Prehospital end-tidal carbon dioxide predicts hemorrhagic shock upon emergency department arrival

Natalie Bulger, MS, Brenna Harrington, BS, Josh Krieger, MD, Andrew Latimer, MD, Saman Arbabi, MD, Catherine R. Counts, PhD, MHA, Michael Sayre, MD, Charles Maynard, PhD, *and* **Eileen M. Bulger, MD**, *Bellevue, Washington*

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BACKGROUND: In addition to reflecting gas exchange within the lungs, end-tidal carbon dioxide ($ETCO_2$) also reflects cardiac output based on CO_2 delivery to the pulmonary parenchyma. We hypothesized that low prehospital $ETCO_2$ values would be predictive of hemorrhagic shock in intubated trauma patients.

METHODS: A retrospective observational study of adult trauma patients intubated in the prehospital setting and transported to a single Level I trauma center from 2016 to 2019. Continuous prehospital $ETCO_2$ data were linked with patient care registries. We developed a novel analytic approach that allows for reflection of prehospital $ETCO_2$ over the entire prehospital course of care. The primary outcome was hemorrhagic shock on emergency department (ED) presentation, defined as either initial ED systolic blood pressure of 90 mm Hg or less or initial Shock Index (SI) > 0.9, and transfusion of at least one unit of blood product during their ED stay. Prehospital $ETCO_2$ less than 25 mm Hg was evaluated for predictive value of hemorrhagic shock.

RESULTS: Three hundred and seven patients (82% men, 34% penetrating injury, 42% in hemorrhagic shock on ED arrival, 27% mortality) were included in the study. Patients in hemorrhagic shock had lower median $ETCO_2$ values (26.5 mm Hg vs. 32.5 mm Hg; $p < 0.001$) than those not in hemorrhagic shock. Patients with prehospital $ETCO_2$ less than 25 mm Hg were 3.0 times (adjusted odds ratio = 3.0; 95% confidence interval, 1.1–7.9) more likely to be in hemorrhagic shock upon ED arrival than patients with $ETCO_2 \geq 25$ mm Hg.

CONCLUSION: Intubated patients with hemorrhagic shock upon ED arrival had significantly lower prehospital $ETCO_2$ values. Incorporating $ETCO_2$ assessment into prehospital care for trauma patients could support decisions regarding prehospital blood transfusion, and triage to higher-level trauma centers, and trauma team activation. (*J Trauma Acute Care Surg.* 2021;91: 457–464. Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Prognostic, level III.

KEY WORDS: Trauma; shock; hemorrhagic shock; end-tidal carbon dioxide; intubation.

In the United States, traumatic injury is the leading cause of death among individuals between ages 1 and 44 years.[1] Rapid hemorrhage is involved in 20% to 40% of traumatic deaths occurring after hospital admission. Some of these deaths may be preventable through early recognition of the extent of hemorrhage and ongoing blood loss.[2] The American College of Surgeons Committee on Trauma has focused on the early recognition of the extent of hemorrhage, ongoing blood loss, and likelihood of hemorrhagic shock as a centerpiece of the Advanced Traumatic Life Support course.

Shock is defined as inadequate delivery of oxygen and nutrients to tissues to maintain normal cellular function.[3] Traditional markers of shock, including systolic blood pressure (SBP) and heart rate, are not always reliable, particularly early after injury or in previously healthy patients, as systolic blood pressure may remain normal until late in the course of shock.[4] While base deficit and venous lactate levels are associated with hemorrhagic shock, these are often not readily available in the prehospital setting.[5,6] End-tidal carbon dioxide ($ETCO_2$), on the other hand, is routinely monitored and easily obtained in patients who are intubated.

End-tidal carbon dioxide is a measure of both ventilation and perfusion and can serve as a noninvasive surrogate for the measurement of cardiac output. End-tidal carbon dioxide is already commonly used by emergency medical services (EMS) providers to assess endotracheal tube (ETT) placement and monitor the quality of chest compressions during cardiopulmonary resuscitation. However, $ETCO_2$ may have greater prognostic value, particularly in patients suffering from hemorrhagic shock. Literature evaluating the association between prehospital $ETCO_2$, specifically measured via an in-line sensor on the ETT, and hemorrhagic shock is limited. Previous studies have found associations between low $ETCO_2$ and hemorrhagic shock, both via nasal cannula and ETT, in the emergency department (ED).[7–9] A recent study by Campion et al.[10] found that lower prehospital $ETCO_2$ was associated with need for massive transfusion and mortality.

