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Comparison of Rocuronium with Succinylcholine for Rapid Sequence Induction Intubation in the Emergency Department: A Retrospective Study at a Single Center in China

Authors' Contribution:

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Statistical Analysis C
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Manuscript Preparation E
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Background: This retrospective study was conducted at a single center in China and aimed to compare rocuronium with succinylcholine for rapid sequence induction intubation in the Emergency Department of a hospital.

Material/Methods: An orotracheal intubation procedure was performed in a total of 267 patients by direct laryngoscopy using an intravenous bolus injection of 1 mg/kg of succinylcholine (n=141; SY group) or 1.2 mg/kg of rocuronium (n=126; RM group) for a rapid sequence induction in the emergency department. The success of orotracheal intubation was evaluated by a capnography curve. The modified Cormack-Lehane score was used to grade the direct laryngoscopy.

Results: There was no statistically significant difference in numbers of patients with successful first-attempt orotracheal intubation between the groups (112 vs. 87, $P=0.067$). Fewer intubation failures under direct laryngoscopy were reported in the SY group than in the RM group (23 [16%] vs. 34 [27%], $P=0.037$). The number of intubation attempts was higher in the RM group than in the SY group (1.52 ± 0.87 per patient vs. 1.27 ± 0.60 per patient, $P=0.032$).

Conclusions: The findings from this study support results from previous studies, showing that even in the Emergency Department setting, rocuronium was equivalent to succinylcholine in achieving rapid sequence induction intubation, when the dose was appropriate. However, as current clinical guidelines highlight, succinylcholine has more contraindications and adverse effects, including hyperkalemia, which should be monitored, and rocuronium has a longer duration of action.

MeSH Keywords: **Emergency Service, Hospital • Intubation • Laryngoscopy • Neuromuscular Blocking Agents • Succinylcholine**

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Background

Tracheal intubation is a crucial intervention in emergency settings [1], and sedation in emergency procedures greatly improves its ease and safety [2]. Therefore, in patients who require emergency tracheal intubation, rapid sequence intubation is the recommended airway management technique [3]. Rapid sequence intubation involves the administration of a hypnotic and paralytic agent that has a rapid onset of action [2]. A neuromuscular blocking agent improves the overall conditions of intubation and the success rate of the first-attempt intubation [4]. Also, intravenous induction using a neuromuscular blocking agent is optimal in the Emergency Department setting [5,6]. The preferred neuromuscular blocking agent is succinylcholine [7] but it has several adverse effects and clinical contraindications [8]. One study reported that rocuronium has the same onset of action as succinylcholine because of its similar pharmacokinetic characteristics and could be used as an alternate to succinylcholine in an emergency setting [9]. Also, except for hypersensitivity, rocuronium has no contraindications and less rapid desaturation and fewer adverse effects, such as increase in oxygen consumption and hyperkalemia, than succinylcholine [8,10]. Also, succinylcholine has a lower tolerance profile than rocuronium [2]. Succinylcholine, a depolarizing muscle relaxant, has a rapid onset of action and works by inducing fasciculations of muscle followed by flaccid muscle paralysis [11]. Rocuronium, a nondepolarizing muscle relaxant [12], has a 2-min to 3-min onset of action and works by competitive blockade of the neuromuscular junction [13]. Also, its effect is possibly antagonized by sugammadex [5].

There has been a remarkable increase in the use of rocuronium in the Emergency Department setting [14]. Several clinical trials showed that succinylcholine performs better than rocuronium in achieving successful intubating conditions [7,15]; however, a retrospective study showed that when rocuronium is used in a concentration of more than 1 mg/kg, it is as successful as succinylcholine in first-attempt emergency intubation [16]. Several studies comparing rocuronium and succinylcholine have been done in operating room settings [7,9,10,15,17,18]. Very few clinical trials [2,19], an observational study [14], prospective study [20], and retrospective study [16] have compared rocuronium and succinylcholine in out-of-hospital settings because there is great need to minimize the risk of aspiration in these settings [21]. However, a randomized trial [2] showed the inferiority of rocuronium when compared with succinylcholine for intubation, whereas a randomized trial [19], observational study [14], prospective study [20], and retrospective study [16] showed that rocuronium is equivalent to succinylcholine for intubation. There is a dilemma regarding the choice of the neuromuscular blocking agent in out-of-hospital settings. Therefore, this retrospective study was conducted at a single center in China and aimed to compare rocuronium with

succinylcholine for rapid sequence induction intubation in the emergency department.

