The association of rocuronium dosing and first-attempt intubation success in adult emergency department patients

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Abstract

Background The recommended rocuronium dose for rapid sequence intubation is 1.0 mg/kg; however, the optimal dose for emergency airway management is not clear. We assessed the relationship between rocuronium dose and first-attempt success among emergency department (ED) patients undergoing rapid sequence intubation.

Methods This is a secondary analysis of the National Emergency Airway Registry (NEAR), an observational 25-center registry of ED intubations. Ninety percent recording compliance was required from each site for data inclusion. We included all patients > 14 years of age who received rocuronium for rapid sequence intubation from 1 Jan 2016 to 31 Dec 2018. We compared first-attempt success between encounters using alternative rocuronium doses (< 1.0, 1.0–1.1, 1.2–1.3 and ≥ 1.4 mg/kg). We performed logistic regressions to control for predictors of difficult airways, indication, pre-intubation hemodynamics, operator, body habitus and device. We also performed subgroup analyses stratified by device (direct vs. video laryngoscopy). We calculated univariate descriptive statistics and odds ratios (OR) from multivariable logistic regressions with cluster-adjusted 95% confidence intervals (CI).

Results 19,071 encounters were recorded during the 3-year period. Of these, 8,034 utilized rocuronium for rapid sequence intubation. Overall, first attempt success was 88.4% for < 1.0 mg/kg, 88.1% for 1.0–1.1 mg/kg, 89.7% for 1.2–1.3 mg/kg, and 92.2% for ≥ 1.4 mg/kg. Logistic regression demonstrated that when direct laryngoscopy was used and when compared to the standard dosing range of 1.0–1.1 mg/kg, the adjusted odds of a first attempt success was significantly higher in ≥ 1.4 mg/kg group at 1.9 (95% CI 1.3–2.7) relative to the other dosing ranges, OR 0.9 (95% CI 0.7–1.2) for < 1.0 mg/kg and OR 1.2 (95% CI 0.9–1.7) for the 1.2–1.3 mg/kg group. First-attempt success was similar across all rocuronium doses among patients utilizing video laryngoscopy. Patients who were hypotensive (SBP < 100 mmHg) prior to intubation had higher first-attempt success 94.9% versus 88.6% when higher doses of rocuronium were used. The rates of all peri-intubation adverse events and desaturation were similar between dosing groups, laryngoscope type utilized and varying pre-intubation hemodynamics.

Conclusions Rocuronium dosed ≥ 1.4 mg/kg was associated with higher first attempt success when using direct laryngoscopy and among patients with pre-intubation hypotension with no increase in adverse events. We recommend further prospective evaluation of the dosing of rocuronium prior to offering definitive clinical guidance.

Keywords Rapid sequence intubation · Emergency medicine · Critical care · Airway · Non-depolarizing paralytics · Depolarizing paralytics

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Résumé

Contexte La dose de rocuronium recommandée pour l'intubation à séquence rapide est de 1,0 mg / kg, mais la dose optimale pour la prise en charge des voies respiratoires d'urgence n'est pas claire. Nous avons évalué la relation entre la dose de rocuronium et la réussite de la première tentative chez les patients des services d'urgence soumis à une intubation à séquence rapide.

Méthodes Il s'agit d'une analyse secondaire du National Emergency Airway Registry (NEAR), un registre d'observation des intubations aux urgences dans 25 centres. Pour que les données soient prises en compte, chaque site devait respecter 90 % des enregistrements. Nous avons inclus tous les patients âgés de plus de 14 ans qui ont reçu du rocuronium pour une intubation à séquence rapide du 1er janvier 2016 au 31 décembre 2018. Nous avons comparé le succès de la première tentative entre les rencontres utilisant des doses alternatives de rocuronium (<1,0 mg/kg, 1,0-1,1 mg/kg, 1,2-1,3 mg/kg et 1,4mg/kg). Nous avons effectué des régressions logistiques pour contrôler les facteurs prédictifs des voies aériennes difficiles, l'indication, l'hémodynamique pré-intubation, l'opérateur, l'habitus corporel et le dispositif. Nous avons également effectué des analyses de sous-groupes stratifiées par dispositif (laryngoscopie directe contre vidéo-laryngoscopie). Nous avons calculé des statistiques descriptives univariées et des rapports des cotes (RC) à partir de régressions logistiques multivariées avec des intervalles de confiance (IC) à 95 % ajustés par groupe.

