Emergency department versus operating room intubation of patients undergoing immediate hemorrhage control surgery

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BACKGROUND: Hemorrhage control surgery is an essential trauma center function. Airway management of the unstable bleeding patient in the

emergency department (ED) presents a challenge. Premature intubation in the ED can exacerbate shock and precipitate extremis. We hypothesized that ED versus operating room intubation of patients requiring urgent hemorrhage control surgery is associated

with adverse outcomes at the patient and hospital-levels.

METHODS: Patients who underwent hemorrhage control within 60 minutes of arrival at level 1 or 2 trauma centers were identified (National

Trauma Data Bank 2017–2019). To minimize confounding, patients dead on arrival, undergoing ED thoracotomy, or with clinical indications for intubation (severe head/neck/face injury or Glasgow Coma Scale score of ≤8) were excluded. Two analytic approaches were used. First, hierarchical logistic regression measured the risk-adjusted association between ED intubation and mortality. Secondary outcomes included ED dwell time, units of blood transfused, and major complications (cardiac arrest, acute respiratory distress syndrome, acute kidney injury, sepsis). Second, a hospital-level analysis determined whether hospital tendency

ED intubation was associated with adverse outcomes.

RESULTS: We identified 9,667 patients who underwent hemorrhage control surgery at 253 trauma centers. Patients were predominantly

young men (median age, 33 years) who suffered penetrating injuries (71%). The median initial Glasgow Coma Scale and systolic blood pressure were 15 and 108 mm Hg, respectively. One in five (20%) of patients underwent ED intubation. After risk-adjustment, ED intubation was associated with significantly increased odds of mortality, longer ED dwell time, greater blood transfusion, and major complications. Hospital-level analysis identified significant variation in use of ED intubation between hospitals not explained by patient case mix. After risk adjustment, patients treated at hospitals with high tendency for ED intubation (compared with those with low tendency) were significantly more likely to suffer in-hospital cardiac arrest (6% vs. 4%; adjusted odds

ratio, 1.46; 95% confidence interval, 1.04–2.03).

CONCLUSION: Emergency department intubation of patients who require urgent hemorrhage control surgery is associated with adverse outcomes.

Significant variation in ED intubation exists between trauma centers not explained by patient characteristics. Where feasible, intubation should be deferred in favor of rapid resuscitation and transport to the operating room. (*J Trauma Acute Care Surg.*

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KEY WORDS: Hemorrhage control surgery; endotracheal intubation; cardiac arrest; trauma center variation; trauma processes of care.

U ncontrolled hemorrhage remains the most common cause of potentially preventable death after trauma. 1-4 Hemorrhage control surgery is an essential function of modern civilian

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trauma centers. For patients who require urgent hemorrhage control surgery, early care processes such as transfusion practices^{5–7} and time to definitive care^{8,9} are known to impact survival.

Airway management in the emergency department (ED) for trauma patients with major bleeding presents a clinical challenge. Such patients are frequently hemodynamically unstable with altered mental status and conventional training prioritizes airway control before all else. ¹⁰ However, premature endotracheal intubation in such patients can exacerbate shock and precipitate extremis. ^{11–14} Therefore, a careful balance of priorities in which intubation is deferred in favor of rapid resuscitation and transport to the operating room (OR) might be preferable. Previous studies evaluating ED intubation of operative trauma patients were limited by small sample size and confounding by indication. ^{15,16} Therefore, there is need to further clarify the impact of intubation location on outcomes for patients requiring urgent hemorrhage control surgery.

The objective of this study was to evaluate the association between ED intubation (vs. OR intubation) and mortality for patients undergoing urgent hemorrhage control surgery at trauma centers in the United States and Canada. We hypothesized that ED intubation would be associated with an increased risk of death and major complications.

PATIENTS AND METHODS

Study Design and Population

This was a retrospective cohort study of adult patients 16 years or older who underwent hemorrhage control surgery at level 1 or 2 trauma centers participating in the National Trauma Data Bank (NTDB) between January 1, 2017, and December 31, 2019. Hemorrhage control surgery is a data field that was added to the National Trauma Data Standard in 2017. This variable captures the type of surgery performed for the purpose of hemorrhage control in patients who received at least 1 U of blood transfusion in the first 4 hours of hospital arrival. The cohort was limited to patients whose ED disposition was to the OR within 60 minutes of hospital arrival to isolate those in which urgent hemorrhage control was prioritized. Patients who suffered prehospital cardiac arrest, those presenting dead on arrival (ED heart rate = 0; systolic blood pressure [SBP] = 0; Glasgow Coma Scale [GCS] motor component = 1), 18 or with nonsurvivable injuries (Abbreviated Injury Scale [AIS] score = 6) were excluded. Because of inherent data limitations the patient-level indication for intubation in the ED could not be known. Therefore, to reduce the potential for confounding by indication, patients were excluded if they underwent ED thoracotomy; suffered severe head, face, or neck injuries (AIS score, \geq 3); or presented with an initial GCS score of \leq 8. In doing so, we sought to limit the cohort to bleeding trauma patients in whom the decision for intubation was guided by physician discretion or local protocol, rather than overt patient-level indications. To allow for hospital-level analyses, the cohort was further limited to trauma centers that treated at least 10 patients undergoing hemorrhage control surgery during the study period.

