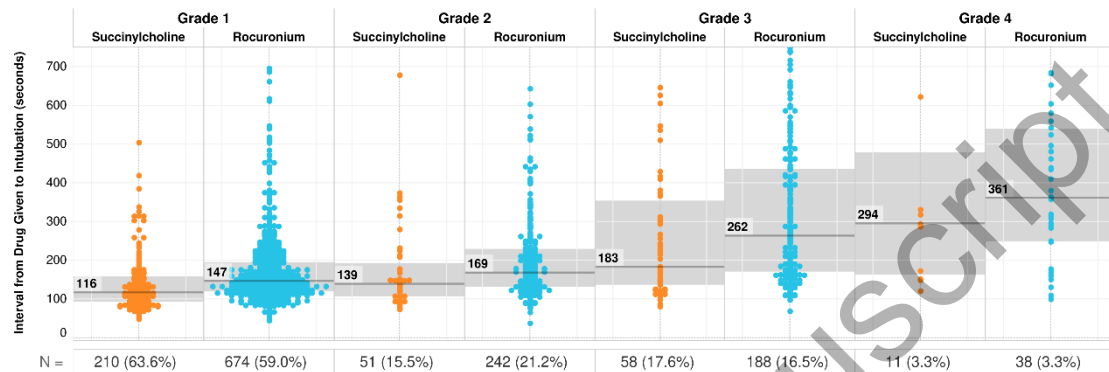


Figure 4. Time intervals by NMBA and Cormack-Lehane view from NMBA to both first attempt and tracheal intubation.

Supplementary Captions

Supplementary Table 1. Pre-NMBA conditions comparing included cases versus cases excluded due to missing data. *NMBA: neuromuscular blocking agent. GCS: Glasgow Coma Scale.*

Supplementary Table 2. Post-NMBA conditions and outcomes comparing included cases versus cases excluded due to missing data. *NMBA: neuromuscular blocking agent. CL: Cormack-Lehane.*

Supplementary Figure 1. Historical NMBA and induction agent use during study period. *NMBA: neuromuscular blocking agent. RSI: Rapid Sequence Intubation.*