Résultats 19 071 consultations ont été enregistrées au cours de la période de trois ans. Parmi celles-ci, 8 034 ont utilisé du rocuronium pour une intubation à séquence rapide. Dans l'ensemble, le succès de la première tentative était de 88,4 % pour <1,0 mg/kg, 88,1 % pour 1,0 à 1,1 mg/kg, 89,7 % pour 1,2 à 1,3 mg/kg et 92,2 % pour $\geq 1,4$ mg/kg. La régression logistique a démontré que lorsque la laryngoscopie directe était utilisée et comparée à la gamme de dosage standard de 1,0-1,1 mg/kg, la probabilité ajustée de réussite de la première tentative était significativement plus élevée dans le groupe $\geq 1,4$ mg/kg à 1,9 (IC 95 % 1,3-2,7) par rapport aux autres gammes de dosage, RC 0,9 (IC 95 % 0,7-1,2) pour < 1,0 mg/kg et RC 1,2 (IC 95 % 0,9-1,7) pour le groupe 1,2-1,3 mg/kg. La réussite de la première tentative était similaire pour toutes les doses de rocuronium chez les patients utilisant la vidéo-laryngoscopie. Les patients qui étaient hypotendus (SBP <100 mmHg) avant l'intubation avaient un taux de réussite de la première tentative plus élevé 94,9% contre 88,6% lorsque des doses plus élevées de rocuronium étaient utilisées. Les taux de tous les effets indésirables péri-intubation et de désaturation étaient similaires entre les groupes de dosage, le type de laryngoscope utilisé et les différentes hémodynamiques pré-intubation.

Conclusions Le rocuronium dosé à $\geq 1,4$ mg/kg a été associé à une meilleure réussite de la première tentative lors de l'utilisation de la laryngoscopie directe et chez les patients présentant une hypotension avant intubation, sans augmentation des effets indésirables. Nous recommandons une évaluation prospective plus poussée du dosage du rocuronium avant de proposer une orientation clinique définitive.

Clinicians' capsule

What is known about the topic?

The recommended dose of rocuronium for rapid sequence intubation is 1.0 mg/kg but evidence from emergency airway management is limited.

What did this study ask?

We assessed the association of rocuronium dosing on first-attempt success and adverse outcomes among emergency department patients.

What did this study find?

Rocuronium dosed ≥ 1.4 mg/kg was associated with higher first attempt success when using direct laryngoscopy and among patients with pre-intubation hypotension.

Why does this matter to clinicians?

The association between accurate weight-based rocuronium dosing and first-attempt success is important and may be further influenced by pre-intubation hypotension.

Background

Emergency intubation is a life-saving procedure commonly performed in the emergency department (ED) and rapid sequence intubation is the most prevalent method used. Rapid sequence intubation involves the near simultaneous administration of sedative and neuromuscular blocking agents to optimize the patient for a fast and safe endotracheal intubation. In the ED, the two most common neuromuscular blocking agents are succinylcholine and rocuronium; however, recent utilization trends show rocuronium use is increasing over time [1].

Previous studies have reported no significant difference in first pass success or peri-intubation adverse events between these two medications [2–4]. However, the differential impact of varying weight-based dosing regimens was not analyzed. While early operating room studies have suggested that escalating doses of rocuronium result in better intubating conditions, the upper limit of rocuronium dosing was 1.0 mg/kg and therefore is hard to extrapolate to emergency department patients [5, 6].

Fig. 1 Flow diagram of patient selection

Objective

To assess the relationship of escalating weight-based dosing for rocuronium on first-attempt intubation success and peri-intubation adverse events in adult ED patients.

Methods

Data source and study population

We analyzed data from the National Emergency Airway Registry (NEAR), an observational 25-center registry of ED intubations. The majority of EDs are affiliated with academic medical centers. Registry-wide recording compliance of 90% was required for data inclusion. Each participating site obtained prior approval from its local institutional review board. Intubating providers completed the standardized data collection instrument after each individual intubation by accessing a centralized electronic data management database (StudyTRAX, Macon, GA). Study investigators reviewed all data using quality assurance algorithms to identify and correct data entry errors. We recorded all data in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology states (STROBE) [7].

