ORIGINAL CLINICAL RESEARCH REPORT

First-Attempt Success Between Anatomically and Physiologically Difficult Airways in the National Emergency Airway Registry

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BACKGROUND: In the emergency department (ED), certain anatomical and physiological airway characteristics may predispose patients to tracheal intubation complications and poor outcomes. We hypothesized that both anatomically difficult airways (ADAs) and physiologically difficult airways (PDAs) would have lower first-attempt success than airways with neither in a cohort of ED intubations.

METHODS: We performed a retrospective, observational study using the National Emergency Airway Registry (NEAR) to examine the association between anticipated difficult airways (ADA, PDA, and combined ADA and PDA) vs those without difficult airway findings (neither ADA nor PDA) with first-attempt success. We included adult (age ≥14 years) ED intubations performed with sedation and paralysis from January 1, 2016 to December 31, 2018 using either direct or video laryngoscopy. We excluded patients in cardiac arrest. The primary outcome was first-attempt success, while secondary outcomes included first-attempt success without adverse events, peri-intubation cardiac arrest, and the total number of airway attempts. Mixed-effects models were used to obtain adjusted estimates and confidence intervals (CIs) for each outcome. Fixed effects included the presence of a difficult airway type (independent variable) and covariates including laryngoscopy device type, intubator postgraduate year, trauma indication, and patient age as well as the site as a random effect. Multiplicative interaction between ADAs and PDAs was assessed using the likelihood ratio (LR) test.

RESULTS: Of the 19,071 subjects intubated during the study period, 13,938 were included in the study. Compared to those without difficult airway findings (neither ADA nor PDA), the adjusted odds ratios (aORs) for first-attempt success were 0.53 (95% CI, 0.40–0.68) for ADAs alone, 0.96 (0.68–1.36) for PDAs alone, and 0.44 (0.34–0.56) for both. The aORs for first-attempt success without adverse events were 0.72 (95% CI, 0.59–0.89) for ADAs alone, 0.79 (0.62–1.01) for PDAs alone, and 0.44 (0.37–0.54) for both. There was no evidence that the interaction between ADAs and PDAs for first-attempt success with or without adverse events was different from additive (ie, not synergistic/multiplicative or antagonistic).

CONCLUSIONS: Compared to no difficult airway characteristics, ADAs were inversely associated with first-attempt success, while PDAs were not. Both ADAs and PDAs, as well as their interaction, were inversely associated with first-attempt success without adverse events. (Anesth Analg 2024;138:1249–59)

KEY POINTS

- **Question:** Are both anatomically and physiologically difficult airways associated with first-attempt success during emergent tracheal intubation in the emergency department?
- **Findings:** Patients with anatomically difficult airways had lower first-attempt success, while those with physiologically difficult airways did not; however, patients meeting the definition of either or both difficult airway types had lower first-attempt success without adverse events.
- **Meaning:** Anatomically and physiologically difficult airways were associated with worse tracheal intubation outcomes in the emergency department.

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Clinicians encounter multiple challenges during emergency airway management.[1] In addition to equipment-, environment-, and team-based factors, certain patient characteristics are associated with challenging airway management and are used to define the "difficult airway."[2] Difficult airway characteristics may impact 1 or more components of emergency airway management, including oxygenation and ventilation, laryngoscopy, and tracheal intubation.[1,2] These characteristics are traditionally anatomical, such as a high Mallampati class (eg, class 4), reduced mouth opening, and reduced thyromental distance.[1,3] However, while anatomical characteristics signify the risk of airway management complications,[4] preintubation physiological characteristics such as hypotension and hypoxemia are also associated with airway management complications in acute care settings.[5–7]

The association between physiological characteristics and poor intubation outcomes highlights a particular challenge in emergency airway management, the "physiologically difficult airway" (PDA).[2,8,9] While prior work has associated physiological characteristics such as preintubation hypotension and hypoxemia with severe peri-intubation complications such as cardiac arrest,[5,6,10–12] little work has been performed on the relationship and interaction between anatomical and physiological factors on intubation complications in the emergency department (ED).[7] A retrospective, single-site study of 1513 ED intubations by Pacheco et al[7] estimated that first-attempt success without adverse events decreased by 10.3% with anatomically difficult airways (ADAs), 10.7% with PDAs, and 21.4% with combined ADAs and PDAs compared to patients without any difficult airway characteristics.

However, aside from being single-site, the Pacheco et al[7] study had some limitations. First, the study was limited by its single composite outcome in the adjusted analysis – first-attempt success without adverse events.[7] While this outcome addresses both the success and safety of intubation, it is unclear how ADAs and PDAs contribute to the components of this outcome. For example, although in theory, PDAs might increase adverse effects without reducing first-attempt success alone, physiological characteristics like the inability to adequately preoxygenate could compromise first-attempt success. This compromise may result from reducing safe-apnea time thereby impairing glottic visualization, which may be a mechanism for reducing first-attempt success.[13,14] Therefore, in this example, it is unclear if PDAs had lower first-attempt success without adverse events by contributing to adverse events or reduced first-attempt success.[7] Furthermore, obesity was evaluated solely as an ADA characteristic despite evidence that it reduces safe-apnea time (physiological mechanism)[13,15] in addition to increasing difficult laryngoscopy (anatomical mechanism).[16]

Our objective, determined a priori, was to examine the difference in first-attempt success between anticipated difficult airways (ADAs alone, PDAs alone, and combined ADAs and PDAs) and those without difficult airway characteristics (neither ADAs nor PDAs) using a multicenter registry of ED intubations. We hypothesized that both difficult airway types would be inversely associated with first-attempt success.

