Rocuronium Versus Succinylcholine for Rapid Sequence Induction of Anesthesia and Endotracheal Intubation: A Prospective, Randomized Trial in Emergent Cases

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When anesthesia is induced with propofol in elective cases, endotracheal intubation conditions are not different between succinylcholine and rocuronium approximately 60 s after the injection of the neuromuscular relaxant. In the present study, we investigated whether, in emergent cases, endotracheal intubation conditions obtained at the actual moment of intubation under succinylcholine differ from those obtained 60 s after the injection of rocuronium. One-hundred-eighty adult patients requiring rapid sequence induction of anesthesia for emergent surgery received propofol (1.5 mg/kg) and either rocuronium (0.6 mg/kg; endotracheal intubation 60 s after injection) or succinylcholine (1 mg/kg; endotracheal intubation as soon as possible). The time from beginning of the induction until completion of the intubation was shorter after the administration of succinylcholine than after rocuronium (median time 95 s versus 130 s; $P < 0.0001$). Endotracheal intubation conditions, rated with a 9-point scale, were better after succinylcholine administration than after rocuronium (8.6 $\pm$ 1.1 versus 8.0 $\pm$ 1.5; $P < 0.001$). There was no significant difference in patients with poor intubation conditions (7 versus 12) or in patients with failed first intubation attempt (4 versus 5) between the groups. We conclude that during rapid sequence induction of anesthesia in emergent cases, succinylcholine allows for a more rapid endotracheal intubation sequence and creates superior intubation conditions compared with rocuronium.

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A rapid sequence induction of anesthesia and endotracheal intubation are indicated in emergency situations in the presence of a full stomach or other conditions with an increased risk of aspiration. Traditionally, succinylcholine has been the neuromuscular blocking drug of choice for rapid sequence induction of anesthesia. However, as a result of its depolarizing effect, succinylcholine can have serious side effects and is contraindicated in many conditions. Rocuronium has the most rapid onset of the currently available nondepolarizing neuromuscular blocking drugs. Therefore, many studies have investigated whether rocuronium may be a suitable alternative to succinylcholine. A meta-analysis of the Cochrane collaboration concluded that when propofol is used to rapidly induce anesthesia, endotracheal intubation conditions are not statistically different between succinylcholine and rocuronium (1). Before applying this evidence in daily practice, some important limitations of the Cochrane Review have to be recognized: (a) most of the patients receiving propofol were elective cases; (b) only a small number of emergent cases actually underwent a rapid sequence induction of anesthesia and endotracheal intubation with propofol and rocuronium; and (c) in most studies included in the meta-analysis, tracheas were intubated approximately 60 s after the injection of the neuromuscular blocking drug, yet clinical practice may allow intubation sooner than 60 s after the injection of succinylcholine. It is currently not known whether endotracheal intubation conditions obtained at the actual moment of intubation under succinylcholine differ from those obtained 60 s after the injection of rocuronium.

Accordingly, the aim of the present study was to compare rocuronium with the current practice of the use of succinylcholine (i.e., endotracheal intubation as soon as possible) in patients requiring rapid sequence induction of anesthesia and endotracheal intubation for emergent surgery. The hypotheses to be tested

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were that (a) succinylcholine would allow for an earlier completion of the endotracheal intubation sequence and (b) succinylcholine would create superior intubation conditions at the actual time of intubation.

Methods

The study took place in the Hospital of Thusis, a rural Level III center. All adult (age, ≥18 yr) patients undergoing emergent surgery under general anesthesia were eligible. Indications for emergent surgery were mainly trauma (the hospital is located in a tourist region with skiing accidents in winter and climbing accidents in summer) and laparotomies. Exclusion criteria were hyperkalemia, neurologic disorders, burns, familial history of malignant hyperthermia, cesarean delivery, complications during birth before delivery, known or anticipated difficult endotracheal intubation warranting awake fiberoptic intubation, contraindication against the use of propofol (e.g., shock) and allergy to rocuronium. The study was approved by the regional Ethics Committee, and written informed consent was obtained during the preoperative visit. The primary outcomes of the study were the duration of the endotracheal intubation sequence and intubation conditions. Using a 9-point grading system for intubation conditions (Table 1), a difference of at least 1.0 points was considered to be of clinical relevance. A power analysis revealed that 85 patients were required for each study group to detect that difference with a power of 0.9 and a two-sided α of 0.05. To account for protocol violations related to an emergent procedure, we planned to enroll 90 patients per group.