Selection of participants

All patients > 14 years of age who underwent rapid sequence intubation with rocuronium between 1 January 2016 and 31 December 2018 were candidates for inclusion. We excluded patients with no documented age, dose, or weight. We also excluded patients who received <0.5 or >2.0 mg/kg of rocuronium as these may have represented data entry errors (Fig. 1).

Study variables and outcomes

We selected encounter variables *a priori* based on their historically known associations with intubation outcomes. This follows the guidance outlined by Lederer et al. on controlling for confounding in casual inference studies [8]. Variables included were patient demographics, indication for intubation, pre-intubation hemodynamics, difficult airway characteristics, preoxygenation modalities, pretreatment medications, induction and neuromuscular blocking agents used along with dosages, intubation position and device, intubator characteristics, best glottic view, first-pass intubation success or failure, peri-intubation adverse events, intubation confirmation method, peri-intubation vitals and disposition.

The primary outcome was first-attempt intubation success. NEAR defines an intubation attempt as a single effort to place an endotracheal tube in which the leading edge of

the laryngoscope blade entered the oral cavity past the alveolar ridge [9].

Secondary outcomes included incidence of any adverse event. Adverse events included cardiac arrest, dental trauma, direct airway injury, bradydysrhythmias, epistaxis, esophageal intubation, hypotension (systolic blood pressure < 100 mm Hg), hypoxemia (oxygen saturation < 90%), iatrogenic bleeding, laryngoscope failure, laryngospasm, lip laceration, main-stem intubation, pharyngeal laceration, pneumothorax, endotracheal tube cuff failure, or vomiting with aspiration. Other outcomes included best Cormack–Lehane view and lowest peri-intubation oxygen saturation [10].

Statistical analysis

We assessed the primary outcome stratified by differing doses of rocuronium, including: < 1.0, 1.0–1.1, 1.2–1.3, and ≥ 1.4 mg/kg. The decision to use these dosing groups was made in part on various historical dosing practices and in part to optimize a similar number of patients in each comparator group. During this process, we also constructed a restricted cubic spline to model the nonlinear relationship between dose and first-pass success using five quintile knots at 0.96, 1.02, 1.18, 1.31, and 1.43 mg/kg (Supplemental Figure 1). We made univariate comparisons among these four groups using Cochran–Armitage trend tests (for nominal variables) and Kruskal–Wallis tests (for non-normal continuous variables).

We extended these comparisons using multivariable logistic regression models to calculate adjusted odds ratios with 95% confidence intervals. These models were clustered by NEAR site and adjusted for sex, body habitus, indication (trauma versus medical patient), initial impression of airway difficulty, intubation position, laryngoscope type, sedative medications, and operator characteristics. We conducted diagnostic tests prior to modeling the data, to include screening for collinearity, assessing outliers, and testing for key assumptions, and found no evidence of violation of the assumptions. We also performed subgroup analyses stratified by device (direct vs. video laryngoscopy) and pre-intubation hemodynamics. We report univariate descriptive statistics and odds ratios (OR) from multivariable logistic regressions with cluster-adjusted 95% confidence intervals (CI).

Results

Over the 3-year period, 19,071 encounters were recorded. Of those, 8,034 were rapid sequence intubations using rocuronium within the defined dosing range (Fig. 1). Among these,

45.7% utilized direct laryngoscopy while 53.4% used video laryngoscopy.

Patients in the lower dose group were more likely to be classified as obese or morbidly obese and had higher mean total body weight, 103.8 kg in the < 1 mg/kg dose group to 67.3 kg in the ≥ 1.4 mg/kg dose group (Table 1). The higher dose groups were also more likely to undergo intubation for a traumatic indication and have facial trauma (23.6 and 12.2% in the ≥ 1.4 mg/kg dose group compared to 15.8% and 6.9% for the 1 mg/kg dose group). A greater proportion of patients, 45.3%, in the < 1 mg/kg dose group had an initial impression of difficult airway compared to 24.3% in the ≥ 1.4 mg/kg dose group.