METHODS

Study Design and Setting

We retrospectively analyzed the National Emergency Airway Registry (NEAR). The most current iteration of NEAR contains intubation data from 25 academic and community EDs and has been described previously.[17] Before participating, ethical approval was obtained from each site's respective institutional review boards and the requirement for written informed consent was waived.

Data Collection

Clinicians submitted intubation data using online forms (StudyTRAX; version 3.47.0011; ScienceTRAX). Study personnel excluded data from sites that submitted completed forms for <90% of intubations performed. Data included intubations performed between January 1, 2016 and December 31, 2018.

Study Population

We included subjects ≥14 years of age undergoing orotracheal intubation with rapid sequence intubation (ie, with both sedation and paralysis) with direct or video laryngoscopy. We excluded cases in cardiac arrest at the time of the first intubation attempt, which would confound the evaluation of peri-intubation cardiac arrest as a secondary outcome. First-attempt intubations using intubating laryngeal mask airways, bronchoscopes, digital intubation, and nonorotracheal routes (ie, nasal and surgical airways) were excluded, since these are infrequently performed in the ED and often indicative of atypical circumstances, such as the use of the nasal route for bronchoscopy-assisted intubation.[18,19] Pediatric cases were excluded, since blood pressure is age-specific, and preintubation systolic blood pressure was collected categorically in the registry with adult-specific cutoffs (Supplemental Digital Content, Supplemental Table 1, http://links.lww.com/AA/E699).

Variables

We collected patient characteristics, intubator characteristics, intubator assessments/findings, and intubation management variables. Patient characteristics included patient age, body habitus, and sex. Clinician characteristics included postgraduate training level. Intubator assessments/ findings included intubation indications (eg, trauma, shock), difficult airway tests (ie, Mallampati class, mouth opening, thyromental distance), difficult airway findings (ie, reduced neck mobility, blood in the airway, airway obstruction, angioedema), facial trauma, neck trauma, preintubation hypoxemia, preintubation hypotension, and intubator impression of difficulty. Intubation management variables included apneic oxygenation, bougie use on the first attempt, external laryngeal manipulation (ie, BURP – backward, upward, rightward, and posterior pressure), preoxygenation time, paralytic medication, induction medication, vasopressor use on the first attempt, preoxygenation device, and laryngoscopy device, direct (DL) or video (VL) laryngoscopy. Additional details on variable coding are presented in the supplement (Supplemental Digital Content, Supplemental Table 1, http://links.lww.com/AA/E699).

We defined difficult airway type, the independent variable, using mechanistic theory. Variables defining ADAs and PDAs were considered if available in NEAR, may contribute to difficult intubation or poor intubation outcomes, and apparent before induction (Table 1). For example, airway obstruction may obscure laryngeal views; therefore, airway obstruction may make intubation anatomically difficult. However, preintubation hypoxemia may increase the risk of postinduction hypoxemia limiting safe-apnea time; therefore, preintubation hypoxemia may make the intubation physiologically difficult. Therefore, we reported difficult airway types as those with no difficult airway findings, ADAs alone, PDAs alone, or findings of both ADAs and PDAs. Additional details on the coding of variables used for the difficult airway definitions are presented in the supplement (Supplemental Digital Content, Supplemental Table 1, http://links.lww.com/AA/E699).

Since obesity may mechanistically impair laryngeal views and safe-apnea time,[13,15,16] we classified all obese patients as combined ADA and PDA. To support this decision, we performed a mediation analysis. A mediation analysis explores the indirect effect of a mediator between the independent variable of interest and the dependent variable, within the causal pathway.[20,21] In contrast, confounders affect the independent and dependent variables from outside the causal pathway.[21] Therefore, we performed a mediation analysis to inspect whether the effect of obesity/ morbid obesity on first-attempt success might be mediated via poor glottic view (anatomic mediator) and/or postinduction hypoxemia (physiological mediator), which supported our decision to use obesity/ morbid obesity as both an ADA and PDA characteristic (Table 1). Additional details on the mediation analysis are presented in the supplement.

Outcomes

Since first-attempt success is a commonly selected end point for ED intubation studies and repeat attempts are associated with severe complications including peri-intubation cardiac arrest,[22–26] we chose first-attempt success *a priori* as the primary outcome. We considered first-attempt success without adverse events as a primary outcome; however, postinduction hypoxemia and hypotension may have been due to persistent preintubation hypoxemia and hypotension rather than a consequence of the intubation. This concern was due to the absolute definitions of these adverse effect variables in the registry where an Spo_2 of <90% and a systolic blood pressure <100 mm Hg after induction qualified as postinduction hypoxemia and hypotension (Supplemental Digital Content, Supplemental Table 1, http://links.lww.com/AA/E699). Due to this potential bias, we chose first-attempt success as the primary outcome rather than first-attempt success without adverse effects.

Secondary outcomes included first-attempt success without adverse events (adverse events included peri-intubation vomiting, esophageal intubation, bradydysrhythmia, cardiac arrest, oxygen saturation <90% or drop of 10%, systolic blood pressure <100 mm Hg, and tachydysrhythmia), poor glottic view (ie, Cormack-Lehane grads 3 or 4), peri-intubation cardiac arrest (not limited to during the first attempt), a rescue surgical airway attempt (not limited to during the first attempt), the total number of airway attempts, and first-attempt peri-intubation adverse events (listed above) at the first attempt. Peri-intubation was

Table 1. Difficult Airway Definitions

Anatomically difficult airway	Physiologically difficult airway
At least one of the following:	At least one of the following:
• Indication of airway obstruction or angioedema	• Preinduction hypoxemia <90% oxygen saturation
• Reduced neck mobility	• Preinduction hypotension <100 mm Hg systolic blood pressure
• Mallampati >2	• Peri-intubation vasopressor medication administration at the first attempt
• Mouth opening <3 fingers	• Shock indication for intubation
• Thyromental distance <3 fingers	• Obese or morbidly obese
• Facial or neck trauma	
• Blood in the airway	
• Obese or morbidly obese	

defined as occurring during or immediately after a tracheal intubation attempt. The supplement presents additional details on the coding of outcomes (Supplemental Digital Content, Supplemental Table 1, http://links.lww.com/AA/E699).