Patients were randomly allocated (sealed envelopes) to receive either 0.6 mg/kg of rocuronium (Esmeron™, Organon, Switzerland) or 1.0 mg/kg of succinylcholine (Lystenon™, Nycomed, Switzerland) as the neuromuscular blocking drug. No premedication was administered. Upon arrival in the operating room, a 18-gauge cannula was inserted in a forearm vein. Routine monitoring was used. End-tidal carbon dioxide was measured using the side-stream method (Cardiocap, Datex, Finland). Electrodes of a nerve stimulator (Healthcare NS 272; Fisher & Paykel, New Zealand) were placed over the left ulnar nerve.

One of three experienced staff anesthesiologists (MS, WU, or SM), assisted by a registered anesthetic nurse and a scrub nurse, was present throughout the whole procedure, guided the injection of drugs, and performed the endotracheal intubation. The staff anesthesiologist was not blinded to the neuromuscular blocking drug used, and the management of difficulties and complications, if any, was left to his discretion. To minimize bias, intubations were performed by three different anesthesiologists who had no personal preference for one of the two neuromuscular blocking drugs.

The endotracheal intubation sequence was defined as time interval between the injection of propofol and the first appearance of end-tidal carbon dioxide on the screen of the monitor. After 3 min of the administration of oxygen, cricoid pressure was applied, and anesthesia was induced with fentanyl 2 μg/kg and propofol 1.5 mg/kg. The neuromuscular blocking drug was injected as soon as the eyelid reflex had disappeared, and the nerve stimulator was switched to the single-twitch mode (rate, one twitch per second). Laryngoscopy was started either after the cessation of fasciculations in the lower extremities (2), if any, the cessation of a visible motor response to continuous single-twitch nerve stimulation, or after 50 s (anticipated time of intubation 60 s after the injection of the neuromuscular blocking drug), whichever was earlier. Endotracheal intubations were performed using a Macintosh size 3 blade and a tracheal tube (Mallinckrodt Hi-Contour, Mallinckrodt, Ireland) with an internal diameter of 7.5 cm in women and of 8.5 cm in men. The timing of events was performed by the anesthetic nurse.

Intubation conditions are usually evaluated using the following factors: (a) ease of laryngoscopy, (b) position and movement of the vocal cords, and (c) response to intubation of the airway and the limbs (3). However, previous studies differ in that either a numerical (1) or a qualitative (4) score was derived from these factors. To allow for a comparison with both types of scoring systems previously used, we provide both a numerical and a qualitative rating. Both ratings are based on a scoring system proposed for good clinical research practice in studies of neuromuscular blocking drugs (3). The intubating anesthesiologist rated the ease of laryngoscopy, the movement and position of the vocal cords, and the reaction to intubation, as demonstrated in Table 1.

Desaturation was defined as either a saturation ≤90% or a decrease in saturation of ≥5% occurring at any time between the start of the induction sequence and 3 min after the completion of the intubation.

Data, presented as mean ± SD unless otherwise stated, were analyzed using SPSS 12.0 for Windows, a commercially available statistical software (SPSS, Chicago, IL). Two-way analysis of variance, unpaired Student's *t*-test, Mann-Whitney test, Fisher's exact test, and the logrank test were applied, as appropriate. General linear modeling was used to assess differences among the 3 intubating anesthesiologists with regard to scoring of the intubation conditions. A $P < 0.05$ was considered to represent statistical significance.