In a cohort of patients who were intubated in the prehospital setting after a traumatic injury, we sought to determine if a low prehospital $ETCO_2$ could predict the presence of hemorrhagic shock upon ED arrival. Our primary objective was to determine a prehospital $ETCO_2$ level that reliably predicts the presence of hemorrhagic shock. We hypothesized that a threshold of prehospital $ETCO_2$ less than 25 mm Hg would predict the presence of hemorrhagic shock on ED arrival.

METHODS

Study Design, Population, and Setting

This was a retrospective, observational cohort study evaluating trauma patients who were intubated and ventilated by Seattle Fire Department paramedics in the prehospital setting as part of their resuscitative care from January 1, 2016, through December 31, 2019. The study a priori excluded patients who were younger than 18 years, were not intubated with an ETT, did not have continuous $ETCO_2$ waveform data, or could not be matched with the in-hospital trauma registry based on the available demographic data (Fig. 1). The study was approved by the University of Washington Institutional Review Board and adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for reporting on observational studies.[11]

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From the Department of Surgery (S.A., E.M.B.), University of Washington, Seattle, Washington; Department of Emergency Medicine (N.B., B.H., A.L., C.R.C., M.S.), University of Washington, Seattle, Washington; Department of Critical Care (J.K.), University of Washington, Seattle, Washington; Seattle Fire Department (A.L., C.R.C., M.S.), Seattle, Washington; and University of Washington School of Public Health (C.M.), Seattle, Washington.

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Address for reprints: Natalie Bulger, MS, Department of Emergency Medicine, University of Washington, Harborview Medical Center, 1835 140th AVE SE, Bellevue, WA 98005; email: nbulger@uw.edu.

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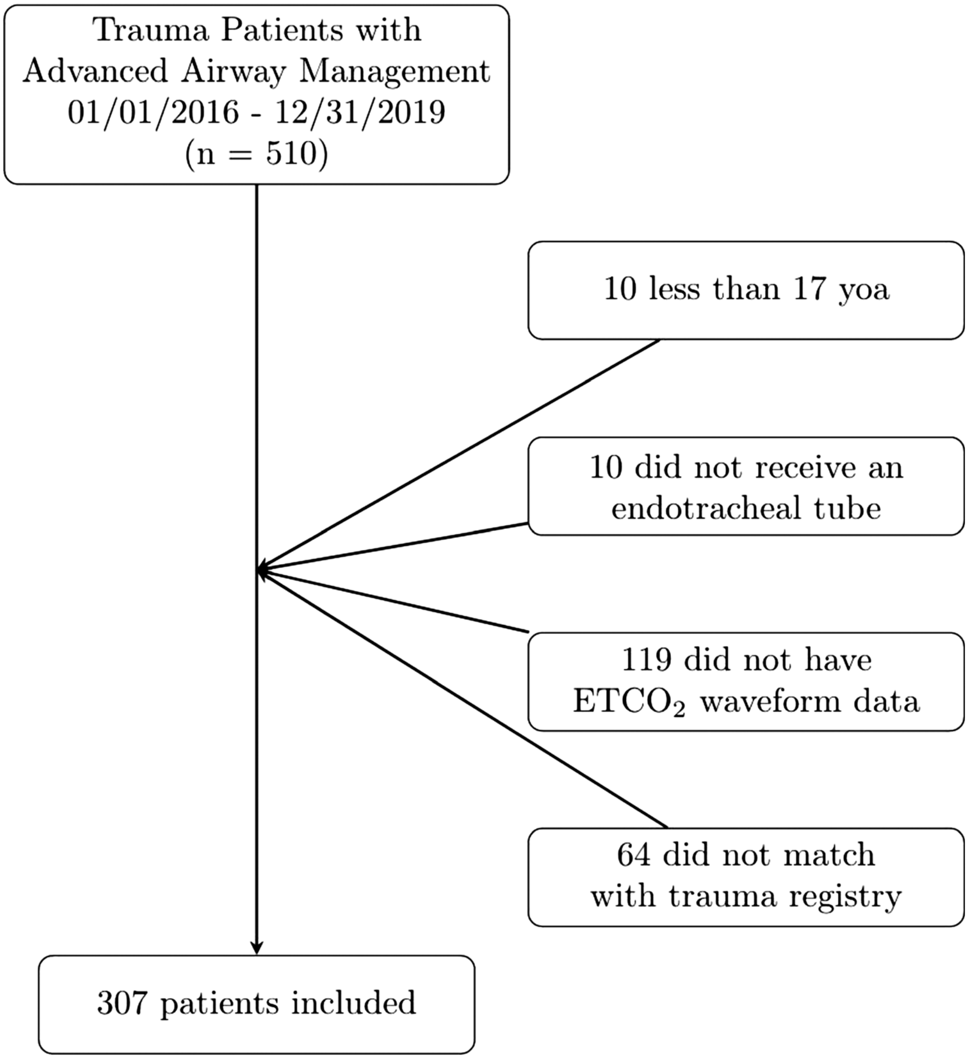