Statistical Analysis

We reported our findings in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology recommendations.[27] We measured variables and unadjusted outcomes between difficult airway types with descriptive statistics. Adjusted estimates for primary and select secondary outcomes were estimated using multiple variable mixed-effects regression models (logistic and Poisson). We use mixed-effects models to account for clustering at the site level by modeling site as a random effect. Fixed effects included the presence of a difficult airway type (independent variable) and covariates including laryngoscopy device type, intubator postgraduate year, trauma indication, and patient age. Sensitivity analyses examined first-attempt success with the same model but with the following alterations: after multiple imputation of the study dataset (Supplemental Digital Content, Supplemental Table 2, http://links.lww.com/AA/E699), after excluding laryngoscopy device type from the model and selecting only direct or video laryngoscopy cases, and after including interaction terms between difficult airway type and laryngoscopy device type. Nonparametric bootstrapping methods were used to calculate adjusted estimates and confidence intervals (CIs), since they do not assume normality of the data.[28,29] Additional modeling details are presented in the supplement.

Lastly, we performed an interaction analysis to examine the potential interaction between ADAs and PDAs with first-attempt success and first-attempt success without adverse events. We tested for the interaction on both multiplicative and additive scales using regression-based methods including the likelihood ratio test. Additional details on the interaction models and analyses are presented in the supplement. We performed the analysis using R (Version 4.2.1 2022-06-23, R Foundation for Statistical Computing, Vienna, Austria) with packages reported in the supplement (Supplemental Digital Content, Supplemental Figure 1, http://links.lww.com/AA/E699).

Sample Size

No prior work has examined the difference in first-attempt success between ADAs, PDAs, and combined ADAs and PDAs compared to those with neither ADAs nor PDAs. However, since obesity is common in NEAR, associated with reduced first-attempt success, and a component of our ADA and PDA definitions (Table 1),[30,31] we used first-attempt success between lean and overweight patients to perform a sample size calculation.[31] In a study of 6889 patients from the Japanese Emergency Airway Network, first-attempt success was 70.9% in lean patients vs 66.4% in overweight patients.[31] Although small, we felt this difference in first-attempt success would be clinically significant given the association between multiple attempts and poor intubation outcomes.[24–26] Therefore, to achieve 80% power at a significance level of 0.05, this study would need 1667 patients per group to detect a similar difference.

RESULTS

Participants

Of the 19,071 subjects intubated during the study period, 13,938 were included in the study cohort after exclusions (Figure 1).

Descriptive Data

Subjects were classified by difficult airway type, and 1867 had neither ADAs nor PDAs, 3664 had ADAs alone, 1304 had PDAs alone, and 7103 had findings of both ADAs and PDAs (Figure 1). The median patient age in years and interquartile ranges for each difficult airway group were 50.00 [32.00–64.00], 48.00 [30.00–63.00], 56.90 [40.00–70.00], and 55.00 [39.00–67.00], respectively (Table 2). Most subjects were intubated by resident physicians in their third postgraduate training year (Table 3).

Mediation Analysis

The effect of obesity/ morbid obesity on first-attempt success was partially mediated via postinduction hypoxemia with an indirect effect of adjusted odds ratio (aOR) 0.992 (95% CI, 0.985–0.998) and a remaining direct effect of aOR 0.986 (95% CI, 0.981–0.999) (Supplemental Digital Content, Supplemental Figure 2, http://links.lww.com/AA/E699). The effect of obesity/ morbid obesity on first-attempt success was partially mediated via poor glottic view with an indirect effect of aOR 0.990 (95% CI, 0.983–0.996) and a remaining direct effect of aOR 0.984 (95% CI, 0.980–0.998) (Supplemental Digital Content, Supplemental Figure 3, http://links.lww.com/AA/E699). Model outputs used for the mediation analysis are presented in the supplement (Supplemental Digital Content, Supplemental Table 3, http://links.lww.com/AA/E699). Therefore, obesity/ morbid obesity was included as a characteristic for both ADAs and PDAs.

Unadjusted Outcome Data

First-attempt success occurred in 1750 of 1867 (93.7%) with neither ADAs nor PDAs, 3268 of 3664 (89.2%) with ADAs, 1212 of 1304 (92.9%) with PDAs, and 6209 of 7103 (87.4%) with both ADAs and PDAs.