Results

During the study period ending with the completion of the protocol in the 180th patient, 234 consecutive

Table 1. Scoring System for Endotracheal Intubation Conditions

	Score 3	Score 2	Score 1
Laryngoscopy			
Jaw relaxation	Relaxed	Acceptable relaxation	Poor relaxation
Resistance to blade	None	Slight resistance	Active resistance
Vocal cords			
Position	Abducted	Intermediate	Closed
Movement	None	Moving	Closing
Intubation response			
Limb movement	None	Slight	Vigorous
Coughing	None	Diaphragmatic	Severe coughing or bucking

The factors laryngoscopy, vocal cords, and response to intubation are individually rated with a score from 1 to 3. The assignment of a score for each of the three factors is based on the lower rating of two variables, e.g., the combination of the variables "no limb movement" and "no coughing" results in a score of 3 for the factor response to intubation, whereas the combination of the variables "no limb movement" and "severe coughing" results in a score of 1. The numerical intubation score was obtained by summing the scores assigned to the factors laryngoscopy, vocal cords, and response to intubation. The maximum score is thus 9, whereas the minimum score is 3. The qualitative intubation scores was defined as follows:

– excellent intubation conditions: all 3 factors were rated with a score of 3.
– good intubation conditions: all 3 factors were rated either with a score of 3 or 2.
– poor intubation conditions: the presence of one factor rated with a score of 1.

Excellent and good intubation conditions are considered clinically acceptable, whereas poor intubation conditions are considered clinically not acceptable (3).

patients underwent emergency surgery under general anesthesia. Five had to be excluded because of predefined exclusion criteria (2 cesarean delivery, 2 hemorrhagic shock, and 1 hyperkalemia), 16 refused to participate, and the enrollment of 33 was missed, mainly because of high workload. One-hundred-eighty patients were randomized, received the allocated treatment, and were included in the analysis (Table 2).

The median time interval between the beginning of the administration of propofol and the disappearance of the eyelid reflex was 30 s (interquartile range, 18.5 s) in the succinylcholine group and 26 s (interquartile range, 20 s) in the rocuronium group ($P = 1.0$). Figure 1 depicts the time interval from injection of the neuromuscular blocking drug to the cessation of a visible motor response to continuous single-twitch nerve stimulation of the ulnar nerve. This time interval was significantly shorter ($P < 0.0001$) in the succinylcholine group (median time, 40 s) compared with the rocuronium group (median time, 70 s). Figure 2 depicts the time interval between the beginning of the administration of propofol and the first appearance of end-tidal carbon dioxide after endotracheal intubation, which was significantly shorter ($P < 0.0001$) in the succinylcholine group (median time, 95 s) compared with the rocuronium group (median time, 130 s).

Scores for endotracheal intubation conditions were significantly higher in the succinylcholine group than in the rocuronium group (8.6 ± 1.1 versus 8.0 ± 1.5; $P < 0.001$). This difference resulted almost exclusively from a difference in the subscore rating the response to intubation (2.8 ± 0.5 versus 2.3 ± 1.0; $P < 0.0001$), whereas there was no difference in the subscores for laryngoscopy (2.9 ± 0.3 versus 2.9 ± 0.3; $P = 0.91$) and vocal cords (2.9 ± 0.4 versus 2.8 ± 0.6; $P = 0.23$). Figure 3 depicts the scores for intubating conditions.

Table 2. Patient Demographics

	Succinylcholine ($n = 90$)	Rocuronium ($n = 90$)
Age (yr)	43 ± 18	49 ± 21
Sex (m/f)	39/51	36/54
ASA Status (I/II/III/IV)	14/50/24/2	14/48/28/0
Height (cm)	170 ± 9	167 ± 9
Weight (kg)	70 ± 14	68 ± 14

Mean ± SD. There was no statistically significant difference between the groups.

Note that compared with the rocuronium group, there were significantly more excellent intubation conditions in the succinylcholine group (Fig. 3). However, there was no difference in patients with poor intubation conditions between the groups (7 versus 12; $P = 0.33$). General linear modeling showed (a) no significant difference among the 3 intubating anesthesiologists with regard to the rating of the intubation conditions ($F_{2,168} = 0.21$; $P = 0.81$), (b) no significant interaction of the 2 between-subject factors intubating anesthesiologist and neuromuscular blocking drug ($F_{2,168} = 1.47$; $P = 0.23$), and (c) no significant interaction of the between-subject factor intubating anesthesiologist and the within-subject factor subscores of intubation conditions ($F_{4,336} = 0.87$; $P = 0.48$). This indicates that there was no systematic difference in scoring among the 3 intubating anesthesiologists.