Material and Methods

Ethics approval and consent to participate

The study protocol (CTGU111620 dated June 29, 2020) was approved by the China Three Gorges University Review Board. The study reporting adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement, the laws of China, and the 2008 Declaration of Helsinki. An informed consent form was signed by relatives (legally authorized persons) of the admitted patients regarding anesthesia and other procedures and the publication of patients' anonymized information in this article. Because this was a retrospective study, Chinese clinical trial registration was waived by the institutional review board.

Study population

Patients (age >18 years) who required emergency tracheal intubation were included in the analysis. Patients with a history of cardiac arrest or allergy to succinylcholine or rocuronium and female patients with pregnancy were excluded.

Sample size calculation

On the basis of the intubation condition and an estimated dropout rate of 20%, at an 80% power ($\beta=0.2$) and 95% of confidence level ($\alpha=0.05$), the required sample size was at least 110 patients in each group [22].

Patient groups

All patients were preoxygenated before induction. In the SY group (n=141), patients received an intravenous bolus injection of 1 mg/kg of succinylcholine (Anectine, Sandoz Inc, Princeton, NJ, USA). In the RM group (n=126), patients received an intravenous bolus injection of 1.2 mg/kg of rocuronium (Zemuron, Mylan NV, Hertfordshire AL, UK) after preoxygenation. All interventions were performed by anesthesiologists with a minimum of 3 years of clinical experience.

Intubation procedure

All patients received 0.3 mg/kg of etomidate (Amidate, Hospira, Inc, Lake Forest, IL, USA) or 2 mg/kg of ketamine (Hospira) after administration of succinylcholine or rocuronium. Propofol (Hospira) was also administered on physicians' recommendation. The Sellick maneuver was performed as per the physicians' preference [2]. Intubation was attempted 60 s after the

administration of succinylcholine or rocuronium. When standard laryngoscopy-assisted intubation (using a Macintosh laryngoscope) was not possible, then a stylet, gum elastic bougie, or intubating laryngeal mask airway (Fastrach) was used or a cricothyrotomy was performed. Sugammadex (Bridion, Merck & Co., Inc., Washington, NJ, USA) was used to antagonize the action of rocuronium in patients in the RM group. Hypotension was managed via intravenous fluid resuscitation using crystalloids and ephedrine (Tedral SA, New York, NY, USA), and prolonged hypotension was managed through norepinephrine (Levophed). Benzodiazepine and opioids were administered as per the conditions of patients and the objective of physicians. The intubation procedure was performed by anesthesiologists. Patients were intubated with the head of the bed elevated, as that can have a direct effect on the grade of visualization.

Outcome measures

The success of orotracheal intubation was evaluated by the anesthesiologists using a capnography curve consistent over 3 respiratory cycles [2].

The modified Cormack-Lehane grading score [23] was used to measure glottis visibility by direct laryngoscopy in the grades of 1 to 4 where 1=full view of vocal cords; 2A=partial view of vocal cords; 2B=only arytenoids and epiglottis seen; 3=only epiglottis seen; and 4=neither glottis nor epiglottis seen. Glottis visibility was evaluated by the anesthesiologists.

The overall difficulty in the process of intubation was measured by the Intubation Difficulty Scale score by anesthesiologists, where 0=easy intubation; 1 through 5=slightly difficult intubation; and a score of more than 5 was considered difficult intubation [22].

Intubation condition was evaluated by anesthesiologists using the Copenhagen score [24] as poor, good, and excellent based on ease of laryngoscopy, coughing and limb movement, the position of vocal cords, and jaw relaxation.

