Low End-Tidal Carbon Dioxide at the Onset of Emergent Trauma Surgery Is Associated With Nonsurvival: A Case Series

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BACKGROUND: End-tidal carbon dioxide ($Etco_2$) is a valuable marker of the return of adequate circulation following cardiac arrest due to medical causes. Previously, the prognostic value of capnography in trauma has been studied among limited populations in prehospital and emergency department settings. We aimed to investigate the relationship between early intraoperative $Etco_2$ and nonsurvival of patients undergoing emergency surgery at a level 1 academic trauma center as a case series. If there is a threshold below which survival was extremely unlikely, it might be useful in guiding decision-making in the early termination of futile resuscitative efforts.

METHODS: Following institutional review board approval, a data set was created to investigate the relationship between $Etco_2$ values at the onset of emergent trauma surgery and nonsurvival. Patients who were admitted and transferred to the operating room (OR) directly from a resuscitation bay were identified using the Ryder Center trauma registry (October 1, 2013, to June 30, 2016). Electronic records from the hospital's anesthesia information management system were queried to identify the matching anesthesia records. The maximum $Etco_2$ values within 5 and 10 minutes of the onset of mechanical ventilation in the OR were determined for patients undergoing general anesthesia with mechanical ventilation. Patients were divided into 2 groups: those who were discharged from the hospital alive (survivors) and those who died in the hospital prior to discharge (nonsurvivors). The threshold $Etco_2$ giving a positive predictive value of 100% for in-hospital mortality was determined from a graphical analysis of the data. Association of determined threshold and mortality was analyzed using the 2-tailed Fisher exact test.

RESULTS: There were 1135 patients who met the inclusion criteria. Within the first 5 minutes of the onset of mechanical ventilation in the OR, if the maximum $Etco_2$ value was ≤20 mm Hg, hospital mortality was 100% (21/21, 95% binomial confidence interval, 83.2% to 100%).

CONCLUSIONS: A maximum $Etco_2$ ≤20 mm Hg within 5 minutes of the onset of mechanical ventilation in the OR may be useful in decision-making related to the termination of resuscitative efforts during emergent trauma surgery. However, a large-scale study is needed to establish the statistical reliability of this finding before potential adoption. (Anesth Analg 2017;XXX:00–00)

Trauma is a leading cause of death in those younger than 44 years throughout the world.[1] In the United States alone, the financial toll of injuries was estimated at $671 billion in 2013.[2] Concerns regarding utilization of resources bear greatly on how to best treat trauma victims, particularly those with the gravest injuries who will succumb despite aggressive resuscitation. Therefore, early identification of patients with nonsurvivable injuries has appreciable clinical utility.[3–5]

Among trauma patients who are alive on hospital arrival, hemorrhagic shock accounts for 82% of all mortality within the first 24 hours after admission, despite ongoing resuscitation.[6] Fatal hemorrhage invariably terminates with a profound decrease in cardiac output due to hypovolemic shock. Because exhaled end-tidal carbon dioxide ($Etco_2$), measured via capnography, indirectly reflects pulmonary blood flow and cardiac output, $Etco_2$ falls during shock states. Capnography has a well-recognized value during resuscitation following cardiac arrest due to medical causes as it helps gauge the adequacy of resuscitative efforts and can herald the return of spontaneous circulation.[7] Recognizing its value in situations when adequate circulation is difficult to assess, quantitative capnography has been incorporated into American Heart Association Advanced Cardiac Support Guidelines (AHA ACLS Guidelines).

In the trauma patient population, the prognostic value of capnography has been examined in the prehospital and emergency department (ED) settings. In a group of young nonintubated patients with penetrating trauma, $Etco_2$ sampled via nasal cannulas correlated with lactate levels and was prognostic of the need for operative intervention.[8] An $Etco_2$ level of <24 mm Hg in blunt trauma patients requiring prehospital intubation was predictive of mortality.[9] An $Etco_2$ to arterial Pco_2 difference >10 mm Hg at the end of resuscitation, likewise, has been associated with mortality.[10,11]

We are unaware of any studies evaluating intraoperative $Etco_2$ at the onset of surgery immediately following patient

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transport to a level 1 trauma center as a prognostic factor for survival. The purpose of this retrospective study was to test our clinical impression that early low $Etco_2$ in mechanically ventilated patients undergoing emergency surgery for trauma is associated with nonsurvival. If a threshold $Etco_2$ value was found below which survival is highly unlikely, it would help refine the decision-making process for early termination of futile resuscitative efforts.