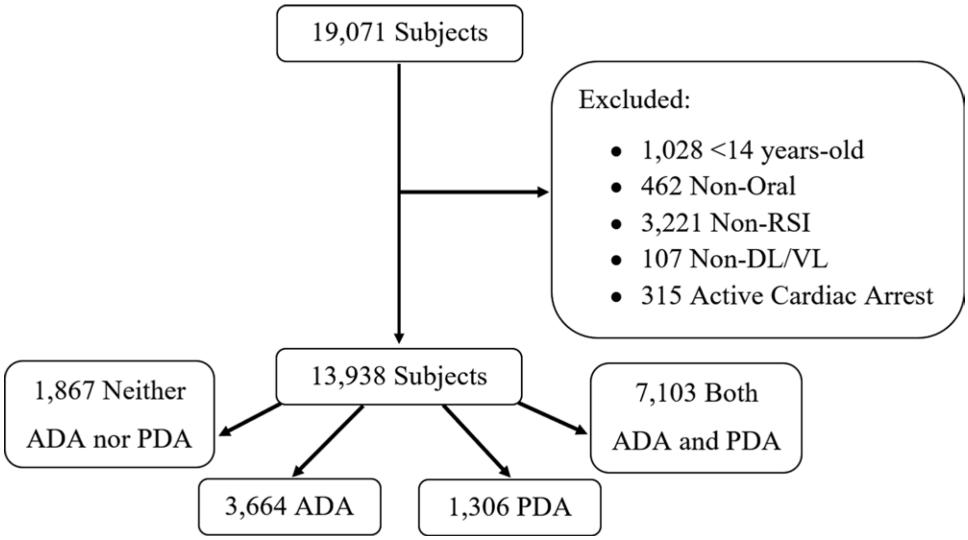

Figure 1. Study flow diagram displaying included and excluded subjects. ADA indicates anatomically difficult airways; DL, direct laryngoscopy; PDA, physiologically difficult airways; RSI, rapid sequence intubation; VL, video laryngoscopy.

Peri-intubation cardiac arrest on any attempt occurred in 7 of 1867 (0.4%) with neither ADAs nor PDAs, 13 of 3664 (0.4%) with ADAs, 19 of 1304 (1.5%) with PDAs, and 107 of 7103 (1.5%) with both ADAs and PDAs (Table 4).

Adjusted And Sensitivity Analyses

Compared to those without difficult airway findings (neither ADAs nor PDAs), the aORs for first-attempt success were 0.53 (95% CI, 0.40–0.68) for ADAs, 0.96 (0.68–1.36) for PDAs, and 0.44 (0.34–0.56) for both (Figure 2, Supplemental Digital Content, Supplemental Table 4, http://links.lww.com/AA/E699), where an aOR of less than 1 indicates a decreased odds of first-attempt success. Comparable results were obtained for first-attempt success despite adding interaction terms between the difficult airway type and laryngoscopy device (ie, DL or VL). These results remained similar and robust after multiple imputation of missing values and performing the analysis in parallel with only DL and VL cases (Supplemental Digital Content, Supplemental Figure 4, Supplemental Table 4, http://links.lww.com/AA/E699).

With the neither ADA nor PDA group as the reference, the aORs for first-attempt success without adverse events were 0.72 (95% CI, 0.59–0.89) for ADAs alone, 0.79 (0.62–1.01) for PDAs alone, and 0.44 (0.37–0.54) for both (Figure 2, Supplemental Digital Content, Supplemental Table 4, http://links.lww.com/AA/E699). The adjusted estimates for total attempts compared to the reference group were 0.06 (95% CI, 0.04–0.08) for ADAs alone, 0.01 (−0.02 to 0.03) for PDAs alone, and 0.08 (0.06–0.10) for both (Figure 2, Supplemental Table 4, http://links.lww.com/AA/E699). Lastly, compared to the neither ADA nor PDA group, aORs for peri-intubation cardiac arrest on any attempt were 1.35 (95% CI, 0.30–23.70) for ADAs alone, 7.71 (2.39–130.94) for PDAs alone, and 8.75 (3.66–152.72) for both (Figure 2, Supplemental Table 4, http://links.lww.com/AA/E699).

Interaction Analysis

In the full interaction model (with ADA-by-PDA interaction term) for first-attempt success, the aORs were 0.58 (95% CI, 0.46–0.72) for ADA versus no ADA, 1.00 (0.76–1.38) for PDA versus no PDA, and 0.84 (0.60–1.14) for the ADA and PDA interaction, indicating no multiplicative interaction, likelihood ratio test P = .275 (Supplemental Digital Content, Supplemental Tables 5 and 6, http://links.lww.com/AA/E699). In the full interaction model for first-attempt success without adverse events, the aORs were 0.78 (0.66–0.92) for ADA versus no ADA, 0.84 (0.68–1.02) for PDA versus no PDA, and 0.72 (0.58–0.91) for the ADA and PDA interaction, indicating a less than multiplicative interaction, likelihood ratio test P = .005 (Supplemental Digital Content, Supplemental Tables 5 and 6, http://links.lww.com/AA/E699). In summary, there was no evidence that the interaction for either analysis (ie, with or without adverse events) was different from additive, since the confidence intervals for 2 measures of additivity both included zero (Supplemental Digital Content, Supplemental Table 6, http://links.lww.com/AA/E699).

DISCUSSION

We found ADAs were adversely associated with first-attempt success and total number of airway attempts, while PDAs were not (Figure 2, Supplemental Digital Content, Supplemental Table 4, http://links.lww.com/AA/E699). In contrast, PDAs were associated with peri-intubation cardiac arrest, while ADAs