Eighty-six of 90 patients in the succinylcholine group and 85 of 90 patients in the rocuronium group were intubated during the first attempt ($P = 1.0$). All remaining nine patients were successfully endotracheally intubated in the second attempt. The reasons for the four failures of the first intubation attempt in the succinylcholine group were one poor intubation condition (numerical score 3), one esophageal intubation

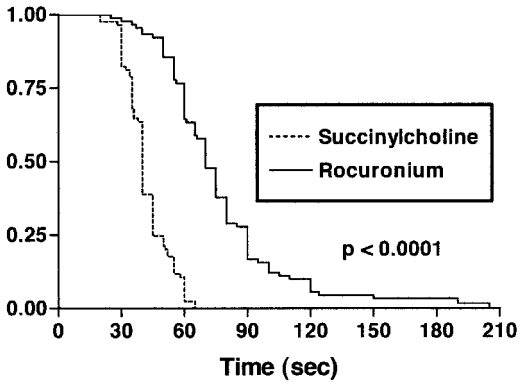

Figure 1. Kaplan-Meyer curve of the probability of the disappearance of a visible motor response to a continuous single-twitch stimulation of the ulnar nerve after injection of succinylcholine or rocuronium. Time 0 denotes the injection of the neuromuscular blocking drug. Curves differ significantly ($P = < 0.0001$; logrank test).

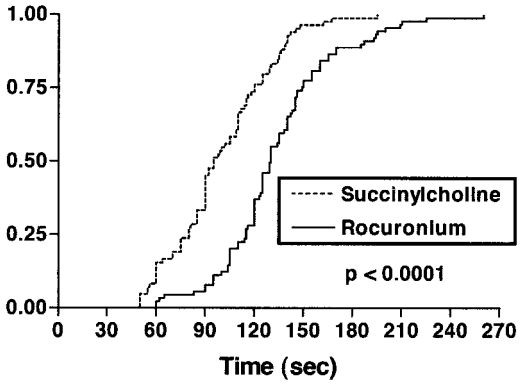

Figure 2. Kaplan-Meyer curve of the probability of the completion of the endotracheal intubation sequence including succinylcholine or rocuronium as the neuromuscular blocking drug. Time 0 denotes the beginning of the injection of the induction drug propofol. The endotracheal intubation sequence was defined to be completed upon the first appearance of end-tidal carbon dioxide after intubation. Curves differ significantly ($P < 0.0001$; logrank test).

(intubation score excellent), and two "difficult anatomy" (intubation scores excellent and good, respectively) that could be mastered in the second attempt by mounting the tube on a stylet. The reasons for the five failures of the first intubation attempt in the rocuronium group were one poor intubation condition (numerical score 4), two esophageal intubations (intubation scores excellent and good, respectively), and two "difficult anatomy" (intubation score excellent in both cases) that could be mastered in the second attempt by mounting the tube on a stylet. Thus, poor intubation conditions were observed in only two of the nine patients (one in each group) not intubated in the first attempt.

A desaturation occurred in 5 of 90 patients in the succinylcholine group and in 9 of 90 patients of the rocuronium group ($P = 0.40$). Poor endotracheal intubation conditions were observed in only 2 of the 14

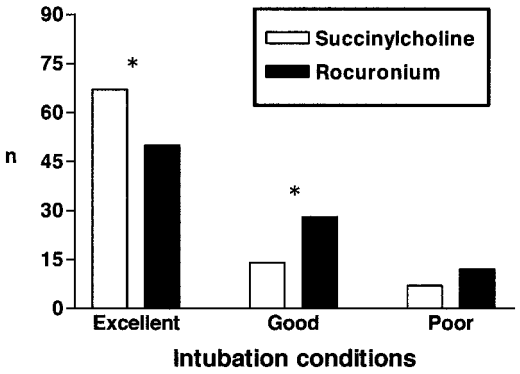

Figure 3. Endotracheal intubation conditions during rapid sequence induction of anesthesia and endotracheal intubation with succinylcholine or rocuronium as the neuromuscular blocking drug. The scoring system is explained in Table 1. *$P < 0.05$ between the 2 neuromuscular blocking drugs (Fisher's exact test).