Data of reported complications related to intubation, including cardiac arrest, arterial hypotension (systolic blood pressure less than 90 mmHg), hypoxemia (occurrence of new oxygen desaturation less than 90%), physician-reported aspiration, severe arrhythmia (ventricular tachycardia or ventricular fibrillation), and allergic reaction, were collected. Intubation-related complications were evaluated by physicians with a minimum of 3 years of clinical experience within the first 15 min after intubation.

Data regarding the number of intubation failures under direct laryngoscopy, the number of intubation attempts, the time

of Emergency Department care, the number of unintentional extubations, the requirements of vasopressors and sedative drugs after intubation, and number of deaths during out-of-hospital care were collected. Exploratory outcomes were evaluated by anesthesiologists.

Statistical analysis

SPSS v25.0 (IBM Corporation, Armonk, NY, USA) was used for statistical analyses. Descriptive data are presented as frequency (percentage) and numerical and ordinal data are presented as mean±SD. A 2-tailed unpaired *t* test was performed for numerical and ordinal data and the Fischer exact test was performed for descriptive data. All results were considered significant when the *P* value was less than 0.05.

Results

Study population

From July 12, 2018 to May 15, 2020, a total of 278 patients required emergency tracheal intubation because of shock, trauma, coma, overdoses, and dyspnea at the Emergency Department of the Yichang Central People's Hospital & The First College of Clinical Medical Science, China Three Gorges University, Hubei, China, and the Dangyang People's Hospital, Dangyang, Hubei, China. Among them, 5 patients had cardiac arrest, 3 were younger than 18 years, 1 was pregnant, 1 had a known allergy to rocuronium, and 1 had a known allergy to succinylcholine. Therefore, the data from these patients (*n*=11) were excluded from the analysis. The data of 267 patients who underwent a rapid sequence induction performed in the Emergency Department were included in the analysis (Figure 1).

Demographic and clinical conditions

The primary reason for intubation was a coma followed by trauma. There were no differences in the demographical, clinical, and anesthetic conditions between the 2 groups (*P*>0.05 for all parameters). The demographical, clinical, and anesthetic conditions of the patients are reported in Table 1.

Orotracheal intubation

A total of 112 (79%) patients in the SY group and 87 (69%) patients in the RM group received successful first-attempt orotracheal intubation. The difference between the groups was not significant (*P*=0.067; Figure 2).