Table 2. Patient Characteristics and Intubator Assessments

	Difficult airway group			
Variable	**Neither**	**ADA**	**PDA**	**Both**
n	1867	3664	1304	7103
Patient age in years, median [IQR]	50.00 [32.00–64.00]	48.00 [30.00–63.00]	56.90 [40.00–70.00]	55.00 [39.00–67.00]
Patient body habitus, n (%)				
Very thin	82 (4.4)	177 (4.8)	92 (7.1)	171 (2.4)
Thin	395 (21.2)	769 (21.0)	328 (25.2)	643 (9.1)
Normal	1377 (73.8)	2704 (73.8)	876 (67.2)	1864 (26.2)
Obese	0 (0.0)	0 (0.0)	0 (0.0)	3706 (52.2)
Morbidly obese (BMI >40)	0 (0.0)	0 (0.0)	0 (0.0)	714 (10.1)
Missing	13 (0.7)	14 (0.4)	8 (0.6)	5 (0.1)
Female patient, n (%)				
Yes	658 (35.2)	1052 (28.7)	474 (36.3)	2583 (36.4)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.0)
Trauma indication for intubation, n (%)	132 (7.1)	1290 (35.2)	116 (8.9)	1836 (25.8)
Face trauma, n (%)				
Yes	0 (0.0)	565 (43.8)	0 (0.0)	774 (42.2)
Missing	3 (2.3)	3 (0.2)	3 (2.6)	1 (0.1)
Neck trauma, n (%)	0 (0.0)	46 (3.6)	0 (0.0)	66 (3.6)
Shock indication for intubation, n (%)	0 (0.0)	0 (0.0)	235 (19.8)	656 (12.5)
Bloody airway, n (%)				
Yes	0 (0.0)	1167 (31.9)	0 (0.0)	2007 (28.3)
Missing	51 (2.7)	12 (0.3)	9 (0.7)	24 (0.3)
Airway obstruction, n (%)				
Yes	0 (0.0)	156 (6.6)	0 (0.0)	307 (5.8)
Missing	20 (1.2)	3 (0.1)	3 (0.3)	12 (0.2)
Angioedema, n (%)	0 (0.0)	20 (0.8)	0 (0.0)	22 (0.4)
Mallampati, n (%)				
Class 1	247 (13.2)	490 (13.4)	171 (13.1)	571 (8.0)
Class 2	196 (10.5)	520 (14.2)	160 (12.3)	872 (12.3)
Class 3	0 (0.0)	362 (9.9)	0 (0.0)	902 (12.7)
Class 4	0 (0.0)	126 (3.4)	0 (0.0)	440 (6.2)
Not assessed	1390 (74.5)	2156 (58.8)	966 (74.1)	4287 (60.4)
Missing	34 (1.8)	10 (0.3)	7 (0.5)	31 (0.4)
Mouth opening, n (%)				
Normal—3+ finger lengths	656 (35.1)	1592 (43.4)	449 (34.4)	2530 (35.6)
Reduced—1–2 finger lengths	0 (0.0)	660 (18.0)	0 (0.0)	1416 (19.9)
Not assessed	1183 (63.4)	1400 (38.2)	848 (65.0)	3129 (44.1)
Missing	28 (1.5)	12 (0.3)	7 (0.5)	28 (0.4)
Reduced neck mobility, n (%)				
Yes	0 (0.0)	1644 (44.9)	0 (0.0)	2336 (32.9)
Missing	43 (2.3)	9 (0.2)	6 (0.5)	19 (0.3)
Intubator impression of difficult, n (%)				
Yes	108 (5.8)	976 (26.6)	104 (8.0)	3171 (44.6)
Missing	54 (2.9)	20 (0.5)	9 (0.7)	40 (0.6)
Thyromental distance, n (%)				
1 finger	9 (0.5)	37 (1.0)	10 (0.8)	137 (1.9)
2 fingers	286 (15.3)	448 (12.2)	194 (14.9)	1236 (17.4)
3 fingers	0 (0.0)	1319 (36.0)	0 (0.0)	1708 (24.0)
4 + fingers	0 (0.0)	144 (3.9)	0 (0.0)	180 (2.5)
Not assessed	1535 (82.2)	1705 (46.5)	1091 (83.7)	3810 (53.6)
Missing	37 (2.0)	11 (0.3)	9 (0.7)	32 (0.5)
Top Indications, n (%)				
Nonoverdose mental status change	530 (28.4)	660 (18.0)	275 (21.1)	1397 (19.7)
Overdose	414 (22.2)	523 (14.3)	166 (12.7)	710 (10.0)
Seizure	201 (10.8)	277 (7.6)	99 (7.6)	380 (5.3)
Head injury with hemorrhage	16 (0.9)	392 (10.7)	12 (0.9)	476 (6.7)
Polytrauma	20 (1.1)	269 (7.3)	17 (1.3)	482 (6.8)
Other	686 (36.7)	1543 (42.1)	735 (56.4)	3658 (51.5)
Preinduction hypoxemia, n (%)				
Yes (<90% Spo_2)	0 (0.0)	0 (0.0)	155 (11.9)	522 (7.3)
Missing	201 (10.8)	216 (5.9)	158 (12.1)	595 (8.4)
Preinduction blood pressure, n (%)				
Hypertensive (SBP >140 mm Hg)	733 (39.3)	1358 (37.1)	311 (23.8)	2472 (34.8)
Normal (SBP 100–139 mm Hg)	1109 (59.4)	2290 (62.5)	465 (35.7)	2910 (41.0)
Hypotensive (<100 mm Hg) —no TX	0 (0.0)	0 (0.0)	110 (8.4)	313 (4.4)
Hypotensive (<100 mm Hg) —IVF	0 (0.0)	0 (0.0)	232 (17.8)	862 (12.1)
Hypotensive (<100 mm Hg) —pressor	0 (0.0)	0 (0.0)	179 (13.7)	517 (7.3)
Missing	25 (1.3)	16 (0.4)	7 (0.5)	29 (0.4)

Abbreviations: ADA, anatomically difficult airway; BMI, body mass index; IQR, interquartile range; IVF, intravenous fluids; PDA, physiologically difficult airway; Pressor, vasopressor medication; SBP, systolic blood pressure; TX, treatment.