First attempt success across dosing ranges was 88.4% for the < 1.0 mg/kg, 88.1% for 1.0–1.1 mg/kg, 89.7% for 1.2–1.3 mg/kg and 92.2% for the ≥ 1.4 mg/kg dose groups (Table 2). When compared to the 1.0–1.1 mg/kg group, the adjusted odds of first-attempt success were highest in the ≥ 1.4 mg/kg group, 1.5 (95% CI 1.1–2.0). The adjusted odds of the remaining dosing groups of < 1.0 mg/kg and 1.2–1.3 mg/kg were 1.1 (95% CI 1.0–1.4) and 1.2 (95% CI 0.9–1.5), respectively (Figs. 2, 3). The rates of all peri-intubation adverse events and desaturation were similar between groups (Supplemental Table 1).

Hypotensive vs. normo-/hypertensive

Patients who were hypotensive (SBP < 100 mmHg) prior to intubation had higher first-attempt success 94.9% versus 88.6% when higher doses of rocuronium were used (Table 2, Fig. 2). Rates of peri-intubation adverse events and desaturation were similar between groups (Supplemental Table 3).

Direct laryngoscopy (DL) vs. video laryngoscopy (VL)

When direct laryngoscopy was used and when comparing to the standard dosing range of 1.0–1.1 mg/kg, the adjusted odds of a first attempt success was significantly higher in ≥ 1.4 mg/kg group at 1.9 (95% CI 1.3–2.7) relative to the other dosing ranges, OR 0.9 (95% CI 0.7–1.2) for < 1.0 mg/kg and OR 1.2 (95% CI 0.9–1.7) for the 1.2–1.3 mg/kg group (Fig. 4). First-attempt success was similar across all dosing ranges with video laryngoscopy. The rates of all peri-intubation adverse events and desaturation were similar between groups (Supplemental Table 2).

Discussion

Interpretation of findings

We observed an association of overall higher first-attempt success with rocuronium doses of 1.4 mg/kg or more

Table 1 Patient characteristics

Variable	Rocuronium, all doses (<i>n</i> =8034)	< 1.0 mg/kg (<i>n</i> =1255)	1.0–1.1 mg/kg (<i>n</i> =2556)	1.2–1.3 mg/kg (<i>n</i> =1919)	≥ 1.4 mg/kg (<i>n</i> =2304)	<i>p</i>
Mean age (SD), years	54.0 (19.4)	55.6 (17.9)	54.7 (18.8)	53.5 (19.5)	52.6 (20.6)	<0.0001
Sex (female), %	35.7	35.3	34.9	32.9	39.1	0.0147
Received 100 mg rocuronium, %	60.2	43.5	45.7	69.5	77.6	<0.0001
Mean weight (SD), kg	80.6 (22.4)	103.8 (31.1)	83.9 (18.8)	77.0 (14.0)	67.3 (13.1)	<0.0001
Body habitus, %						
Very thin	4.2	1.9	3.4	3.7	6.7	<0.0001
Thin	16.2	7.6	12.8	15.1	25.5	<0.0001
Normal	46.3	27.5	42.7	53.6	54.6	<0.0001
Obese	28.0	44.1	36.3	25.4	12.1	<0.0001
Morbidly obese	5.1	18.4	4.4	2.1	1.1	<0.0001
Starting oxygen saturation (SD), %	97.3 (7.2)	96.7 (7.0)	97.4 (7.3)	97.4 (7.0)	97.3 (7.5)	<0.0001
Pre-intubation hypotension (SBP < 100), %	16.3	17.5	16.3	16.5	15.5	0.1014
Indication, %						
Medical	80.2	84.1	82.7	79.0	76.2	<0.0001
Traumatic	19.6	15.8	17.2	20.5	23.6	<0.0001
Initial impression of difficult airway, %	30.6	45.3	31.0	28.1	24.3	<0.0001
Reduced neck mobility, %	25.9	23.2	24.4	27.0	28.3	<0.0001
Median Mallampati score (IQR)	2 (1–3)	3 (2–3)	2 (1–3)	2 (1–3)	2 (1–3)	<0.0001
Reduced mouth opening, %	15.0	17.8	15.0	15.0	13.5	0.0008
Airway obstruction, %	3.0	3.4	2.9	3.0	2.9	0.5106
Facial trauma, %	9.7	6.9	8.4	10.1	12.2	<0.0001
Blood or vomit in airway, %	22.7	21.7	22.3	24.1	22.4	0.3954
Any difficult airway characteristic, ^a %	60.0	61.8	58.8	60.5	59.9	0.7362
Device, %						
Direct laryngoscope	45.7	42.1	48.7	45.9	44.0	0.6747
Video laryngoscope	53.4	56.7	50.8	53.0	54.9	0.5469
Other	0.4	0.8	0.3	0.5	0.3	0.1550
Sedation agent, %						
Etomidate	78.9	79.3	80.4	77.6	78.3	0.1094
Ketamine	13.9	11.2	12.9	15.3	15.2	0.0002
Propofol	2.4	3.2	2.7	2.2	2.0	0.0146
Midazolam	0.8	1.1	0.7	0.8	0.7	0.2147
None	4.0	5.3	3.2	4.1	3.9	0.3949
Intubator characteristics, %						
Emergency medicine PGY1	2.4	3.1	2.3	2.0	2.3	0.1427
Emergency medicine PGY2	12.0	12.6	12.0	13.1	10.8	0.1606
Emergency medicine PGY3	34.2	34.6	33.6	32.1	36.5	0.1925
Emergency medicine PGY4	39.2	36.7	39.7	39.3	39.9	0.1567
Emergency medicine fellow	7.1	7.4	7.4	7.8	6.2	0.1467
Emergency medicine attending physician	1.1	1.2	1.1	1.4	1.0	0.6647
Other (non-emergency medicine)	3.9	4.4	3.8	4.0	3.5	0.2718