METHODS

The Institutional Review Boards of the University of Miami and Jackson Memorial Hospital approved this study with a waiver of informed consent.

The Ryder Trauma Center Registry was queried to identify patients who arrived in the ED resuscitation bays between October 1, 2013, and September 30, 2015, and went directly to the operating room (OR) without first being admitted to an inpatient bed. Data from the registry included patient name, medical record number, age, sex, race, ethnicity, Glasgow Coma Scale, Trauma Score, Injury Severity Score, total length of stay, in-hospital mortality, time from dispatch of emergency services to ED arrival, injury type (blunt or penetrating), and mode of transport (private or rescue vehicle). Electronic records from the hospital's anesthesia information management system (PICIS Clinical Solutions, Wakefield, MA) were queried to identify the matching anesthesia records for the emergency surgery. Matching was complex and involved multiple parameters, including patient names (many misspelled or listed as "unknown"), medical record number (some incorrectly entered or missing), dates (some incorrectly listed), OR location, and manual inspection of anesthesia records and the hospital's enterprise electronic health record (PowerChart 4.2.1; Cerner, Kansas City, MO). All patients in the trauma registry were ultimately identified, with several determined not to have gone to the OR emergently or only having a paper anesthesia record. Time-stamped $Etco_2$ values, ventilation mode, tidal volume, and peak inspiratory pressures were retrieved. The maximum $Etco_2$ values within 5 and 10 minutes of the onset of mechanical ventilation in the OR were determined for patients undergoing general anesthesia. Cases excluded from the analysis are listed in Figure 1. Patients were divided into 2 groups: those who were discharged from the hospital alive (survivors) and those who died during their hospitalization (nonsurvivors).

Data relating to intraoperative transfusion were collected for nonsurvivors who had a maximum $Etco_2$ ≤20 mm Hg within 5 minutes of the onset of mechanical ventilation. The total amount of intraoperatively transfused packed red blood cells and fresh frozen plasma (FFP) were gathered.

Statistical Methods

A power analysis was not performed as this was an exploratory retrospective case series intended to confirm our clinical impression and determine the sample size needed for a multicenter follow-up study. Patient demographics and transport times were compared using a χ^2 test with Dunn-Šidák correction for multiple comparisons among these parameters. The primary outcome was in-hospital mortality. The 2-sided Student *t* test was used to compare the differences between survivors and nonsurvivors for the maximal $Etco_2$ within 5 and 10 minutes of the onset of mechanical ventilation in the OR. The highest $Etco_2$ for a positive predictive value of 100% for in-hospital mortality was determined from a graphical evaluation of the data. Association of determined threshold and mortality was analyzed using the 2-tailed Fisher exact test. Descriptive data are presented as the mean ± SD with the interquartile range (IQR) listed for ventilation parameters. Systat version 13 (Systat Software, San Jose, CA) was used for all statistical tests. A corrected *P* value <.05 was required to claim statistical significance.

RESULTS

There were 1135 patients who met the inclusion criteria (Figure 1). Overall mortality was 13.1% (95% binomial confidence interval [CI], 11.2%–15.2%). Patients who died during their hospitalization were sicker as judged by their initial Glasgow Coma Scale, Trauma Score, or Injury Severity Score (Table 1). However, transport times from initial dispatch of the rescue team until the patient arrived in the trauma resuscitation bay did not differ between survivors and nonsurvivors (Table 1).

If the maximum $Etco_2$ value was ≤20 mm Hg within the first 5 minutes of the onset of mechanical ventilation in the OR, in-hospital mortality was 100% (21/21; 95% binomial CI, 83.2%–100%; $P < .001$; Figure 2; Table 2). If the maximum $Etco_2$ value was ≤20 mm Hg within the first 10 minutes of the onset of mechanical ventilation in OR, hospital mortality was also 100% (11/11; 95% binomial CI, 71.5%–100%; $P < .001$; Figure 3; Table 3).