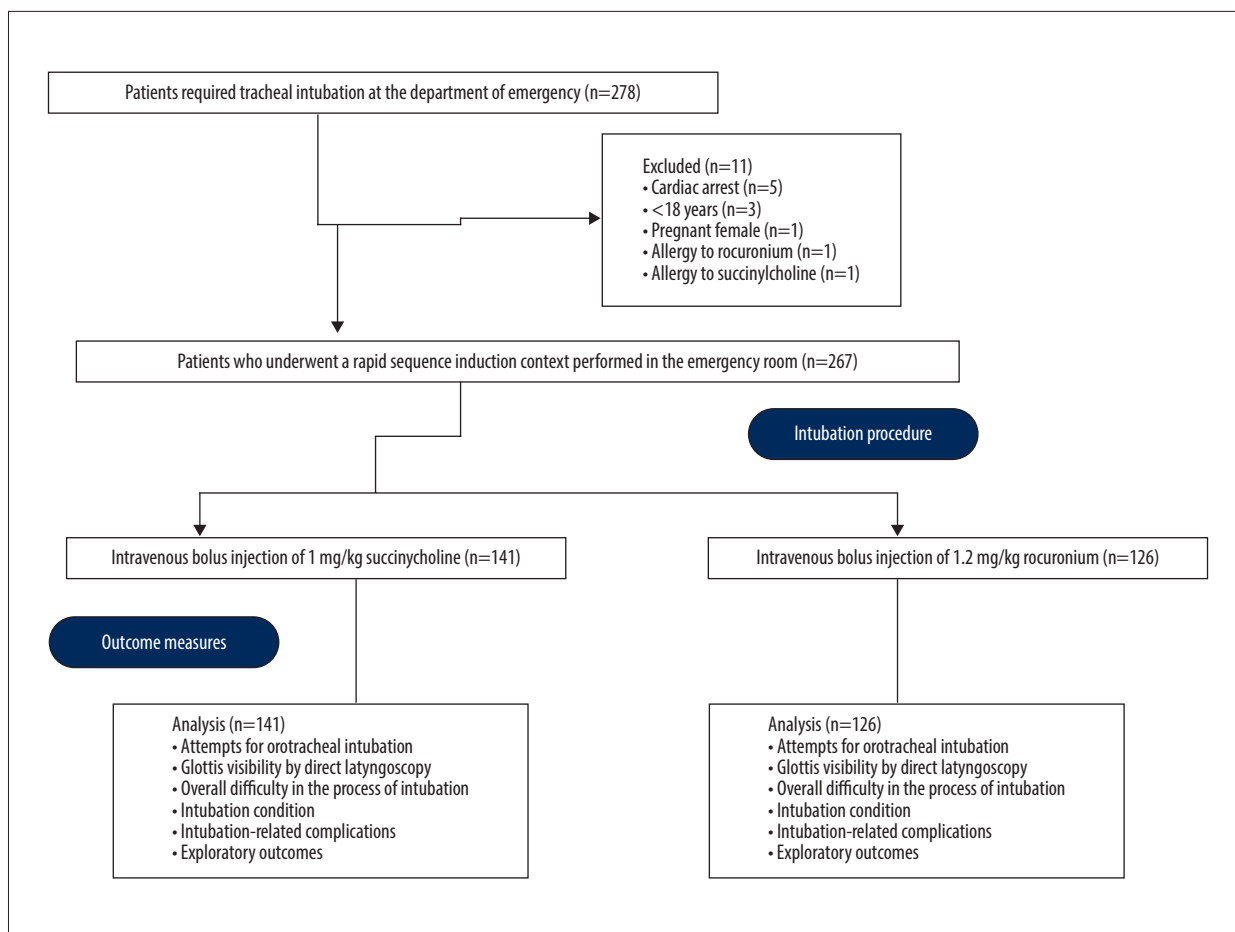


Figure 1. Rapid sequence induction intubation in the Emergency Department.

Grading of direct laryngoscopy

There was no significant difference in the modified Cormack-Lehane grading score between the SY and RM groups ($P=0.528$; **Table 2**).

The intubation difficulty scale

There was no significant difference in the Intubation Difficulty Scale between the SY and RM groups (3.92 ± 0.98 vs. 4.11 ± 0.65 , $P=0.066$; **Figure 3**).

Intubation condition

There was no statistical difference for the Copenhagen scores between the SY and RM groups ($P=0.509$; **Table 3**).

Alternative intubation techniques used

There was no significant difference in the requirement of alternative intubation techniques between the SY and RM groups ($P=0.711$; **Table 4**).

Intubation-related complications

More patients in the SY group had at least 1 intubation-related complication compared to that of the RM group. However, overall, there was no statistical significance difference in intubation-related complications between the 2 groups (**Table 5**).

Exploratory outcomes

Fewer intubation failures under direct laryngoscopy were reported in the SY group than in the RM group (23 [16%] vs. 34 [27%], $P=0.037$; **Figure 4**). The number of intubation attempts was higher in the RM group than in the SY group (1.52 ± 0.87 per patient vs. 1.27 ± 0.60 per patient; $P=0.032$). More patients in the SY group required vasopressors after intubation than in the RM group (34 [24%] vs. 18 [14%], $P=0.046$; **Figure 5**). More patients required sedative drugs after intubation in the SY group than in the RM group (69 [49%] vs. 45 [36%], $P=0.035$; **Figure 6**). However, there were no significant differences in the duration of Emergency Department care, the number of deaths during Emergency Department care, and the requirements of unintentional extubations between the

Table 1. Demographical, clinical, and anesthetic conditions of the enrolled patients at the Emergency Department.