^aDifficult airway characteristics include reduced neck mobility, Mallampati score > 1, reduced mouth opening, airway obstruction, facial trauma, and blood or vomit in airway

p values are for Cochran–Armitage trend test or Kruskal–Wallis test

Table 2 First-attempt outcomes for overall sample and stratified by pre-intubation SBP and device

Variable	Rocuronium, all doses (<i>n</i> = 8034)	< 1.0 mg/kg (<i>n</i> = 1255)	1.0–1.1 mg/kg (<i>n</i> = 2556)	1.2–1.3 mg/kg (<i>n</i> = 1919)	≥ 1.4 mg/kg (<i>n</i> = 2304)	<i>p</i>
Overall						
First-pass intubation success, %	89.7	88.4	88.1	89.7	92.2	< 0.0001
Any adverse event, %	14.0	15.7	15.2	13.4	12.3	0.0007
Peri-intubation desaturation, %	8.0	10.2	9.0	7.6	6.1	< 0.0001
Pre-intubation SBP < 100						
First-pass intubation success, %	89.8	88.6	86.1	89.9	94.9	0.0006
Any adverse event, %	20.7	17.7	23.1	21.2	19.4	0.9276
Peri-intubation desaturation, %	8.9	7.7	10.8	9.2	7.0	0.3937
Pre-intubation SBP ≥ 100						
First-pass intubation success, %	89.9	88.8	88.6	90.1	91.9	0.0004
Any adverse event, %	12.9	16.2	13.8	12.0	11.0	< 0.0001
Peri-intubation desaturation, %	8.2	11.4	9.1	7.6	6.1	< 0.0001
Direct laryngoscopy						
First-pass intubation success, %	87.6	83.0	85.6	88.2	92.0	< 0.0001
Any adverse event, %	13.1	15.5	13.6	12.6	11.5	0.0216
Peri-intubation desaturation, %	7.0	8.7	7.7	6.8	5.2	0.0020
Video laryngoscopy						
First-pass intubation success, %	91.6	92.3	90.5	91.3	92.4	0.3856
Any adverse event, %	14.8	15.9	16.8	13.9	13.0	0.0115
Peri-intubation desaturation, %	9.0	11.5	10.4	8.1	6.8	< 0.0001

p values are for Cochran–Armitage trend test

Fig. 2 First-attempt success among varying rocuronium dosing groups compared to 1.0–1.1 mg/kg. Error bars represent cluster-adjusted 95% confidence intervals. Comparisons are statistically significant if the confidence interval does not cross 1 (dotted line)