Figure 1. Inclusion criteria. Included patients were 18 years or older, received an ETT as their advanced airway, had usable $ETCO_2$ waveform downloaded from the cardiac monitors, and were matched with the in-hospital trauma registry based on available patient identifiers. Because of the changes in cardiac monitor configuration in the earlier years, there were patients who randomly did not have an analyzable $ETCO_2$ waveform.

The Seattle Fire Department is the primary provider of emergency response in the city of Seattle, with firefighter emergency medical technicians and paramedics providing basic life support and advanced life support, respectively. Paramedics use direct laryngoscopy for endotracheal intubation as the primary advanced airway, following a standardized rapid sequence intubation airway management algorithm.[12] To avoid hyperventilation among patients with suspected traumatic brain injury, paramedics have been taught to target an $ETCO_2$ range of 35 to 40 mm Hg.[13] Primary indications for intubation include inability to protect the airway from aspiration due to decreased level of consciousness, ineffective spontaneous ventilation, and concern for airway obstruction due to injury of the face or neck.

Data Variables and Collection

Continuous $ETCO_2$ data, downloaded directly from the cardiac monitor (LifePak 15; Stryker Medical, Redmond, WA), were linked with the EMS airway registry and in-hospital trauma registry based on available patient identifiers. The cardiac monitors record real-time audio, continuous electrocardiographic waveforms, continuous quantitative $ETCO_2$, peripheral arterial oxygen saturation, and continuous transthoracic impedance. Information for the airway registry is collected and maintained using Research Electronic Data Capture tools hosted at the Institute of Translational Health Sciences at the University of Washington.[14] A digital airway survey is completed following every patient encounter involving an attempted advanced airway procedure. The paramedic who managed the airway documents patient characteristics, including age and reason for intubation, method, and outcome for each placement attempt, the use of any adjunctive medications, and details related to the procedure process.[15] The airway survey is then compared with the time-synchronized audio defibrillator recording by trained data abstractors who adjudicate any differences between the airway

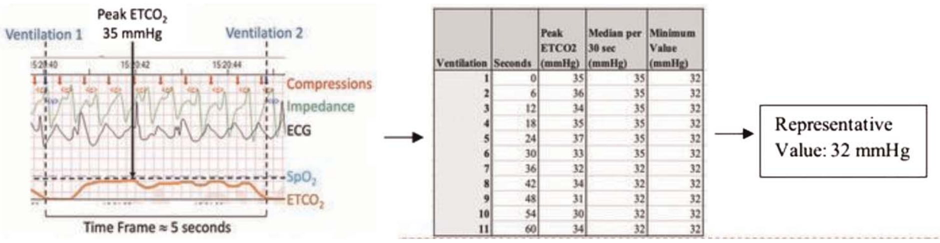

Figure 2. Representative $ETCO_2$ calculation method. A representative $ETCO_2$ value for each patient was determined in a stepwise fashion. All data were uploaded by the paramedics from the Lifepak 15 monitors to a centralized database using CODESTAT software. The continuous, raw waveform data for $ETCO_2$ were retrieved for this project. As $ETCO_2$ values vary during ventilation, the peak $ETCO_2$ was calculated for each ventilation and then the median value was determined for every 30 seconds following intubation. The minimum of these median values was then used to represent the lowest $ETCO_2$ value for this episode of care.