Nonsurvivors with maximum $Etco_2$ ≤ 20 mm Hg within 5 minutes of the onset of mechanical ventilation in the OR had a mean respiratory rate of 12.9 ± 3.7 breaths per minute (IQR, 10–15 breaths per minute), and a mean tidal volume of 476 ± 140 mL (IQR, 413–558 mL). There was no difference in minute ventilation between patients who expired in the OR (all with maximum $Etco_2$ ≤20 mm Hg within 5 minutes of the onset of mechanical ventilation) and those who left the OR alive, 6.4 ± 2.0 L/min vs 6.5 ± 1.7 L/min, respectively ($P = .83$). The difference between the means of the maximum $Etco_2$ within 5 minutes of the onset of mechanical ventilation in the OR of nonsurvivors and survivors was −9.0 mm Hg (95% CI, −10.2 to −7.7 mm Hg; $P < 10^{-6}$).

Of the patients with maximum $Etco_2$ ≤20 mm Hg within 5 minutes of the onset of mechanical ventilation in the OR, the majority died in the OR, and none survived >3 days postoperatively (Table 4).

Among the 21 nonsurvivors with maximum $Etco_2$ ≤20 mm Hg within 5 minutes of the onset of mechanical ventilation in the OR, 80% (N = 17) had damage control laparotomy and thoracotomy, 15% (N = 3) underwent thoracotomy only, and 5% (N = 1) underwent laparotomy only.

Blood Product Use

Among the 21 patients who had a maximum $Etco_2$ ≤20 mm Hg within 5 minutes of the onset of mechanical ventilation in the OR (all of whom were nonsurvivors), the average amounts of packed red blood cells and FFP transfused were 9.4 ± 9.8 units and 5.3 ± 5.6 units, respectively. We were unable to determine how much of this blood product use might have been avoided had resuscitative efforts been