Table 3. Intubator Characteristics and Intubation Management

	Difficult airway group			
Variable	**Neither**	**ADA**	**PDA**	**Both**
n	1867	3664	1304	7103
Intubator training level, n (%)				
PGY-1	224 (12.0)	422 (11.5)	135 (10.4)	861 (12.1)
PGY-2	499 (26.7)	1095 (29.9)	436 (33.4)	2375 (33.4)
PGY-3	872 (46.7)	1511 (41.2)	514 (39.4)	2688 (37.8)
PGY-4	139 (7.4)	304 (8.3)	120 (9.2)	590 (8.3)
PGY≥5 or fellow	54 (2.9)	131 (3.6)	35 (2.7)	194 (2.7)
Attending	53 (2.8)	113 (3.1)	35 (2.7)	232 (3.3)
Missing	26 (1.4)	88 (2.4)	29 (2.2)	163 (2.3)
Preoxygenation time, n (%)				
Less than 1 min	36 (2.4)	65 (2.2)	8 (0.7)	72 (1.2)
1–3 min	289 (19.5)	655 (21.8)	67 (5.7)	595 (9.6)
Greater than 3 min	1158 (78.1)	2281 (76.0)	272 (23.0)	2426 (39.0)
Immediate intubation—no preoxygenation	0 (0.0)	0 (0.0)	834 (70.6)	3129 (50.3)
Peri-intubation pressor (first attempt), n (%)				
Epinephrine	0 (0.0)	0 (0.0)	15 (1.2)	44 (0.6)
Norepinephrine	0 (0.0)	0 (0.0)	18 (1.4)	70 (1.0)
Phenylephrine	0 (0.0)	0 (0.0)	19 (1.5)	79 (1.1)
Multiple	0 (0.0)	0 (0.0)	4 (0.3)	11 (0.2)
Apneic oxygenation, n (%)				
Yes	973 (52.1)	2085 (56.9)	218 (16.7)	2095 (29.5)
Missing	382 (20.5)	664 (18.1)	952 (73.0)	4005 (56.4)
Preoxygenation devices, n (%)				
Nonrebreather facemask	964 (51.6)	1909 (52.1)	222 (17.0)	1815 (25.6)
CPAP/BPAP	169 (9.1)	168 (4.6)	63 (4.8)	502 (7.1)
Bag valve mask	167 (8.9)	485 (13.2)	42 (3.2)	396 (5.6)
Nasal cannula	142 (7.6)	259 (7.1)	12 (0.9)	228 (3.2)
Missing	350 (18.7)	649 (17.7)	947 (72.6)	3987 (56.1)
Other	75 (4.0)	194 (5.3)	18 (1.4)	175 (2.5)
Video laryngoscopy, n (%)	1238 (66.3)	2635 (71.9)	801 (61.4)	5074 (71.4)
Bougie use on first attempt, n (%)				
Yes	458 (24.5)	726 (19.8)	203 (15.6)	1189 (16.7)
Missing	91 (4.9)	44 (1.2)	26 (2.0)	79 (1.1)
BURP maneuver, n (%)				
Yes	386 (20.7)	963 (26.3)	274 (21.0)	1863 (26.2)
Missing	130 (7.0)	65 (1.8)	39 (3.0)	124 (1.7)
Induction medication, n (%)				
Etomidate	1631 (87.4)	3179 (86.8)	1077 (82.6)	5885 (82.9)
Ketamine	152 (8.1)	334 (9.1)	188 (14.4)	1017 (14.3)
Midazolam	17 (0.9)	30 (0.8)	13 (1.0)	52 (0.7)
Propofol	67 (3.6)	121 (3.3)	26 (2.0)	149 (2.1)
Paralytic medication, n (%)				
Rocuronium	1034 (55.4)	1791 (48.9)	761 (58.4)	3807 (53.6)
Succinylcholine	826 (44.2)	1869 (51.0)	538 (41.3)	3279 (46.2)
Vecuronium	4 (0.2)	4 (0.1)	4 (0.3)	16 (0.2)
Missing	3 (0.2)	0 (0.0)	1 (0.1)	1 (0.0)

Abbreviations: ADA, anatomically difficult airway; BMI, body mass index; BPAP, bilevel positive airway pressure; BURP, backward, upward, rightward, and posterior pressure on the larynx; CPAP, continuous positive airway pressure; PDA, physiologically difficult airway; PGY, postgraduate year.

were not (Figure 2, Supplemental Digital Content, Supplemental Table 4). These results suggest that ADAs and PDAs appear to be associated with intubation sequelae via different mechanisms. Nevertheless, ADAs and PDAs, individually and combined, were adversely associated with first-attempt success without adverse events (Figure 2, Supplemental Digital Content, Supplemental Tables 4 and 5, http://links.lww.com/AA/E699). Furthermore, the combined ADA and PDA group had a lower aOR for first-attempt success without adverse events than either the ADA or PDA groups individually (Figure 2, Supplemental Digital Content, Supplemental Table 4, http://links.lww.com/AA/E699), and the interaction between ADAs and PDAs for first-attempt success without adverse events was found to be less than multiplicative and not different from additive (Supplemental Digital Content, Supplemental Tables 5 and 6, http://links.lww.com/AA/E699). This indicates that ADA and PDA characteristics are likely additive regarding their association with first-attempt success without adverse events, and so neither synergistic nor antagonistic.[32] Therefore, in the ED, the risk of difficult intubation and peri-intubation adverse events may be modified by the type of difficult airway (ADA versus PDA) and the combination of both types