TABLE 1. Patient Demographics

	Overall (n = 307)	Hemorrhagic Shock (n = 128)	Nonhemorrhagic Shock (n = 179)
Male (%)	252 (82.1%)	105 (82.0%)	147 (82.1%)
Mean age (SD), y	40.3 (17.0)	41.3 (17.3)	39.6 (16.9)
ISS, ≥15 (%)	208 (67.8%)	105 (82.0%)	103 (57.5%)
Max head AIS score > 2	127 (41.3%)	43 (33.6%)	84 (47.0%)
Preintubation neuromuscular blockade			
Succinylcholine (%)	130 (42.3%)	40 (31.3%)	90 (50.3%)
Rocuronium (%)	139 (45.3%)	56 (43.8%)	83 (46.7%)
None (%)	38 (12.4%)	32 (35.0%)	6 (3.6%)
Postintubation neuromuscular blockade			
Succinylcholine (%)	1 (0.32%)	0 (0.0%)	1 (0.6%)
Rocuronium (%)	20 (6.5%)	6 (4.7%)	14 (7.8%)
None (%)	286 (93.2%)	122 (95.3%)	165 (92.2%)
Trauma type			
Penetrating (%)	103 (33.6%)	58 (45.3%)	45 (24.2%)
Blunt (%)	190 (61.9%)	70 (54.7%)	120 (67.0%)
Burn/other (%)	14 (4.6%)	0 (0.0%)	14 (7.8%)
Mean initial ED vital signs (SD)			
Systolic blood pressure	115.7 (46.0)	85.8 (50.4)	136.6 (28.0)
Respiratory rate	14.9 (6.1)	13.0 (7.8)	16.3 (4.0)
Heart rate	96.0 (37.8)	93.5 (53.1)	97.8 (21.7)
Mean initial ED laboratory values (SD)			
Lactate	5.2 (3.8)	7.4 (4.6)	3.8 (2.4)
Base deficit	6.6 (5.5)	9.4 (6.5)	4.7 (3.8)
Shock Index	0.88 (0.36)	1.1 (0.4)	0.7 (0.2)
Total GCS	3.6 (2.4)	3.0 (0.4)	3.6 (2.4)
Motor	1.5 (1.4)	1.1 (0.7)	1.5 (1.4)
Mean fluid administration (SD)			
RBCs	7.2 (9.5)	7.9 (10.0)	2.6 (2.8)
Fresh frozen plasma	6.1 (8.6)	6.7 (9.0)	2.1 (2.6)
Platelets	0.88 (1.4)	0.99 (1.4)	0.17 (0.38)
Cryoprecipitate	0.33 (0.76)	0.35 (0.80)	0.17 (0.38)
ED disposition			
Morgue (%)	34 (11.0%)	31 (24.2%)	3 (1.7%)
OR or angiography (%)	83 (27.3%)	47 (36.7%)	36 (20.1%)
ICU (%)	174 (56.7%)	49 (38.3%)	125 (69.8%)
Admitted to floor (%)	4 (1.3%)	0 (0.0%)	4 (2.2%)
Discharged (%)	12 (3.9%)	1 (0.8%)	11 (6.1%)
Mortality	83 (27.0%)	61 (47.7%)	22 (12.3%)

Demographics and characteristics of clinical care of patients who experienced significant injury, stratified by occurrence of hemorrhagic shock.
SD, standard deviation; GCS, Glasgow Coma Scale; ICU, intensive care unit; OR, operating room; RBCs, red blood cells.

report and audio recording. The trauma registry is managed by the single Level I trauma center in Seattle and contains variables pertaining to patient care both prehospital and in-hospital for patients admitted following a traumatic injury, including initial vital signs and blood gas values obtained in the ED.