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline. ¹⁹ The project was approved by our institutional review board.

Exposure: Intubation in the ED

The exposure was defined as endotracheal intubation performed in the ED (identified using *International Classification of Diseases, Tenth Revision*, procedure codes 0BH17EZ or 0BH18EZ with procedure time less than total ED dwell time).

Outcomes

The primary outcome was in-hospital mortality. Secondary outcomes included total ED dwell time, units of blood transfused in the first 4 hours, and major complications. Major complications included in-hospital cardiac arrest with cardiopulmonary resuscitation (CPR), acute kidney injury, acute respiratory distress syndrome, ventilator-associated pneumonia, and severe sepsis as defined in the National Trauma Data Standard. ¹⁷

Potential Confounders

We considered several variables that might confound the association between ED intubation and the outcomes. These included patient baseline and injury characteristics. Patient baseline characteristics included age, sex, race, and insurance status. Injury characteristics included the mechanism of injury, global

(Injury Severity Score [ISS]) and anatomic injury severity (AIS by body region), specific injury diagnoses, and ED vital signs. The type of hemorrhage control surgery performed was also considered. Specific injury diagnoses were included because specific patterns of injury might affect clinical presentation, thereby influencing the decision for intubation, and mortality risk. Specific injury diagnoses were identified using AIS diagnosis codes.

We also considered that hospital characteristics might be associated with processes of care that could impact the location of intubation and outcomes for patients undergoing hemorrhage control surgery. For this reason, trauma center level of designation (level 1 vs. 2), teaching status (university affiliated, community, or nonteaching), funding status (for profit vs. nonprofit), and volume of patients treated with hemorrhage control surgery over the study period were evaluated.

Statistical Analysis

Univariable analyses compared patient baseline and injury characteristics between those who underwent ED versus OR intubation. Wilcoxon rank sum and χ^2 tests were used to compare median values and frequencies of categorical variables, respectively. We then used two analytic approaches to achieve the stated study objective.

First, we performed a patient-level analysis to estimate the association between location of intubation (ED vs. OR) and the outcomes. To accomplish this, we used multivariable logistic regression models to estimate risk-adjusted odds ratios for binary outcomes (mortality and major complications) and negative binomial models to estimate rate ratios for outcomes operationalized as count data (ED dwell time and blood transfusion). All models were multilevel mixed models that included a random intercept term to account for clustering of patients within trauma centers. Variables were included in multivariable analyses if the p value was ≤ 0.1 in univariable comparison between ED and OR intubation groups or were otherwise specifically selected based on clinical importance.

Second, we performed a hospital-level analysis to evaluate whether hospital tendency for ED intubation was associated with risk of adverse outcomes. A multilevel logistic regression model was used to estimate the unique risk-adjusted odds ratio and 80% confidence interval (CI) for ED intubation at each trauma center. This approach has been previously used to quantify risk-adjusted differences in patient care between hospitals for the purpose of quality improvement.²¹ Trauma centers were then categorized as high, average, or low tendency for ED intubation by outlier status. Specifically, trauma centers with a lower limit of the 80% CI greater than 1 were high outliers—significantly more likely than average to perform intubation in the ED. Conversely, trauma centers with an upper limit of the 80% CI less than 1 were low outliers—significantly less likely than average to perform intubation in the ED. Risk-adjusted outcomes were then compared across hospital tendency for ED intubation.

To quantify hospital-level variation in ED intubation, we used the median odds ratio (MOR).²² The MOR represented the median value of the odds ratio obtained when comparing the likelihood of ED intubation for patients treated at two randomly selected hospitals in our study. In this way, the MOR showed the

degree to which differences in ED intubation were a hospital-level phenomenon, independent of patient characteristics.

Because trauma center characteristics might reflect differences in structures and processes of care that impact the location of intubation, we compared trauma center characteristics across hospital tendency for ED intubation. We then used the proportional change in variance (PCV) to measure the proportion of hospital-level variation in ED intubation that could be explained by trauma center characteristics. The PCV is estimated using the following equation²³:

$$PCV = \left(\frac{V_1 - V_2}{V_1}\right) \times 100\%$$

where V_1 is the hospital-level variance in the multilevel model including only patient-level characteristics and V_2 is the hospital-level variance in the same model after adding trauma center characteristics. In this way, the PCV represented the degree to which hospital-level differences in ED intubation are explained by trauma center characteristics independent of patient characteristics.

Emergency department vital signs (heart rate, SBP, and GCS) were missing in up to 8% of patients and were therefore imputed using a multiple imputation technique.²⁴ All statistical analyses were performed using SAS statistical software version 9.4 (SAS Institute Inc., Cary, NC). Threshold for statistical significance was set to p < 0.05.

RESULTS

Derivation of the study population is shown in Supplemental Digital Content (Supplementary Fig. 1, http://links.lww.com/TA/C892). During the study period, we identified 9,667 patients who underwent urgent hemorrhage control surgery at 253 levels 1 and 2 trauma centers. Patients were predominantly young men (8,046 male [83%]; median age, 33 years [interquartile range (IQR), 24–46 years]) who suffered penetrating injuries (4,887 firearm injury [51%]; 2,019 stab injury [21%]). The median ISS was 18 (IQR, 10–26). The median GCS score on arrival was 15 (IQR, 14–15), and the median SBP was 108 mm Hg (IQR, 88–130 mm Hg). The most common operations for hemorrhage control were laparotomy (6,534 patients [68%]), extremity (1,444 patients [15%]), and thoracotomy procedures (598 patients [6%]). Emergency department intubation was performed in 1,972 patients (20%), and 877 (9%) died.