patients (one in each group) with desaturation, whereas 8 of 14 desaturations were associated with an excellent intubation score. Four of 14 desaturations (2 in each group) occurred in patients with a second intubation attempt. Compared with the patients without desaturation, the time interval from the beginning of the administration of propofol and the completion of the intubation was longer in patients with desaturation (134 ± 9 s versus 116 ± 3 s; $P = 0.047$).

Discussion

In the present study, we compared rocuronium with the current practice of the use of succinylcholine (i.e., endotracheal intubation as soon as possible) in patients requiring rapid sequence induction of anesthesia and endotracheal intubation for emergent surgery. When succinylcholine was used as the neuromuscular blocking drug for rapid sequence induction of anesthesia, the median intubation sequence was 35 s shorter than when rocuronium was used. Succinylcholine created excellent intubation conditions more often than rocuronium, and there was a statistically significant difference of 0.5 points on a 9-point grading scale of intubation conditions in favor of succinylcholine. However, as far as clinically acceptable intubating conditions and failed intubation attempts are concerned, the two relaxants were not statistically different.

Analyzing the available evidence up to the year 2000, a Cochrane Review concluded that for rapid sequence induction of anesthesia, succinylcholine created superior endotracheal intubation conditions to rocuronium when comparing excellent intubation conditions. Using the less stringent clinically acceptable intubation conditions, the two drugs were not statistically different (1). Moreover, based on a subgroup analysis, the Cochrane Review concluded that

intubation conditions did not statistically differ between the administration of succinylcholine and rocuronium when propofol was used as the drug to induce anesthesia (1). Several potential limitations of these conclusions are noteworthy. Only 24 of the 1606 patients included in the Cochrane Review were emergent cases that actually underwent a true rapid sequence induction of anesthesia and endotracheal intubation with both propofol and rocuronium. All 24 patients were part of a single study and received 1 mg/kg of rocuronium (4). Moreover, only 47 of the 640 patients included in the subgroup using propofol as the induction drug (4–12) were emergency cases undergoing a true rapid sequence induction of anesthesia and endotracheal intubation. From the remaining 593 elective cases, approximately 50% ($n = 290$) did not undergo a true rapid sequence induction of anesthesia. Most previous studies comparing succinylcholine and rocuronium assessed endotracheal intubation conditions approximately 60 seconds after the injection of the neuromuscular blocking drug (1). Whereas this is an appropriate time interval for rocuronium, a delay between injection of succinylcholine and start of laryngoscopy of 50 seconds or more does not reflect current practice; most, if not all, anesthesiologists choosing succinylcholine for rapid sequence induction of anesthesia and endotracheal intubation take advantage of its rapid onset of action and start laryngoscopy as quickly as possible, i.e., after the cessation of fasciculations. Indeed, 50 seconds after the injection of the neuromuscular blocking drug, i.e., the time of the beginning of the laryngoscopy in previous studies, the intubation sequence was already completed in more than one-third of the patients in the succinylcholine group of the present study.