Fig. 3 First-attempt success among rocuronium doses. Error bars represent 95% confidence intervals

Fig. 4 First-attempt success among rocuronium doses, stratified by device. Error bars represent 95% confidence intervals

compared with lower dosing among rapid sequence intubations in the ED. An even higher effect estimate of first pass success was noted with direct laryngoscopy as there appeared to be a near-linear increase in intubation success with escalating doses of rocuronium ranging from 83% (< 1.0 mg/kg) to 92% (at or above 1.4 mg/kg). Intubations utilizing video laryngoscopy, however, had high rates of first

pass success (90–92%) across all doses of rocuronium. We believe this discrepancy is likely related to improved glottic exposure offered by VL compared with DL as several studies have shown that VL facilitates better glottic visualizations, reduced esophageal intubations, and higher rates of first pass success [11–16]. Presumably, patients who received a lower weight-based dose of rocuronium either had slower onset

or incomplete paralysis making direct laryngoscopy more challenging while having minimal impact on VL.

Our study additionally suggests that utilizing higher dose rocuronium in patients exhibiting pre-intubation hypotension is associated with improved intubation success. As previously reported, pre-intubation hemodynamic instability is associated with worse outcomes [17]. As decreases in cardiac output affect rocuronium pharmacokinetics, hypotensive patients likely have reduced drug delivery and delayed onset or incomplete neuromuscular blockade at the time laryngoscopy is attempted [18]. Our observation of higher rates of first attempt success associated with higher doses of rocuronium may reflect a counterbalancing of reduced drug delivery with administration of more drug.

Based on our observation that heavier and obese body habitus patients were more likely to received lower weight-based doses of rocuronium suggests that EM providers are either bound by institutional limits for maximum rocuronium administration or providers are reflexively giving a standard dose (i.e., 100 mg of rocuronium) irrespective of the patient's actual body weight. In our dataset, the mean weight of patients in the < 1.0 mg/kg group was 103.8 kg compared to 67.3 kg in the ≥ 1.4 mg/kg group; both equate to approximately 100 mg of rocuronium administered. This is likely a consequence of it being an easy number to remember and also happens to be the standard size of the vials [19]. While standard doses offer simplicity, this study highlights the importance of accurate weight-based dosing to avoid the undesirable combination of a morbidly obese difficult airway who is inadvertently underdosed and therefore only partially relaxed during laryngoscopy. This benefit should be appropriately weighed against the risk of making errors while attempting bedside calculations during high-acuity and stressful situations.

Comparison to previous studies

In emergency medicine, the standard rapid sequence intubation dose for rocuronium is 1.0–1.2 mg/kg [20, 21]. In contrast, in the operating room a dosing range of 0.45–0.9 mg/kg is advocated [22]. This practice variation likely reflects differences in the setting and goals of airway management as higher doses may result in faster onset at the expense of prolonged paralysis [23, 24]. Anesthesia providers more often intubate in a controlled setting and prefer a shorter duration of neuromuscular blockade to facilitate operating room turnover, whereas emergency medicine providers prioritize efficient and optimal intubating conditions with less concern about titrating to a short anesthetic time.

The majority of rocuronium dosing research to date comes from the anesthesia literature and is the basis for the manufacturer's package insert guidance that for rapid sequence intubation, "0.6 to 1.2 mg/kg will provide

excellent or good intubating conditions in most patients in less than 2 min". TEVA pharmaceutical cites 11 studies where the doses ranged 0.6–0.85 mg/kg and only two studies that evaluated larger dose rocuronium ranging from 0.9–1.2 mg/kg [19]. This was acknowledged as a limitation for comparisons to succinylcholine intubations in a recent Cochrane review [3].