Univariable Comparisons: ED Versus OR Intubation

Table 1 compares baseline and injury characteristics between patients based on location of intubation. Compared with those in which intubation was deferred to the OR, patients who underwent ED intubation were significantly more likely to suffer blunt trauma (669 of 1,972 patients [34%] vs. 2,092 of 7,695 patients [27%], p < 0.001), with higher median ISS (22 vs. 17, p < 0.001) because of severe injuries to the chest and extremities. Specific injury diagnoses more common among patients who underwent ED intubation included lung, thoracic vascular, cardiac, liver, and abdominal vascular injuries. While ED vital signs differed significantly between ED and OR

TABLE 1. Univariable Comparison of Patients Who Underwent ED Versus OR Intubation

	ED Intubation (n = 1,972)	OR Intubation (n = 7,695)	p
Baseline characteristics			
Age, median (IQR), y	32 (25–46)	33 (24-46)	0.683
Male sex, n (%)	1,664 (84.4)	6,382 (82.9)	0.126
Race, n (%)	, , ,	, , ,	0.031
Black	776 (39.4)	3,269 (42.5)	
White	862 (43.7)	3,241 (42.1)	
Other	334 (16.9)	1,185 (15.4)	
Insurance, n (%)	` /	, , ,	0.720
Public	906 (45.9)	3,576 (46.5)	
Private	578 (29.3)	2,282 (29.7)	
Self-pay	488 (24.8)	1,837 (23.9)	
Injury characteristics	(= 1.13)	-, ()	
Mechanism, n (%)			< 0.001
Firearm	953 (48.3)	3,934 (51.1)	
Stab	350 (17.8)	1,669 (21.7)	
MVC	304 (15.4)	968 (12.6)	
Motorcycle	121 (6.1)	319 (4.2)	
Pedestrian	132 (6.7)	270 (3.5)	
Fall	34 (1.7)	195 (2.5)	
Other blunt injury	78 (4.0)	340 (4.4)	
ISS, median (IQR)	22 (14–30)	17 (10–26)	< 0.001
Severe injury AIS score ≥3, n (%)	22 (14–30)	17 (10-20)	<0.001
Chest	985 (50.0)	2,662 (34.6)	< 0.001
Abdomen			0.589
Extremity	1,084 (55.0)	4,282 (55.7)	
External/soft tissue	762 (38.6)	2,554 (33.2)	<0.001
Injury diagnoses, n (%)	117 (5.9)	407 (5.3)	0.200
Rib or sternum fracture	606 (25.2)	2710 (25.2)	0.072
	696 (35.3)	2719 (35.3)	0.973
Lung	572 (29.0)	1,265 (16.4)	<0.001
Thoracic vascular	156 (7.9)	317 (4.1)	< 0.001
Heart	142 (7.2)	357 (4.6)	< 0.001
Abdominal vascular	380 (19.3)	1,308 (17.0)	0.018
Liver	612 (31.0)	2,047 (26.6)	< 0.001
Spleen	400 (20.3)	1,430 (18.6)	0.086
Kidney	278 (14.1)	1,057 (13.7)	0.678
Pancreas	171 (8.7)	599 (7.8)	0.194
GI/mesenteric	842 (42.7)	3,495 (45.4)	0.030
Extremity vascular	327 (16.6)	1,459 (19.0)	0.015
Long bone fracture	397 (20.1)	1,529 (19.9)	0.795
Pelvic fracture	17 (0.9)	112 (1.5)	0.041
ED vital signs			
GCS score, median (IQR)	15 (13–15)	15 (15–15)	< 0.001
SBP, median (IQR), mm Hg	107 (85–130)	109 (90–130)	0.026
HR, median (IQR), bpm	116 (94–135)	102 (85–121)	< 0.001
Hemorrhage control surgery, n (%)			< 0.001
Laparotomy	1,284 (65.1)	5,250 (68.2)	
Thoracotomy	220 (11.2)	378 (4.9)	
Sternotomy	46 (2.3)	162 (2.1)	
Neck	50 (2.5)	118 (1.5)	
Extremity	209 (10.6)	1,235 (16.1)	
Mangled extremity/soft tissue	163 (8.3)	552 (7.2)	

AIS, Abbreviated Injury Scale; bpm, beats per minute; ED, emergency department; GI, gastrointestinal; HR, heart rate; ISS, Injury Severity Score; IQR, interquartile range; MVC, motor vehicle collision.