Outcomes

The primary outcome was hemorrhagic shock, which was defined as transfusion of at least one unit of any blood component in the ED along with either an initial ED systolic blood pressure less than or equal to 90 mm Hg or an initial ED shock index greater than 0.9. This definition for hemorrhagic shock was developed based the enrollment criteria used in the Pragmatic, Randomized Optimal Platelet and Plasma Ratios trial, which was designed to capture a patient population likely to need a massive transfusion. The Pragmatic, Randomized Optimal Platelet and Plasma Ratios trial defined patients with severe bleeding as those who received at least one unit of any blood component within 1 hour of hospital admission and an ABC score greater than or equal to 2.[16] Deaths in the ED, who met the study definition of hemorrhagic shock, were also included. Subgroup analyses included stratification of patients based on mechanism of injury (blunt vs. penetrating), Injury Severity Score (ISS, ≥15), traumatic brain injury (head Abbreviated Injury Scale [AIS] score >2), and mortality.

Analysis

A representative $ETCO_2$ value for each patient was determined in a stepwise fashion (Fig. 2). The continuous, raw waveform data for $ETCO_2$ was exported from the CodeStat database (Stryker Medical, Redmond, WA). As $ETCO_2$ values vary during ventilation, the peak $ETCO_2$ was calculated for each ventilation using Stata/MP 16.1 (Statacorp, College Station, TX) and then the median value of those peak values was determined for each 30-second epoch following successful tracheal intubation. The minimum of these median values was then used to represent the lowest $ETCO_2$ value for this episode of care.

The median prehospital $ETCO_2$ values were compared for patients with and without hemorrhagic shock and subgroup analyses were performed stratifying patients based on mechanism of injury (blunt vs. penetrating), injury severity (ISS ≥15), traumatic brain injury (head AIS score >2), and mortality. All results were analyzed for significance using a Wilcoxon Rank Sum test. We then constructed receiver operating characteristic (ROC) curves to evaluate the ability of prehospital $ETCO_2$ to predict hemorrhagic shock and in-hospital mortality compared with initial ED lactate and initial prehospital systolic blood pressure.

We also used logistic regression to evaluate the association between prehospital $ETCO_2 < 25$ mm Hg and hemorrhagic shock on ED presentation, using prehospital $ETCO_2$ as a single categorical variable. A threshold value of 25 mm Hg was chosen to validate previous reports.[10,17,18] The model was adjusted for age, sex, and mechanism of injury. Standard errors of regression coefficients were adjusted for clustering of patients within paramedics. Analyses were performed using Stata/MP 16.1 (Statacorp, College Station, TX).

RESULTS

Characteristics of Study Subjects

Of the 510 patients with significant injury who received advanced airway management during the study period, 307 were eligible for inclusion (Fig. 1). Of these, 82% were male, 34% had a penetrating mechanism of injury, 42% were in hemorrhagic shock on ED arrival, and 27% died in the hospital (Table 1). Patients in hemorrhagic shock had higher mortality (48% vs. 12%), were more likely to have an ISS > 15 (82% vs. 58%), had a higher initial ED lactate (7.4 vs. 3.8), and a higher rate of penetrating injury (45% vs. 25%) (Table 1).

The Relationship of $ETCO_2$ and Hemorrhagic Shock

Patients in hemorrhagic shock had significantly lower minimum median $ETCO_2$ values than those not in hemorrhagic shock (26.5; interquartile range [IQR], 11.3–32.0) vs. 32.5;

TABLE 2. Median Prehospital ETCO2 Values (IQR)

	Overall (n = 307)	Hemorrhagic Shock (n = 128)	Nonhemorrhagic Shock (n = 179)	*p*
Overall	31 (24–36)	26.5 (11.3–32)	32.5 (28.5–37)	< 0.0001*
Mechanism of injury				
Penetrating (n = 103)	29 (17–34)	21 (9–32)	31.5 (28–37)	< 0.0001*
Blunt (n = 190)	31 (25.5–36)	28.5 (21–32)	32.5 (28.25–37)	< 0.0001*
ISS				
<15 (n = 99)	32 (26.5–39)	27 (9–32)	32.75 (28.5–40.5)	< 0.001*
≥15 (n = 208)	30 (22–34.75)	26 (12–32)	32 (28.5–36)	< 0.0001*
Mortality				
Alive (n = 224)	32 (28–37)	29 (24–33)	33 (29–38)	< 0.001*
Dead (n = 83)	21.5 (9–31)	12 (8–30)	27 (23–31)	0.004*
Head AIS score				
>2 (n = 127)	31 (25–36)	27.5 (21.5–34)	32.8 (27.5–36.3)	< 0.01*
≤2 (n = 180)	30 (21–35)	25 (9–32)	32 (29–38)	< 0.0001*

*Significant difference between median values as determined by Wilcoxon Rank Sum Test.