Table 4. Outcomes and Adverse Events

	Difficult airway group			
Variable	**Neither**	**ADA**	**PDA**	**Both**
n	1867	3664	1304	7103
First-attempt success, n (%)				
Yes	1750 (93.7)	3268 (89.2)	1212 (92.9)	6209 (87.4)
Missing	2 (0.1)	9 (0.2)	1 (0.1)	7 (0.1)
First-attempt success without AE, n (%)[a]				
Yes	1628 (87.2)	3057 (83.4)	1093 (83.8)	5344 (75.2)
Missing	2 (0.1)	9 (0.2)	1 (0.1)	7 (0.1)
Total airway attempts, median [IQR]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]
Peri-intubation cardiac arrest (on any attempt), n (%)	7 (0.4)	13 (0.4)	19 (1.5)	107 (1.5)
Any first attempt AE, n (%)[a]	144 (7.7)	309 (8.4)	136 (10.4)	1166 (16.4)
First-attempt AEs, n (%)				
Hypotension	52 (2.8)	69 (1.9)	64 (4.9)	332 (4.7)
Bradydysrhythmia	6 (0.3)	10 (0.3)	7 (0.5)	66 (0.9)
Cardiac arrest	7 (0.4)	12 (0.3)	18 (1.4)	93 (1.3)
Hypoxemia	81 (4.3)	205 (5.6)	54 (4.1)	759 (10.7)
Tachydysrhythmia	2 (0.1)	7 (0.2)	2 (0.2)	19 (0.3)
Esophageal intubation—delayed recognition	0 (0.0)	4 (0.1)	0 (0.0)	2 (0.0)
Esophageal intubation—immediate recognition	7 (0.4)	23 (0.6)	5 (0.4)	43 (0.6)
Vomiting	2 (0.1)	22 (0.6)	3 (0.2)	55 (0.8)
Poor glottic view (Grade 3–4), n (%)				
Yes	95 (5.1)	289 (7.9)	74 (5.7)	699 (9.8)
Missing	126 (6.7)	61 (1.7)	31 (2.4)	127 (1.8)
Rescue surgical airway (on any attempt), n (%)	1 (0.1)	3 (0.1)	0 (0.0)	21 (0.3)

Abbreviations: ADA, anatomically difficult airway; AE, adverse events; IQR, interquartile range; PDA, physiologically difficult airway.
[a]Adverse events include first-attempt peri-intubation vomiting, esophageal intubation (immediately recognized and delayed recognition), bradydysrhythmia, cardiac arrest, hypoxemia (<90% or drop of 10% of oxygen saturation), hypotension systolic blood pressure <100 mm Hg, and tachydysrhythmia.

(ADA and PDA) (Figure 2, Supplemental Digital Content, Supplemental Tables 4–6, http://links.lww.com/AA/E699).

Our results align with a prior single-site study examining the association between ADAs and PDAs with first-attempt success without adverse events.[7] In that study, compared to airways with no difficult airway characteristics, ADAs and PDAs had aORs for first-attempt success without adverse events of 0.37 (95% CI, 0.21–0.66) and 0.36 (0.19–0.67), respectively. In addition, they observed the presence of both difficult airway types having a lower adverse association with first-attempt success without adverse events than either individually, aOR 0.19 (0.11–0.33). Differences between our results might reflect slightly different definitions for hypoxemia and hypotension adverse events. The prior study required a decrease in oxygen saturation or blood pressure from preintubation levels.[7] In contrast, we defined peri-intubation hypoxemia as an oxygen saturation <90% or a decrease of 10% and hypotension as a systolic blood pressure <100 mm Hg (Supplemental Digital Content, Supplemental Table 1, http://links.lww.com/AA/E699). Additionally, the prior study included obesity as only an ADA characteristic; whereas, we included it as both an ADA and PDA characteristic (Table 1).[7] Nevertheless, despite different definitions for ADAs and PDAs, we observed similar relationships between difficult airway types and first-attempt success without adverse events (Figure 2, Supplemental Digital Content, Supplemental Table 4, http://links.lww.com/AA/E699).

Although our study was intended to be exploratory and informative, it may guide clinical practice in some ways. First, clinicians should anticipate both anatomical and physiological challenges when intubating obese/ morbidly obese ED patients (Supplemental Digital Content, Supplemental Figures 2 and 3, http://links.lww.com/AA/E699).[33] Next, PDAs are associated with peri-intubation cardiac arrest (Figure 2, Supplemental Digital Content, Supplemental Table 4, http://links.lww.com/AA/E699); therefore, clinicians must critically weigh the need for immediate intubation versus optimizing hemodynamic and respiratory parameters.[2] Also, although ADAs were not directly associated with peri-intubation cardiac arrest in our study, ADAs were associated with multiple airway attempts, which has been associated with peri-intubation cardiac arrest and other severe complications in various other studies.[24–26] Lastly, while technological advances such as VL have mitigated anatomical challenges to difficult laryngoscopy and intubation,[34] we observed a similar association between ADAs and first-attempt success among both the DL and VL cohorts (Supplemental Digital Content, Supplemental Figure 4, Supplemental Table 4, http://links.lww.com/AA/E699). Additional work is necessary to better understand the relationship between hemodynamic and respiratory optimization before and during intubation and intubation outcomes.[2,9,35]