TABLE 2. Comparison of Unadjusted Outcomes for Patients Who Underwent ED Versus OR Intubation

	ED Intubation $(n = 1,972)$	OR Intubation $(n = 7.695)$	p
Duimoury outcome	(11 1,5/12)	(ii 7,023)	Р
Primary outcome			
Overall mortality, n (%)	343 (17.4)	544 (7.1)	< 0.001
Secondary outcomes			
ED dwell time, median (IQR), min	31 (22–42)	22 (13–36)	< 0.001
RBC transfusion at 4 h, median (IQR), units	6 (3–12)	4 (2–7)	< 0.001
Major complication, n (%)			
Cardiac arrest with CPR	198 (10.0)	304 (4.0)	< 0.001
AKI	120 (6.1)	268 (3.5)	< 0.001
ARDS	61 (3.1)	104 (1.4)	< 0.001
VAP	63 (3.2)	125 (1.6)	< 0.001
Sepsis	59 (3.0)	153 (2.0)	0.007

AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; RBC, red blood cell; VAP, ventilator-associated pneumonia.

intubation groups, these differences were of marginal clinical significance.

Significant differences in unadjusted outcomes were observed between ED and OR intubation groups (Table 2). Specifically, patients intubated in the ED were significantly more likely to die (17% vs. 7%, p < 0.001). Emergency department intubation was also associated with significantly longer ED dwell time, greater blood transfusion in the first 4 hours, and higher risk of major complications.

Patient-Level Analysis

Risk-adjusted patient outcomes as a function of location of intubation are shown in Table 3. After adjusting for patient baseline and injury characteristics, patients who underwent intubation in the ED versus the OR had significantly higher odds of mortality (adjusted odds ratio [aOR], 1.85; 95% CI, 1.54–2.23). Patients intubated in the ED also had significantly longer ED dwell time, greater blood transfusion, and higher odds of major complications. Specifically, ED intubation was associated with significantly greater risk of in-hospital cardiac arrest with CPR, acute kidney injury, and acute respiratory distress syndrome.

TABLE 3. Risk-Adjusted Outcomes Associated With ED Versus OR Intubation

	Odds Ratio/Rate Ratio	95% CI	
Primary outcome		_	
Overall mortality	1.85	1.54-2.23	
Secondary outcomes			
ED dwell time	1.25	1.24-1.27	
RBC transfusion at 4 h	1.23	1.21-1.26	
Major complication			
Cardiac arrest with CPR	1.72	1.38-2.15	
AKI	1.44	1.13-1.85	
ARDS	1.57	1.10-2.25	
VAP	1.21	0.85 - 1.75	
Sepsis	1.30	0.93-1.83	

AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; RBC, red blood cell; VAP, ventilator-associated pneumonia.

Hospital-Level Analysis

Hospital Variation in ED Intubation and Impact on Outcomes

There was wide variation in the rate of ED intubation for patients undergoing hemorrhage control surgery across trauma centers (Fig. 1A). After adjusting for patient baseline and injury characteristics, the hospital-specific odds of ED intubation varied significantly (Fig. 1B). Specifically, 66 hospitals (26%) were high outliers—with significantly higher-than-average tendency for ED intubation (high EDI centers). Conversely, 50 hospitals (20%) were low outliers—with significantly lower-than-average tendency for ED intubation (low EDI centers). High EDI centers performed intubation in the ED five times more frequently than low EDI centers (ED intubation rate, 40% vs. 8%) for reasons not explained by differences in patient case mix.

The MOR for ED intubation across trauma centers was 2.5. In other words, the risk-adjusted odds of ED intubation differed by a median of 2.5-fold between any two randomly selected hospitals.

After risk adjustment, there was no significant difference in mortality, blood transfusion, or most major complications across hospital tendency for ED intubation (Table 4). However, patients treated at high EDI centers were significantly more likely to suffer in-hospital cardiac arrest with CPR compared with those treated at low EDI centers (6% vs. 4%; aOR, 1.46; 95% CI, 1.04–2.03).

Trauma Center Characteristics and ED Intubation

Having identified significant variation in hospital tendency for ED intubation, we evaluated the contributing role of trauma center characteristics (Table 5). Low EDI hospitals were significantly more likely to be level 1, university-affiliated, nonprofit trauma centers. There was also a strong tendency for hospitals with higher volumes of hemorrhage control surgery to defer intubation to the OR. Specifically, 72% of low EDI trauma centers were in the highest quartile of hemorrhage control surgery volume.

Finally, we calculated the PCV to estimate the degree to which hospital variation in ED intubation is explained by trauma center characteristics. The results of this analysis are shown in

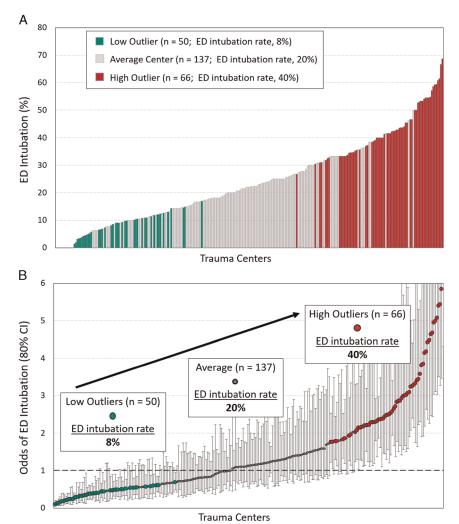


Figure 1. Variation in use of ED intubation across trauma centers. The range in crude rate of ED intubation across all trauma centers is shown (*A*). Significant variation in trauma center odds of ED intubation was observed after adjusting for patient characteristics (*B*). Specifically, 66 trauma centers were high outliers, with higher-than-average odds of ED intubation (ED intubation rate, 40%). Conversely, 50 trauma centers were low outliers, with lower-than-average odds of ED intubation (ED intubation rate, 8%).