Median end-tidal carbon dioxide, with IQR, values based on the representative minimum median value generated for each patient. Values are provided for the overall cohort as well as divided into mechanism of injury, injury severity score, mortality, and head abbreviated injury score.

IQR, 28.5–37.0; $p < 0.0001$) (Table 2). This pattern was consistent when stratified by mechanism of injury, injury severity, traumatic brain injury, and mortality (Table 2). We observed a dose-response relationship. Of the 87 patients with a minimum median prehospital $ETCO_2$ 25 mm Hg, 69% were in hemorrhagic shock on ED arrival; and of the 56 patients with an $ETCO_2 \leq 20$ mm Hg, 82% were in hemorrhagic shock. The logistic regression analysis revealed that patients with prehospital $ETCO_2 < 25$ mm Hg were 3.0 times (adjusted odds ratio = 3.0; 95% confidence interval [CI], 1.1–7.9) more likely to be in hemorrhagic shock upon ED arrival than patients with $ETCO_2 \geq 25$ mm Hg.

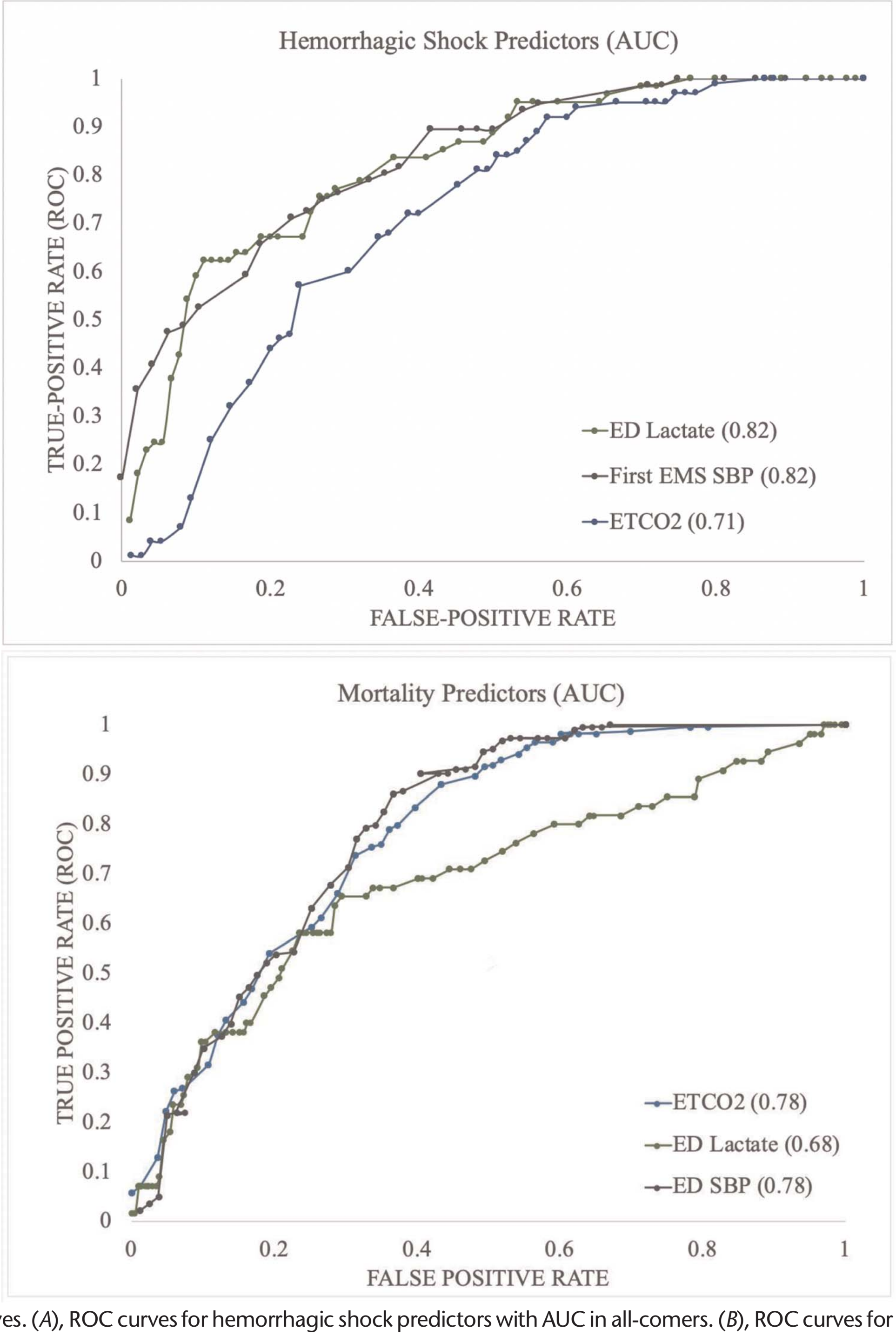

Figure 3. ROC curves. (*A*), ROC curves for hemorrhagic shock predictors with AUC in all-comers. (*B*), ROC curves for mortality predictors with AUC in all-comers.

The area under the receiver operating characteristic curve (AUC ROC) for minimum median $ETCO_2$ was 0.72 (95% CI, 0.65–0.78) for prediction of ED hemorrhagic shock (Fig. 3, Table 3). This compared favorably to first EMS systolic blood pressure and ED lactate (Fig. 3). When stratified by mechanism of injury, the AUC of the ROC curve for minimum $ETCO_2$ within penetrating trauma patients was 0.75 (95% CI, 0.65–0.84) (Table 3). When predicting mortality, the AUC for minimum median $ETCO_2$ was 0.78 (95% CI, 0.71–0.84) overall and increased to 0.89 (95% CI, 0.82–0.96) when limiting the analysis to patients suffering from penetrating trauma (Fig. 3, Table 3).

DISCUSSION

This study demonstrates an association between low $ETCO_2$ in the prehospital setting and hemorrhagic shock in the ED among a cohort of severely injured patients requiring prehospital tracheal intubation. Furthermore, prehospital $ETCO_2$ < 25 mm Hg was a predictor of hemorrhagic shock upon ED arrival. These results were consistent across patient subgroups. Thus, the continuous assessment of prehospital $ETCO_2$ may support the early identification of patients in hemorrhagic shock.