Despite limited investigations into higher doses of rocuronium typically used during emergency airway management, several studies point to improved outcomes with increasing doses. One double-blind comparison of elective surgical cases found that 0.9 mg/kg of rocuronium or 1.5 mg/kg succinylcholine provided similar intubating conditions at 1 min and found that these doses were superior to 0.7 mg/kg of rocuronium [6]. Similarly, a study examining the effectiveness of neuromuscular blockade at varying rocuronium dosing found that 100% blockade occurred at 1.0 min for 0.9 mg/kg and 1.2 mg/kg but 1.3 min for 0.6 mg/kg [23]. An earlier randomized trial of operating room patients given varying doses of rocuronium ranging from 0.4 mg/kg to 2.0 mg/kg found that large doses of rocuronium (2.0 mg/kg) were necessary to obtain a greater than 90% probability of achieving ideal conditions for rapid sequence intubation [5]. They acknowledged this higher dose may be more appropriate for traumatic indications as the prolonged paralysis would not be ideal for typical elective surgery cases.

More recently, April et al. compared patient outcomes with succinylcholine versus rocuronium but only dichotomized rocuronium doses to ≥ 1.2 or < 1.2 mg/kg. They reported a better first attempt intubation success with higher rocuronium dosing among patients without difficult airway characteristics [2]. Our study expanded upon that analysis as we observed an association of overall higher first-attempt success with rocuronium doses of 1.4 mg/kg or more compared with lower dosing strategies. As repeated attempts of endotracheal intubation are associated with increased adverse events, we offer modest evidence to support utilizing larger doses of rocuronium for ED rapid sequence intubation [25].

Strengths and limitations

While our study is strengthened by inclusion of over eight thousand ED intubations from a multicenter dataset, it also comes with several limitations. Our self-reported data collection is susceptible to recall bias. As an attempt to reduce this, we required participating centers to maintain > 90% compliance with reporting and to complete the research surveys as soon as possible.

This analysis comprised an analysis of observational data. Consequently, we cannot determine causation between varying dosing groups and outcomes. In our data collection and subsequently in our multivariate regression analysis, we

attempted to capture and include as many of these potentially confounding variables to account for their influence on outcomes. However, we cannot control for unmeasured confounders. Related to this and as stated previously, in the lower dosing group patients were more obese and more likely to have the initial impression of a difficult airway and generally these patients are inherently higher risk for poorer outcomes. While these variables were included into our multi-variate analysis, additional unmeasured characteristics of these patients could potentially contribute to the observed differences in first-attempt intubation success.

Improved first attempt success is best thought of as a process outcome. While there is an association between first-pass success and decreased in peri-intubation adverse events we did not observe an increase in adverse events across our dosing groups [17, 26]. This may reflect underreporting. In addition, we are unable to make a causal statement about increased rocuronium dosing and patient morbidity or mortality.

While our study assesses the association between rocuronium dose and first pass success, our primary outcome may be impacted by unmeasured confounders such as time to laryngoscopy following drug administration. While not recorded in our registry, we have no reason to believe differences in time to first laryngoscopy would be unevenly distributed across dosing regimens. In fact, higher dosing may precipitate more rapid onset of neuromuscular blockade and provide better intubating conditions for “early lookers”. Nevertheless, this and other provider level variations remain potential confounders.

Another potential limitation of our study is that our dosing thresholds were largely determined based upon sample size convenience and historical norms. While several of the group’s cutoffs follow typical dosing regimens (i.e., < 1.0 and > 1.0 mg/kg), other cutoffs are more arbitrary. Should different cutoffs been selected, it is possible different associations could have been observed although it is very likely ≥ 1.4 mg/kg would still have shown a larger effect estimate for first pass success.

Clinical and research implications

For practitioners, our observations highlight the importance of calculating accurate weight-based rapid sequence intubation dosing patients with greater BMIs. For researchers, our observations offer guidance for further prospective study on the possible benefit of higher dose rocuronium for rapid sequence intubation with direct laryngoscopy and in patients with hypotension or shock.

Conclusions

In this large observational series, we observed an association of higher first attempt success with rocuronium dosed ≥ 1.4 mg/kg and higher among all ED intubations, particularly when direct laryngoscopy was used and among patients with pre-intubation hypotension, without an increase in adverse events.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s43678-021-00119-6>.

Author contributions NL, MF, and CB conceived of the study. MF, MA, and CB supervised the study. AA provided statistical advice and analyzed the data. NL drafted the article, and all authors contributed substantially to its revision. RW is a senior NEAR investigator, founded the registry and contributed to manuscript development.

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Declarations

Conflict of interest None of the authors have significant conflicts of interest to disclose.

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