Supplemental Digital Content (Supplementary Table 1, http://links.lww.com/TA/C892). Hospital teaching status explained the largest proportion of the observed variation in hospital tendency for ED intubation (PCV, 26%), followed by hemorrhage control surgery volume (PCV, 20%) and level of designation (PCV, 19%). Hospital funding status appeared to contribute negligibly to center-level variation in ED intubation (PCV, 3%). With all trauma center characteristic included in the model, the PCV was 35%, indicating that structures and processes of care associated with these hospital-level factors account for 35% of observed differences in ED intubation.

DISCUSSION

In this study of patients who underwent urgent hemorrhage control surgery at levels 1 and 2 trauma centers in the United States and Canada, endotracheal intubation in the ED versus OR was associated with higher mortality, longer ED dwell time, greater blood transfusion, and risk of major complications. Significant

trauma center variation in use of ED intubation was identified, which could not be explained by differences in patient characteristics. Patients treated at trauma centers with high tendency for ED intubation were significantly more likely to suffer in-hospital cardiac arrest.

These findings emphasize that early decision-making in the emergency care of bleeding trauma patients can have a meaningful impact on outcomes. Hemorrhage control surgery is an essential trauma center function, and early care processes, such as transfusion practices or time to operative hemorrhage control, are associated with survival. ^{6–9} Our study adds to the literature by providing evidence that deferring intubation in eligible patients in lieu of prioritizing resuscitation and rapid transport to the OR might confer a survival advantage.

These observations are intuitive and recognizable to those who care for patients with major injury. Patients with intravascular volume depletion secondary to hemorrhage depend on compensatory mechanisms to maintain cardiac output and end organ perfusion. Endotracheal intubation can compromise these

TABLE 4. Comparison of Patient Outcomes by Hospital Tendency for ED Intubation

	Low Outlier	Average Center	High Outlier	
Patients, n	3,613	3,814	2,240	
Centers, n	50	137	66	
ED intubation, n (%)	304 (8.4)	770 (20.2)	898 (40.1)	
Primary outcome				
Overall mortality, n (%)	305 (8.4)	366 (9.6)	216 (9.6)	
Adjusted OR (95% CI)	Reference	1.11 (0.89–1.40)	1.27 (0.97-1.65)	
Secondary outcomes				
ED dwell time, median (IQR), min	21 (13–34)	25 (15–39)	28 (18-41)	
Adjusted RR (95% CI)	Reference	1.11 (1.04–1.18)*	1.20 (1.11-1.29)*	
RBC transfusion at 4 h, median (IQR), U	4 (2–8)	4 (2–8)	4 (2–9)	
Adjusted RR (95% CI)	Reference	0.92 (0.84–1.00)	1.05 (0.95–1.16)	
Cardiac arrest with CPR, n (%)	160 (4.4)	198 (5.2)	136 (6.1)	
Adjusted OR (95% CI)	Reference	1.16 (0.87–1.56)	1.46 (1.04-2.03)*	
AKI, n (%)	132 (3.7)	166 (4.4)	90 (4.0)	
Adjusted OR (95% CI)	Reference	1.19 (0.90–1.57)	1.17 (0.85-1.63)	
ARDS, n (%)	58 (1.6)	57 (1.5)	50 (2.2)	
Adjusted OR (95% CI)	Reference	0.91 (0.58–1.42)	1.42 (0.88-2.29)	
Sepsis, n (%)	75 (2.1)	83 (2.2)	54 (2.4)	
Adjusted OR (95% CI)	Reference	1.04 (0.68–1.59)	1.10 (0.67-1.80)	

^{*}Statistically significant.

AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; RBC, red blood cell; RR, rate ratio; VAP, ventilator-associated pneumonia.

mechanisms through the effects of induction medications or neuromuscular blockade, positive-pressure ventilation, or procedural complications. 11–14,25,26 As a result, the premature intubation of underresuscitated bleeding patients will often exacerbate shock, lead to compensatory increases in blood transfusion, delay to operative hemorrhage control, and higher likelihood of subsequent organ dysfunction. Our findings support this biologic rationale and suggest that, where feasible, intubation should be deferred in carefully selected patients without clear indications for intubation.

In-hospital cardiac arrest was a major contributor to the observed association between ED intubation and mortality in our study. Cardiac arrest occurs in 3% of trauma patients who require emergency intubation.²⁷ In contrast, the rate of cardiac arrest

associated with ED intubation in our study was 10%, reflecting the underlying physiologic risk profile of our hemorrhage control cohort. Relative hypotension and increased shock index are known risk factors for intubation-related cardiac arrest. ^{26–29} In recent studies, the median SBP and shock index for patients who experienced cardiac arrest after intubation ranged 98 to 110 mm Hg^{26,27,29} and 0.9 to 0.98, respectively. ^{26–28} In our cohort, the median SBP and shock index were 108 mm Hg and 0.96, emphasizing that hemorrhage control surgery patients are at high risk for intubation-related cardiac arrest. The observation that ED intubation was associated with 72% increased odds of cardiac arrest further validates the biological rational for a causal link between premature intubation and death in

TABLE 5. Comparison of Trauma Center Characteristics by Hospital Tendency for ED Intubation