Typically, systolic blood pressure does not start to decline until the later stages of shock when the body can no longer compensate for the severe blood loss.[4] Early recognition of hemorrhagic shock is vital to prehospital decision-making, and many patients suffering from early hemorrhagic shock may be difficult to identify due to their seemingly normal traditional vital signs.[4] Improving prehospital triage for patients in occult or compensated shock can increase the likelihood of survival because of their favorable response to timely intervention.[4,5,7,9,19] Earlier identification may facilitate prehospital triage, administration of blood products, and rapid transport to an appropriate trauma center with access to key resources for hemorrhage control.[20]

Previous studies have assessed the predictive value of a variety of metrics for hemorrhagic shock including point-of-care lactate, base deficit, and shock index.[6,7,19,21,22] All of these demonstrated strong correlation in a hospital setting. While point of care lactate has been studied in the prehospital environment, it requires invasive measurements and is not readily available.[21] Traditional vital signs, such SBP and shock index, cannot be measured continuously throughout the course of care. Prehospital $ETCO_2$ is advantageous because it can be measured continuously to assess for effectiveness of interventions, as well as changes in physiology.

$ETCO_2$ is readily available in most urban EMS agencies. Our findings are consistent with previous studies of the utility of $ETCO_2$ in identifying patient need for rapid transfusion and mortality.[10,17,18] Campion et al.[10] found that lower prehospital $ETCO_2$ values were predictive of mortality and need for massive transfusion postinjury in 173 intubated trauma patients over a two-year period. Campion et al.[10] suggested that a prehospital $ETCO_2$ < 25 mm Hg was predictive of hemorrhagic shock. Wilson et al.[18] found lower prehospital $ETCO_2$ values were associated with need for transfusion or operative intervention in 105 intubated and nonintubated trauma patients over a 1-year period. Childress et al.[17] similarly found lower prehospital $ETCO_2$ predicted in-hospital mortality in intubated and nonintubated trauma patients.