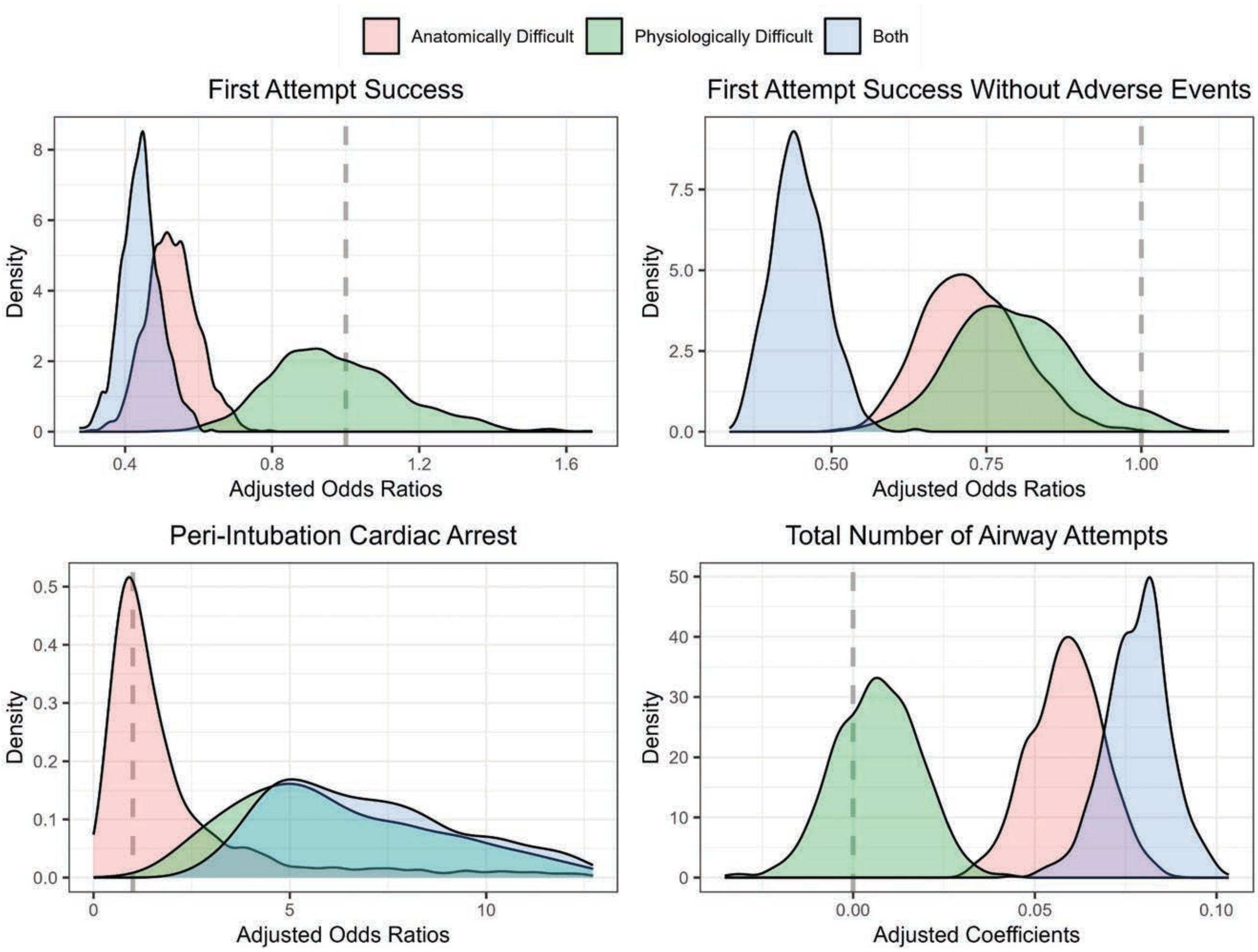

Figure 2. Density plots of bootstrapped adjusted regression estimates for the primary outcome (first-attempt success) and select secondary outcomes. Each *y*-axis presents probability densities for the *x*-axis variable. In addition to the difficulty airway type (independent variable), model fixed effects included device type (ie, direct and video laryngoscopy), intubator training level (ie, postgraduate training level), trauma, and age as well as the site as a random effect.

LIMITATIONS

First, confounding by indication and unmeasured confounders may have biased the results from our observational data. For example, recognition of and preparation for the difficult airway was not captured in the registry and might impact aspects of care such as intubator selection (ie, trainee versus attending) and interventions intended to mitigate peri-intubation adverse effects (eg, choice of DL versus VL). Similarly, we could not differentiate the cause of postinduction hypoxemia and hypotension. For example, these complications may have been the result of persistent preintubation hypoxemia and hypotension rather than a true adverse effect of the intubation. Also, hindsight and self-report bias may have impacted our results, given that intubating clinicians completed the data forms after the intubation. In addition, many factors may cue an intubator that a particular patient has an ADA or PDA; therefore, a classification with limited criteria will never be entirely sensitive or specific. NEAR does collect a variable representing the intubator's gestalt impression of airway difficulty; however, this variable may be confounded by knowledge of the intubation outcome. Similarly, the mediation analysis assumes there is no unmeasured confounding between the exposure-outcome, mediator-outcome, and exposure-mediator, as well as no mediator-outcome confounder that is affected by the exposure.[36] And, we did not investigate for the presence of an exposure-mediator interaction. We did not investigate all clinical interventions meant to mitigate ADA or PDA characteristics, such as glucocorticoids for airway edema or hypotension. Similarly, we excluded awake and flexible fiberoptic intubations, since these occur infrequently in NEAR.[19,37] Intubator-specific skill and experience with ADA and PDA characteristics was unknown and may have affected measured outcomes. Lastly, most intubations were performed by residents in the ED; therefore, the results may not be generalizable to all clinicians and practice settings.

CONCLUSIONS

Compared to those without difficult airway findings, ADAs alone were adversely associated with first-attempt success, while PDAs alone were not. Both ADAs and PDAs, as well as their additive interaction, were inversely associated with first-attempt success without adverse events.

DISCLOSURES

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