	Low Outlier	Average Center	High Outlier	
Centers, n	50	137	66	
Rate of ED intubation, %	8.4	20.2	40.1	
Trauma center level, n (%)				< 0.001
Level 1 vs. level 2	45 (90.0)	81 (59.1)	28 (42.4)	
Teaching status, n (%)				< 0.001
University	41 (82.0)	67 (48.9)	18 (27.3)	
Community	8 (16.0)	54 (39.4)	36 (54.5)	
Nonteaching	1 (2.0)	16 (11.7)	12 (18.2)	
Hospital type, n (%)				
For profit vs. nonprofit	3 (6.0)	17 (12.4)	15 (22.7)	0.033
Volume of hemorrhage control surgery, n (%)				< 0.001
<50 patients	2 (4.0)	37 (27.0)	15 (22.7)	
50–89 patients	8 (16.0)	52 (38.0)	23 (34.9)	
90–130 patients	4 (8.0)	26 (19.0)	18 (27.3)	
>130 patients	36 (72.0)	22 (16.1)	10 (15.2)	

these patients. Taken together, trauma providers should prioritize blood-based resuscitation to optimize physiology before intubation while minimizing delay to surgical hemorrhage control.

Previous studies sought to evaluate the impact of ED intubation on trauma outcomes. Dumas et al. 15 compared ED with OR intubation among operative trauma patients in their single-center study. In 241 patients, they found that ED intubation was associated with higher risk of ED thoracotomy, massive transfusion, and death. There was no difference in time to surgery between ED and OR intubation groups. However, a major limitation of this study was confounding by indication due to inclusion of patients who underwent ED thoracotomy. As a result, ED intubation was an event along the causal pathway to mortality among patients with the most critical injuries. The observation that 35% of ED intubation patients received massive transfusion, whereas more than 50% of OR intubation patients received no blood transfusion, was evidence of this confounding. Similar limitations affect interpretation of the forthcoming paper by Duchesne et al. 16 Among 237 patients undergoing surgery for noncompressible torso hemorrhage, the median GCS score before ED intubation was 8, compared with the median GCS score of 15 among patients treated with deferred intubation. Such profound confounding could not be reliably adjusted for in either study.

In contrast, a major strength of our study was the exclusion of patients with clear clinical indications for intubation (severe head/face/neck injury, GCS score of ≤8, ED thoracotomy). This was done to minimize confounding by indication. As a result, differences in presenting vital signs between ED and OR intubation groups, while statistically significant, were only of marginal clinical significance (median GCS score, 15 vs. 15; median SBP, 107 vs. 109 mm Hg). Therefore, the decision for ED intubation in our study was more likely to be guided by physician discretion or local protocol (structures and processes of care), rather than a direct reflection of injury severity.

In this way, the results of our center-level analysis are even more meaningful. Wide variation in ED intubation was observed across trauma centers. Specifically, there was fivefold difference in rate of ED intubation between high versus low EDI centers. The MOR indicated a median 2.5-fold difference in the odds of ED intubation when comparing any two randomly selected trauma centers. This variation was not explained by differences in patient characteristics. Therefore, we believe that this variation likely reflects differences in structures and processes of care—the infrastructure, resources, people, and decisions that impact care for patients requiring urgent hemorrhage control surgery. These differences in care matter because patients treated at high EDI hospitals (compared with low EDI hospitals) had 46% higher odds of cardiac arrest and tendency to higher odds of overall mortality (although not statistically significant after risk-adjustment).

It is notable that only in-hospital cardiac arrest was significantly associated with hospital tendency for ED intubation. Overall mortality, blood transfusion, or other major complications were not significantly different based on hospital use of ED intubation. We believe that this can be explained by the nature of the hospital-level analysis. By grouping centers into three categories, sample size is negatively impacted. The exposure in the hospital-level analysis (high, average, and low tendency for ED intubation) becomes an ecological variable applied to the

group, rather than individual patients. Therefore, although the difference in rate of ED intubation between high versus low EDI centers (40% vs. 8%) was remarkable, the increased risk of mortality associated with ED intubation becomes muted in hospital-level comparisons. This interpretation is supported by the fact that, although marginally nonsignificant, there was a tendency toward higher odds of mortality at high EDI centers (aOR, 1.27; 95% CI, 0.97–1.65).

Trauma center characteristics were strongly associated with variation in hospital tendency for ED intubation. Specifically, ED intubation was less likely to occur at universityaffiliated, level 1 trauma centers with high volumes of hemorrhage control surgery. Teaching status, trauma center level, and hemorrhage control surgery volume together explained 35% of the variation in ED intubation across hospitals after adjusting for patient characteristics. This might be explained by differences in structures and processes of care that correlate with these factors. For example, the integration of trainees at university-affiliated trauma centers will likely involve continued team-building efforts and education that promote evidence-based practices and patient safety. Level 1 trauma centers with high volumes of hemorrhage control surgery likely organize resources to respond to high acuity in ways that expedite treatment and optimize outcomes.³⁰ Altogether, our findings suggest that the decision for ED intubation is heavily influenced by institutional resources and experience in caring for bleeding trauma patients. Future work is needed to clarify which structures and processes of care are characteristic of trauma centers that perform highly in caring for patients who undergo hemorrhage control surgery. Such study may allow for the definition of key performance indicators with the goal of elevating the quality of care at all centers.