Based on current evidence, the induction of anesthesia sequence of the present study was chosen to achieve the best possible endotracheal intubation conditions for the rocuronium group. Propofol was used as the induction drug because this anesthetic seems to be superior to all other drugs with regard to intubating conditions after rocuronium injection (1). Fentanyl (2 μg/kg) was added to the induction sequence because opioids, in doses equivalent to alfentanil 20 μg/kg, were found to significantly improve intubating conditions after rocuronium administration (13). Intubation was attempted 60 seconds after the injection of rocuronium because this seemed to be the earliest moment when acceptable intubation conditions can be reliably achieved (1). Rocuronium was used in a dose of 0.6 mg/kg because there seemed to be no benefit of larger rocuronium doses on intubation conditions when propofol was used as the induction drug (1). Previous work demonstrated a dose-dependent effect of rocuronium on both onset and duration of neuromuscular block (14). Thus, there is the possibility that larger doses of rocuronium would allow for an earlier intubation. However, all studies comparing intubation conditions after different doses of rocuronium did so after a predefined time interval (usually 60 seconds after the injection of rocuronium). Thus, it is unknown whether the earlier onset of neuromuscular block associated with doses larger than 0.6 mg/kg of rocuronium would translate into a clinical advantage, i.e., the possibility for an earlier intubation with at least the same intubation conditions that are achievable at 60 seconds.

An important limitation of our study is the lack of a double-blind design. Concealing the effects of drugs that have visible effects such as fasciculations is inherently difficult. Moreover, because the two neuromuscular blocking drugs studied differ in onset time, awareness of the time of the injection of the drug results in unblinding. Thus, a perfect double-blind design implies that the intubating anesthesiologist is not able to see or overhear the patient and the team performing the induction sequence and is immediately available to intubate the patient's trachea after the cessation of fasciculations. A rapid sequence induction of anesthesia is a high-risk procedure requiring the full attention of an appropriately trained anesthesiologist. Because, in our settings, the simultaneous achievement of perfect blinding and optimal patient safety was not feasible, we opted for a single-blind study design. The statistical analysis of the effects and interactions of neuromuscular blocking drugs and the intubation scores revealed a homogenous rating with no systematic differences among the anesthesiologists performing the intubations.

The power of the present study was too small to allow reliable conclusions on the incidence of complications. These issues should be addressed in large multicenter trials. Interestingly, in the present study, only a minority of failed first endotracheal intubation attempts and desaturations were associated with a low score of intubation conditions. If confirmed in further trials, these findings may lead to a modification of the scoring system presently used.

What are the practical implications of our findings? Choosing rocuronium instead of succinylcholine for rapid sequence induction of anesthesia prolongs the time of unprotected airway, i.e., the time interval from beginning of the induction until completion of endotracheal intubation, from a median time of 95 seconds to a median time of 130 seconds. The additional risk of aspiration and desaturation resulting from a prolongation of the intubation sequence by a median time of 35 seconds is unknown, but it is most likely very small in most patients. However, patients with an especially high risk for aspiration or a desaturation may benefit from a more rapid intubation. Choosing rocuronium instead of succinylcholine for rapid sequence induction of anesthesia results in less optimal intubating conditions. However, the difference between the two

relaxants is small and mainly results from lower ratings in the subscore addressing the reaction to intubation, i.e., coughing or bucking. Because the reaction to intubation occurs after the placement of the tube, the relevance for patients' safety is marginal. Until more data on complications are available, we suggest that anesthesiologists select the best treatment for their patients undergoing a rapid sequence induction of anesthesia on an individual basis by balancing intubation conditions and duration of the intubation sequence against potential side effects.

Compared with the subgroup of patients receiving propofol included in the recent Cochrane Review on rapid sequence induction (1), in the present study, we observed significantly more poor intubation conditions after both neuromuscular blocking drugs (19 of 180 versus 27 of 640 poor intubation conditions; $P = 0.007$). Because most patients included in the Cochrane Review were elective cases not undergoing a true rapid sequence induction of anesthesia, this difference is most likely explained by differences in the patient population and the procedure. Although elective cases are valuable models for investigating the effects of neuromuscular blocking drugs, findings obtained in this setting may thus not be necessarily extrapolated to emergency situations.

In conclusion, in the context of a rapid sequence induction of anesthesia with propofol and fentanyl in emergent cases, succinylcholine allowed for a more rapid endotracheal intubation sequence and created superior intubation conditions than rocuronium. Presently, practitioners have to balance the quality of intubation conditions and the duration of the intubation sequence against the potential for side effects. Large-scale trials are required to address important safety issues such as failed intubation attempts and desaturations associated with the use of succinylcholine or rocuronium.

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