Characteristic		Groups		Comparison
		SY	RM	
Neuromuscular blocking agent used		Succinylcholine	Rocuronium	
Patients included in analysis		141	126	P value
Sex	Male	95 (67)	73 (58)	0.128
	Female	46 (33)	53 (42)	
Age (y)	Minimum	18	18	0.344
	Maximum	64	63	
	Mean±SD	51.15±11.41	52.41±10.19	
Body mass index (kg/m ²)		24.12±2.22	24.41±1.45	0.213
Reason for intubation	Shock	18 (13)	17 (13)	0.998
	Trauma	22 (16)	21 (17)	
	Coma due to neurological disease	37 (26)	33 (26)	
	Coma due to poisoning	31 (22)	25 (20)	
	Overdoses	17 (12)	16 (13)	
	Dyspnea	16 (11)	14 (11)	
Glasgow Coma Scale score	Minimum	3	3	0.828
	Maximum	7	7	
	Mean±SD	5.45±1.45	5.41±1.56	
Heart rate (beats/min)		105±11	102±15	0.062
Breaths/min		24±4	25±5	0.071
Arterial diastolic pressure (mmHg)	<90 but ≥50	115 (82)	101 (80)	0.876
	<50	26 (18)	25 (20)	
Arterial systolic pressure (mmHg)	<140 but ≥90	109 (77)	88 (70)	0.211
	≥140	32 (23)	38 (30)	
% Peripheral oxygen saturation		94.51±4.55	94.01±4.01	0.344
Total etomidate administered (mg)		22.12±4.15 (n=115)	21.15±4.11 (n=107)	0.057
Total ketamine administered (mg)		39±4 (n=26)	41±5 (n=19)	0.143
Total propofol administered (mg)		527±21	531±25	0.197
Cancer history		9 (6)	2 (2)	0.065
Cardiac disease history		15 (11)	7 (6)	0.181
Renal disease history		4 (3)	11 (9)	0.059
Patient position during intubation	Lying on a stretcher	87 (62)	79 (63)	0.897
	Lying on a bed	54 (38)	47 (37)	

Descriptive data are demonstrated as frequency (percentage) and numerical and ordinal data are demonstrated as mean±SD. Two-tailed unpaired *t* test was performed for numerical and ordinal data and the Fischer exact test was performed for descriptive data. All results were considered significant if the *P* value was less than 0.05.

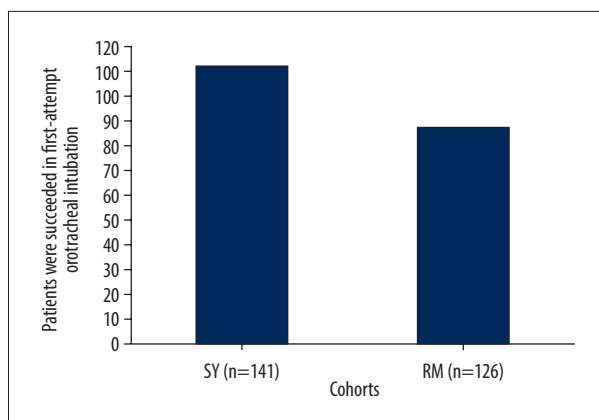


Figure 2. Successful first-attempt orotracheal intubation analysis. Data are presented as frequency. The success of orotracheal intubation was evaluated by a capnography curve.

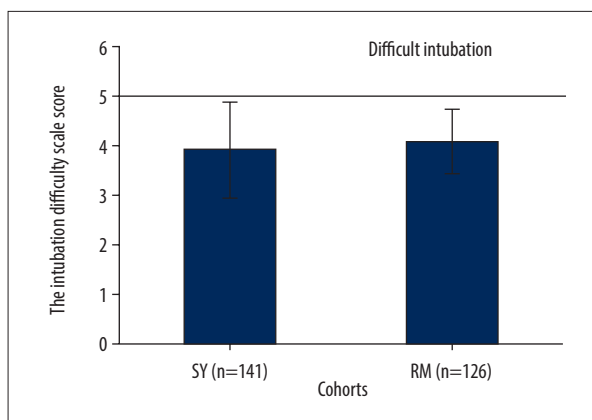


Figure 3. The Intubation Difficulty Scale analysis. Data are presented as mean ± SD.

Table 2. The modified Cormack-Lehane score by direct laryngoscopy.