There are several important limitations that must be considered when interpreting the results of this study. First, confounding due to unmeasured factors is likely to exist despite our best efforts to minimize this through study design and analysis. Specific event-level information is not available beyond the variables in the data set. We are unable to know the true indications for intubation in the ED. Therefore, there may be unmeasured clinical indicators associated with mortality that influenced decisions to intubate early. However, we were successful in reducing confounding by indication through exclusion of patients with hard indications for intubation (severe head/face/neck injury, GCS score of ≤8, ED thoracotomy) as evidenced by the median GCS score of 15 and SBP of 108 mm Hg in our cohort. Remaining differences in patient baseline and injury characteristics were adjusted for in our multivariable logistic regression model, which showed excellent performance (c statistic in model for mortality, 0.87). For these reasons, we believe that confounding alone is unlikely to explain our observations.

Second, the timing of major complications was unknown. Therefore, we are unable to demonstrate a temporal association between ED intubation and cardiac arrest. We are also unable to determine the true cause of cardiac arrest. However, the finding that cardiac arrest and other major complications were more common after ED intubation is evidence that the observed association between ED intubation and risk of death is mediated through these adverse events.

Third, it is important to acknowledge that our hospital-level observations likely reflect multiple factors related to patient care,

of which timing and location of intubation is only one. For example, hospitals that treat high volumes of patients requiring hemorrhage control surgery have likely established numerous processes of care that confer benefit to patient outcomes. We are not able to quantify to what degree our findings truly reflect the impact of intubation location above and beyond what may be overall better care at such centers. It is for this reason that further study is needed to define optimal care practices for patients undergoing hemorrhage control surgery.

Finally, the American College of Surgeons NTDB was not designed for the purpose of this study, and reliability of important variables could not be confirmed. However, data collection at levels 1 and 2 trauma centers is performed by trained registrars, and data fields are clearly defined to ensure consistency and minimize abstraction errors. The explicit purpose of the NTDB is to allow for research and quality improvement efforts. Our analysis embodies this mission of quality improvement: to clarify best practices that might be implemented broadly with the goal of improving trauma patient outcomes.

CONCLUSION

In this study of patients who underwent urgent hemorrhage control surgery at levels 1 and 2 trauma centers in the United States and Canada, ED intubation was associated with increased odds of mortality and major complications. Significant trauma center variation in use of ED intubation exists independent of differences in patient characteristics. Patients treated at trauma centers where ED intubation is most common are at significantly increased risk of suffering in-hospital cardiac arrest. These data suggest that, where feasible, intubation should be deferred in favor of rapid resuscitation and transport to surgical hemorrhage control.

AUTHORSHIP

Z.D. contributed in the literature search, study design, data analysis, interpretation, and writing. M.J.S. contributed in the study design, interpretation, and critical revision. M.S., J.J., M.M., A.K., J.V.S., K.S., and E.H. contributed in the interpretation and critical revision. J.P.B. contributed in the literature search, study design, data analysis, interpretation, and writing.

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DISCLOSURE

The authors declare no conflicts of interest.

REFERENCES

- Holcomb JB, del Junco DJ, Fox EE, Wade CE, Cohen MJ, Schreiber MA, et al. The prospective, observational, multicenter, major trauma transfusion (PROMMTT) study: comparative effectiveness of a time-varying treatment with competing risks. *JAMA Surg*. 2013;148(2):127–136.
- Eastridge BJ, Mabry RL, Seguin P, Cantrell J, Tops T, Uribe P, et al. Death on the battlefield (2001–2011): implications for the future of combat casualty care. *J Trauma Acute Care Surg*. 2012;73(6 Suppl 5):S431–S437.
- Dutton RP, Stansbury LG, Leone S, Kramer E, Hess JR, Scalea TM. Trauma mortality in mature trauma systems: are we doing better? An analysis of trauma mortality patterns, 1997–2008. *J Trauma*. 2010;69(3):620–626.
- 4. Cannon JW. Hemorrhagic shock. N Engl J Med. 2018;378(4):370-379.