Our study adds support to this body of literature and also introduces a novel method of determining the prehospital $ETCO_2$. Previous studies have used manually abstracted mean or median values across the prehospital course or an initial $ETCO_2$ once the level was stable.[10,17,18] We have developed a method which reflects the $ETCO_2$ across the prehospital course using more granular data capture and which is easily automated and replicable. An algorithm which incorporated this analytical approach, if incorporated directly into the prehospital monitors, could allow real time assessment of these values along with alerts to the paramedics when readings are consistently below a predefined threshold.

Limitations

This study is limited in its generalizability, as it reflects only intubated patients transported by a single urban EMS system with short transport times. In addition, the inability to match some EMS records with the hospital registry data, due to differing patient identifiers, could have created some selection bias. A fraction of patients received rocuronium during their course of care and may have had higher $ETCO_2$ values as a result of the ventilation target of 35 mm Hg to 40 mm Hg used by the EMS agency. Previous studies have demonstrated the challenge of identifying hemorrhagic shock patients based solely on prehospital or ED vital signs.[23,24] Thus, there is no uniform definition. We chose to use a definition which has supported enrollment in previous trials for massive transfusion and our data support that the patients evaluated were critically ill however it

TABLE 3. Area Under the Receiver Operating Characteristic Curve

Populations	All-comers (n = 307)	Penetrating (n = 103)	Blunt (n = 190)
Predictor of hemorrhagic shock, AUC (95% CI)			
$ETCO_2$	0.72 (0.65–0.78)	0.75 (0.65–0.84)	0.69 (0.60–0.77)
Initial ED lactate	0.77 (0.71–0.83)	0.80 (0.71–0.90)	0.76 (0.67–0.84)
Initial EMS SBP	0.83 (0.78–0.88)	0.86 (0.79–0.93)	0.82 (0.75–0.88)
Predictor of mortality, AUC (95% CI)			
$ETCO_2$	0.78 (0.71–0.84)	0.89 (0.82–0.96)	0.70 (0.61–0.80)
Initial ED lactate	0.68 (0.60–0.77)	0.73 (0.59–0.86)	0.67 (0.55–0.78)
Initial EMS SBP	0.78 (0.72–0.85)	0.91 (0.85–0.98)	0.69 (0.59–0.79)
			*14 burn/other mechanism

AUC ROC (95% (CI)) for three different predictors of hemorrhagic shock and mortality for all-comer, penetrating, and blunt trauma. Patients suffering burns or other mechanisms of injury were excluded.

is possible that a small number of patients meeting the definition did not have significant hemorrhage.[16] The study's limitations should be considered in the context of its strengths, including the large sample size of critically injured patients requiring prehospital intubation with a mix of penetrating and blunt trauma and a high frequency of patients in hemorrhagic shock. In addition, the granularity of the $ETCO_2$ data is greater than previous studies which allowed development of a novel analytic approach which is more reflective of the patient's entire prehospital course.

CONCLUSIONS

Patients in hemorrhagic shock upon ED arrival have significantly lower prehospital $ETCO_2$ values, and prehospital $ETCO_2$ less than 25 mm Hg is predictive of hemorrhagic shock. These data support training of prehospital and ED providers about the importance of monitoring $ETCO_2$ in this patient population. These findings suggest there is evidence for incorporating $ETCO_2$ into vital signs utilized for prehospital clinical decision making, including blood product transfusion and rapid triage to higher-level trauma centers. $ETCO_2$ has the advantage of continuous monitoring in the field which is not possible for SBP. However, the additive value of $ETCO_2$ to traditional vitals in predicting hemorrhagic shock will require further prospective study. Other future studies should focus on the value of incorporating $ETCO_2$ thresholds into both prehospital triage and trauma team activation criteria and the development of predictive algorithms that could be incorporated into prehospital monitoring devices.

AUTHORSHIP

S.A., A.L., J.K., M.S., and E.M.B. conceived the study. N.B., B.H., C.R.C. and C.M. managed the data, including quality control, as well as provided statistical advice on study design. N.B., B.H., and C.M. analyzed the data. N.B. drafted the manuscript, and all authors contributed substantially to its revision.

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DISCLOSURE

The authors declare no conflicts of interest.

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