The modified Cormack-Lehane score	Groups		Comparison
	SY	RM	
Neuromuscular blocking agent used	Succinylcholine	Rocuronium	
Patients included in analysis	141	126	P value
1	81 (57)	71 (56)	0.528
2A	29 (20)	20 (16)	
2B	15 (11)	14 (11)	
3	11 (8)	11 (9)	
4	5 (4)	10 (8)	

Data are presented as frequency (percentage). The Fischer exact test was performed for statistical analysis. The results were considered significant if the P value was less than 0.05.

Table 3. The intubation conditions.

The Copenhagen scores	Groups		Comparison
	SY	RM	
Neuromuscular blocking agent used	Succinylcholine	Rocuronium	
Patients included in analysis	141	126	P value
Excellent	85 (60)	81 (64)	0.509
Good	41 (29)	29 (23)	
Poor	15 (11)	16 (13)	

Data are presented as frequency (percentage). The Fischer exact test was performed for statistical analysis. The results were considered significant if the P value was less than 0.05.

Table 4. Alternative intubation techniques used.

Alternative intubation techniques	Groups		Comparison
	SY	RM	
Neuromuscular blocking agent used	Succinylcholine	Rocuronium	
Patients included in analysis	141	126	P value
Stylet	9 (7)	15 (11)	0.711
Gum elastic bougie	12 (10)	14 (10)	
The intubating laryngeal mask airway (Fastrach)	1 (1)	4 (3)	
Cricothyrotomy	1 (1)	1 (1)	

Data are presented as frequency (percentage). The Fischer exact test was performed for statistical analysis. The results were considered significant if the *P* value was less than 0.05.

Table 5. Intubation-related complications within the first 15 min after intubation.

Intubation-related complications	Groups		Comparison
	SY	RM	
Neuromuscular blocking agent used	Succinylcholine	Rocuronium	
Patients included in analysis	141	126	P value
Cardiac arrest	4 (3)	3 (2)	0.998
Arterial hypotension	7 (5)	11 (9)	0.234
Hypoxemia	13 (9)	12 (10)	0.997
Physician-reported aspiration	4 (3)	5 (4)	0.739
Severe arrhythmia	5 (4)	4 (3)	0.739
Allergic reaction	2 (1)	1 (1)	0.985
Numbers of patients with at least one complication	31 (22)	21 (17)	0.284

Data are presented as frequency (percentage). The Fischer exact test was performed for statistical analysis. The results were considered significant if the *P* value was less than 0.05.

2 groups. Three patients of the RM group required sugammadex treatment. Also, no death was attributed to difficult intubation (Table 6).

Discussion

This observational study of the use of anesthesiology in the Emergency Department setting aimed to compare rocuronium with succinylcholine for rapid sequence induction intubation. The results showed that there was no statistical difference between the 2 drugs ($P=0.067$) in the successful first-attempt orotracheal intubation. Therefore, the complication rate of rocuronium is equivalent to that of succinylcholine regarding airway control because the complication rate

generally increases with an increase in the number of intubation attempts [25,26]. The results for the orotracheal intubation of the present study agree with those of a randomized trial [19], observational study [14], prospective study [20], and a retrospective study [16] but do not agree with the results of a randomized clinical trial [2]. The reason for the contradictory results is that the randomized clinical trial [2] used a one-sided 97.5% confidence level for a statistical difference from expert opinion (no reference is available), while the present study used a two-sided 95% confidence level for statistical difference. However, if the present study had used a one-sided 97.5% confidence level for statistical significance, there would be a statistically significant difference between the SY and RM groups in successful first-attempt orotracheal intubation. In general, the results of the present observational study

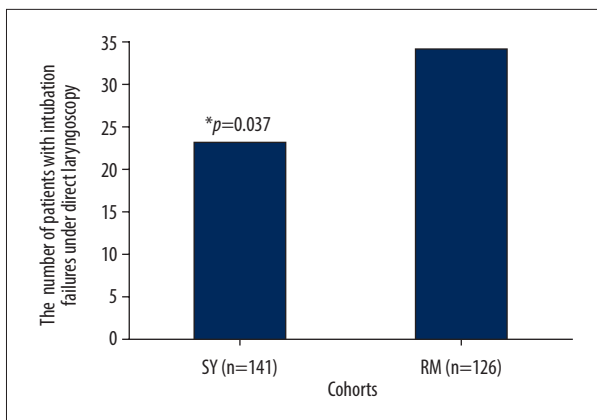


Figure 4. Intubation failures under direct laryngoscopy analysis. Data are presented as frequencies. * Significantly lower than the rocuronium (RM) group.