- Holcomb JB, Tilley BC, Baraniuk S, Fox EE, Wade CE, Podbielski JM, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. *JAMA*. 2015;313(5):471–482.
- Hynes AM, Geng Z, Schmulevich D, Fox EE, Meador CL, Scantling DR, et al. Staying on target: maintaining a balanced resuscitation during damage-control resuscitation improves survival. *J Trauma Acute Care Surg*. 2021;91(5):841–848.
- Hazelton JP, Ssentongo AE, Oh JS, Ssentongo P, Seamon MJ, Byrne JP, et al. Use of cold-stored whole blood is associated with improved mortality in hemostatic resuscitation of major bleeding: a multicenter study. *Ann Surg*. 2022;276(4):579–588.
- 8. Meizoso JP, Ray JJ, Karcutskie CA 4th, Allen CJ, Zakrison TL, Pust GD, et al. Effect of time to operation on mortality for hypotensive patients with gunshot wounds to the torso: the golden 10 minutes. *J Trauma Acute Care Surg.* 2016;81(4):685–691.
- Barbosa RR, Rowell SE, Fox EE, Holcomb JB, Bulger EM, Phelan HA, et al. Increasing time to operation is associated with decreased survival in patients with a positive FAST examination requiring emergent laparotomy. *J Trauma Acute Care Surg*. 2013;75(1 Suppl 1):S48–S52.
- American College of Surgeons Committee on Trauma. Chapter 1: Initial Assessment and Management. In: Advanced Trauma Life Support: Student Course Manual. 10th ed. Chicago, IL: American College of Surgeons; 2018:2–21.
- Shafi S, Gentilello L. Pre-hospital endotracheal intubation and positive pressure ventilation is associated with hypotension and decreased survival in hypovolemic trauma patients: an analysis of the National Trauma Data Bank. *J Trauma*. 2005;59(5):1140–1145.
- Naguib M, Samarkandi AH, Bakhamees HS, Magboul MA, el-Bakry AK. Histamine-release haemodynamic changes produced by rocuronium, vecuronium, mivacurium, atracurium and tubocurarine. *Br J Anaesth*. 1995;75(5):588–592.
- Mayglothling J, Duane TM, Gibbs M, McCunn M, Legome E, Eastman AL, et al. Emergency tracheal intubation immediately following traumatic injury: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg.* 2012;73(5 Suppl 4):S333–S340.
- Davis DP, Kimbro TA, Vilke GM. The use of midazolam for prehospital rapid-sequence intubation may be associated with a dose-related increase in hypotension. *Prehosp Emerg Care*. 2001;5(2):163–168.
- Dumas RP, Jafari D, Moore SA, Ruffolo L, Holena DN, Seamon MJ. Emergency department versus operating suite intubation in operative trauma patients: does location matter? World J Surg. 2020;44(3):780–787.
- Duchesne J TS, Jackson-Weaver O, Tatum D (2022). Not so fast with ABC for non-compressible torso hemorrhage: an ad-hoc review of AAST MIT. In: American Association for the Surgery of Trauma 2022 Annual Meeting; September 21, 2022, Chicago, IL.
- American College of Surgeons Committee on Trauma. National Trauma Data Standard 2019. Available at: https://www.facs.org/media/p1scq2jf/ ntdb_data_dictionary_2019_revision.pdf. Accessed November 1, 2022.
- Byrne JP, Xiong W, Gomez D, Mason S, Karanicolas P, Rizoli S, et al. Redefining "dead on arrival": identifying the unsalvageable patient for the purpose of performance improvement. J Trauma Acute Care Surg. 2015; 79(5):850–857.
- Strengthening the Reporting of Observational Studies in Epidemiology (STROBE). Checklist for Cohort Studies 2021. Available at: https://www. strobe-statement.org/fileadmin/Strobe/uploads/checklists/STROBE_checklist_cohort.doc. Accessed November 1, 2022.
- Hubbard AE, Ahern J, Fleischer NL, Van der Laan M, Lippman SA, Jewell N, et al. To GEE or not to GEE: comparing population average and mixed models for estimating the associations between neighborhood risk factors and health. *Epidemiology*. 2010;21(4):467–474.
- Glance LG, Dick AW, Meredith JW, Mukamel DB. Variation in hospital complication rates and failure-to-rescue for trauma patients. *Ann Surg*. 2011;253(4):811–816.
- Merlo J, Chaix B, Ohlsson H, Beckman A, Johnell K, Hjerpe P, et al. A brief conceptual tutorial of multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic regression to investigate contextual phenomena. *J Epidemiol Community Health*. 2006;60(4):290–297.
- Merlo J, Yang M, Chaix B, Lynch J, Rastam L. A brief conceptual tutorial on multilevel analysis in social epidemiology: investigating contextual phenomena in different groups of people. *J Epidemiol Community Health*. 2005;59(9):729–736.

- Yuan Y. Multiple imputation using SAS software. J Stat Softw. 2011;45(6).
 Available at: https://www.jstatsoft.org/article/view/v045i06. Accessed March 21, 2023.
- Smischney NJ, Demirci O, Diedrich DA, Barbara DW, Sandefur BJ, Trivedi S, et al. Incidence of and risk factors for post-intubation hypotension in the critically ill. *Med Sci Monit*. 2016;22:346–355.
- Yang TH, Chen KF, Gao SY, Lin CC. Risk factors associated with peri-intubation cardiac arrest in the emergency department. Am J Emerg Med. 2022;58:229–234.
- Heffner AC, Swords DS, Neale MN, Jones AE. Incidence and factors associated with cardiac arrest complicating emergency airway management. *Resuscitation*. 2013;84(11):1500–1504.
- Wardi G, Villar J, Nguyen T, Vyas A, Pokrajac N, Minokadeh A, et al. Factors and outcomes associated with inpatient cardiac arrest following emergent endotracheal intubation. *Resuscitation*. 2017;121:76–80.
- De Jong A, Rolle A, Molinari N, Paugam-Burtz C, Constantin JM, Lefrant JY, et al. Cardiac arrest and mortality related to intubation procedure in critically ill adult patients: a multicenter cohort study. *Crit Care Med.* 2018; 46(4):532–539.
- Thomas AC, Campbell BT, Subacius H, Bilimoria KY, Stey AM, Hamad D, et al. Time to OR for patients with abdominal gunshot wounds: a potential process measure to assess the quality of trauma care? *J Trauma Acute Care Surg*. 2022;92(4):708–716.