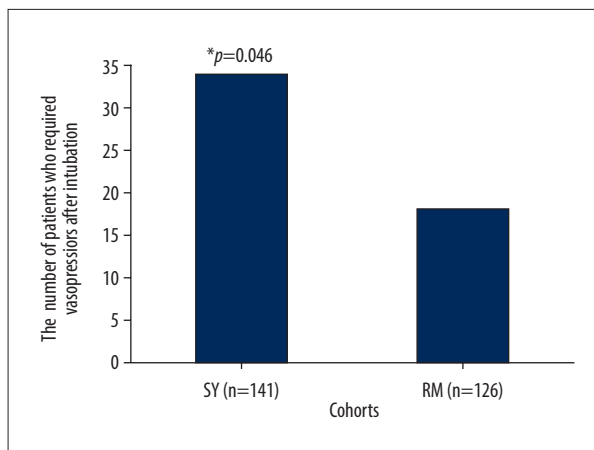


Figure 5. Requirements of vasopressors after intubation analysis. Data are presented as frequencies. * Significantly higher than the rocuronium (RM) group.

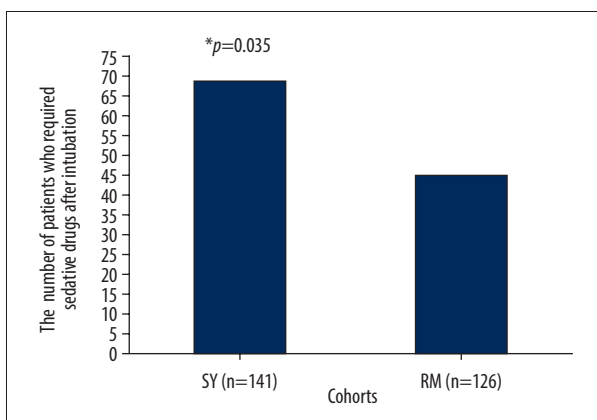


Figure 6. Sedative drugs required after intubation. Data are presented as frequencies. * Significantly higher than the rocuronium (RM) group.

showed that rocuronium is as successful as succinylcholine for first-attempt orotracheal intubation in patients who underwent a rapid sequence induction performed in the Emergency Department setting.

The results of the present study showed fewer intubation failures under direct laryngoscopy in patients in the SY group than in the RM group. The number of intubation failures in

Table 6. Exploratory outcomes.

Exploratory outcomes		Groups		Comparison
		SY	RM	
Neuromuscular blocking agent used		Succinylcholine	Rocuronium	
Patients included in analysis		141	126	P value
The number of intubation attempts	2	22 (15)	19 (15)	0.032
	3	5 (4)	14 (11)	
	≥4	2 (2)	6 (5)	
	Mean±SD	1.27±0.60*	1.52±0.87	
The time of out-of-hospital care (min)	Minimum	33	35	0.071
	Maximum	79	85	
	Mean±SD	54±4	55±5	
The number of deaths during out-of-hospital care		1 (1)	3 (2)	0.346
The number of unintentional extubations		1 (1)	2 (2)	0.604

Descriptive are data presented as frequency (percentage) and numerical and ordinal data are presented as mean±standard deviation (SD). The Fischer exact test was performed for statistical data. All results were considered significant if the P value was less than 0.05. * Significantly lower than the RM group.

the present study were similar with the intubation failure results of one randomized clinical trial [2] but not with the results of another randomized clinical trial [19]. The reason for these conflicting results is the differences in inclusion criteria between the studies. These results supported that the recovery of profound neuromuscular block from rocuronium is significantly slower than the recovery from succinylcholine.

In the present study, no statistically significant differences were found for the modified Cormack-Lehane grading score, the Intubation Difficulty Scale score, the Copenhagen scores, alternative intubation techniques used, intubation-related complications, and most exploratory outcomes between the SY and RM groups. The results of these outcome measures were similar with those of a randomized clinical trial [2], an observational study [14], and the guidelines for tracheal intubation management [5]. These results also supported the statistically equivalent performance of rocuronium and succinylcholine in patients who underwent a rapid sequence induction performed in the Emergency Department setting. Whether rocuronium or succinylcholine, the choice of paralytic should not have a direct effect on the difficulty of intubation, as long as paralysis has taken effect, which is operator-dependent and varies according to the situation.

Compared to the RM group, more patients required vasopressors and sedative drugs after intubation in the SY group. Succinylcholine induces hemodynamic instability which requires the administration of vasopressors [2]. Also, succinylcholine induces adverse respiratory events [27] that require the administration of sedative drugs after intubation. Compared to succinylcholine, rocuronium has the advantages of fewer adverse effects and contraindications and the disadvantages of a shorter of duration of effect.

This study had several limitations. The results showed that rocuronium was statistically equivalent to succinylcholine for the successful first-attempt orotracheal intubation, but the difference in group size of 112 vs. 87 patients was clinically significant. In clinical practice, rocuronium was inferior to succinylcholine for the successful first-attempt orotracheal intubation in patients who underwent a rapid sequence induction performed in the Emergency Department setting. This was supported by the finding that the number of intubation attempts per patient was higher in the RM group than in the SY group (1.52 ± 0.87 per patient vs. 1.27 ± 0.60 per patient). During the study, anesthesiologists performed direct laryngoscopy using the Macintosh laryngoscope for intubations. However, the use of video laryngoscopy may decrease the risk of complications related to a lack of expertise of anesthesiologists by improving glottis visualization [28]. However, although video laryngoscopy is used in anesthesiology practice, a randomized clinical trial [2] reported that compared with direct laryngoscopy, video laryngoscopy

does not improve orotracheal intubation rates. Also, video laryngoscopy is associated with severe life-threatening complications [29]. The present study was not a double-blind randomized trial. However, a double-blind randomized trial is nearly impossible to design in the emergency department, where the priority is saving lives and not meeting study objectives.

The standard dose of succinylcholine is 1.5 mg/kg for excellent intubation [30], but we used 1 mg/kg succinylcholine or 1.2 mg/kg rocuronium for intubation, using first-pass intubation as an endpoint. Paralysis does not occur on a continuum as does sedation, whereby one can have various depths of anesthesia. Depending on the dose of the agent selected for the appropriate clinical circumstance, as well as sufficient time for said dose to take effect, a patient will be either paralyzed or not. In our study, the effect of paralysis was identical in both groups. It is standard practice in emergency rapid sequence intubation in many centers to aim for doses of rocuronium as high as 1.5 mg/kg in patients who are hypotensive, otherwise the time to onset of paralysis is delayed. Hence, with emergency rapid sequence intubation of the current study comparing relatively low doses of rocuronium (1.2 mg/kg) and succinylcholine (1 mg/kg), the context of considering the hemodynamics of the patient population was minimal. Intubation is normally done by hospital anesthesiologists, but in the emergency department, intubation is performed mostly by emergency physicians. The purpose of this article is to identify optimal intubating conditions in the emergency department. However, in many cases, Emergency Department physicians are performing the procedure, which is a very significant distinction in physician expertise level. However, the specialty and experience of the proceduralists in emergency departments may vary based on country, region, and institution. A final limitation is that the adverse-effect profile of each drug, such as oxygen consumption and rates of desaturation, malignant hyperthermia, or hyperkalemia in the setting of multi-trauma, burns, and sepsis were not discussed.

Conclusions

The findings from this study support the results of previous studies and have shown that even in the Emergency Department setting, rocuronium was equivalent to succinylcholine in achieving rapid sequence induction intubation, when the dose was appropriate. However, as current clinical guidelines highlight, succinylcholine has more contraindications and adverse effects, including hyperkalemia, which should be monitored, and rocuronium has a longer duration of action.

Availability of data

The datasets were used and analyzed during the current study available from the corresponding author on request.

Acknowledgments

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Conflict of interest

None.

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