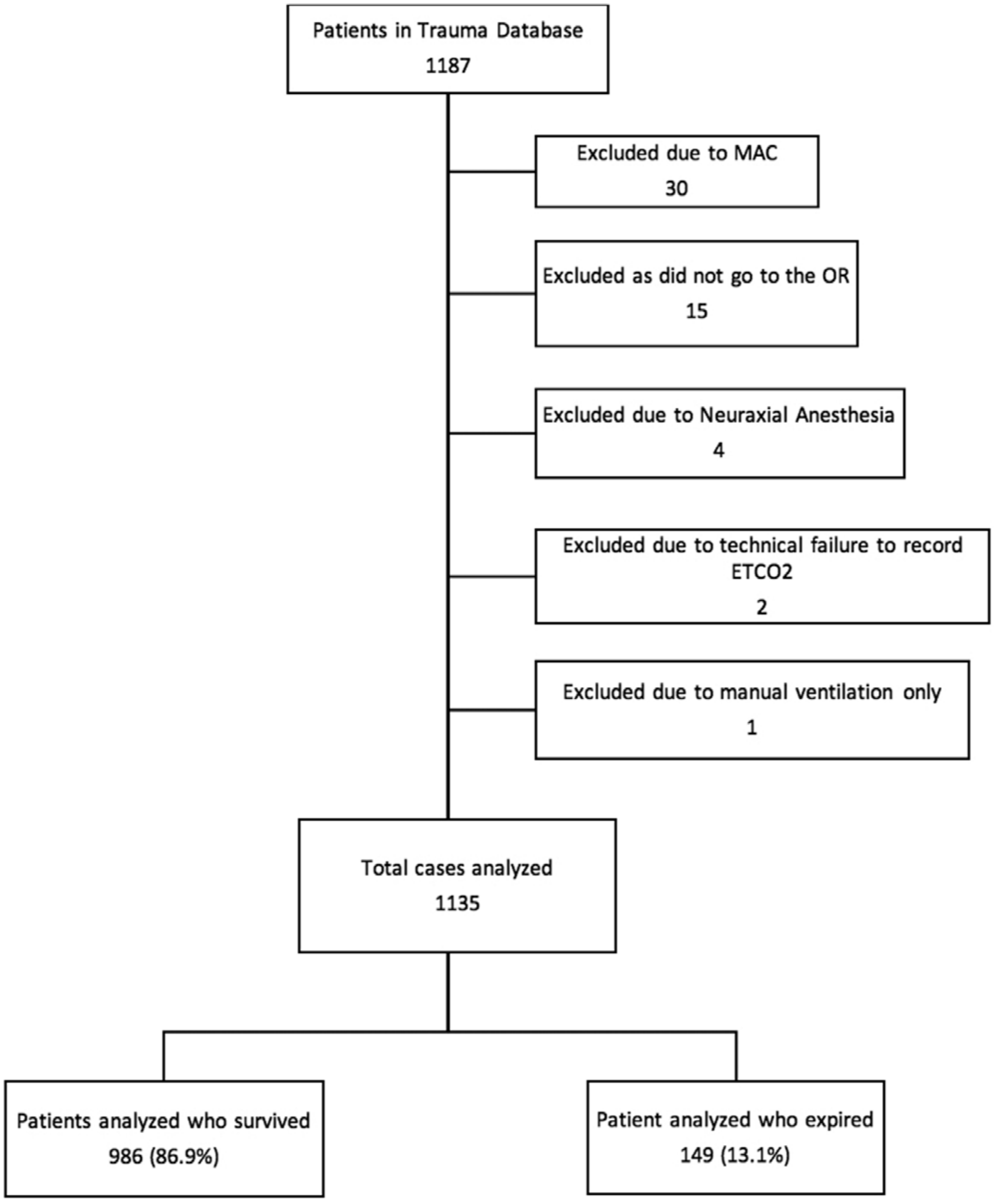

Figure 1. Flow diagram of patients included in the study. $Etco_2$ indicates end-tidal carbon dioxide concentration; MAC, monitored anesthesia care; OR, operating room.

Table 1. Patient Demographics and Transport Information

Parameter	Survived N[a] Mean ± SD	Died N[a] Mean ± SD	Difference Died – Survived	Difference 95% CI	*P* Value[b]
Age (y)	986	149			
	36.5 ± 17.0	42.1 ± 20.4	5.7	2.2 to 9.1	.007
GCS	804	137			
	13.9 ± 2.8	8.2 ± 5.1	−5.8	−6.6 to −4.9	$<10^{-6}$
Trauma Score	754	119			
	4.9 ± 2.6	7.5 ± 1.0	−2.6	−3.1 to −2.1	$<10^{-6}$
ISS	984	149			
	15.5 ± 13.0	44.0 ± 18.5	28.4	25.3 to 31.5	$<10^{-6}$
Dispatch to ED Time (min)	745	127			
	29.0 ± 14.3	30.2 ± 26.6	1.2	−3.6 to 5.9	.993

Abbreviations: CI, confidence interval; ED, emergency department; GCS, Glasgow coma score; ISS, Injury Severity Score.
[a]There were 149 nonsurvivors and 986 survivors among the 1135 patients studied. Data were missing for some patients, as indicated by the varying values of N for each row.
[b]Dunn-Šidák corrected for multiple comparisons.

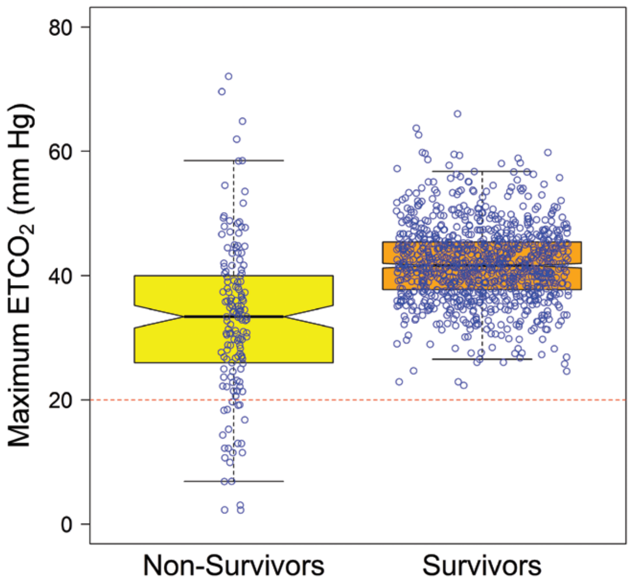

Figure 2. Maximum end-tidal carbon dioxide ($Etco_2$) within 5 minutes of the onset of mechanical ventilation in the operating room (OR). Box plot with data points overlaid. The hinges represent the first and third quartiles, the notches represent the 95% confidence interval (CI) of the median, and the whiskers extend to 1.5 × interquartile range. The red dotted line is at 20 mm Hg $Etco_2$. All patients who had a maximum $Etco_2$ ≤20 mm Hg within 5 minutes of the onset of mechanical ventilation in the OR expired. All surviving patients had an $Etco_2$ >20 mm Hg within 5 minutes of mechanical ventilation in the OR. The difference between the means of the maximum $Etco_2$ was −9.0 mm Hg (95% CI, −10.2 to −7.7; $P < 10^{-6}$).

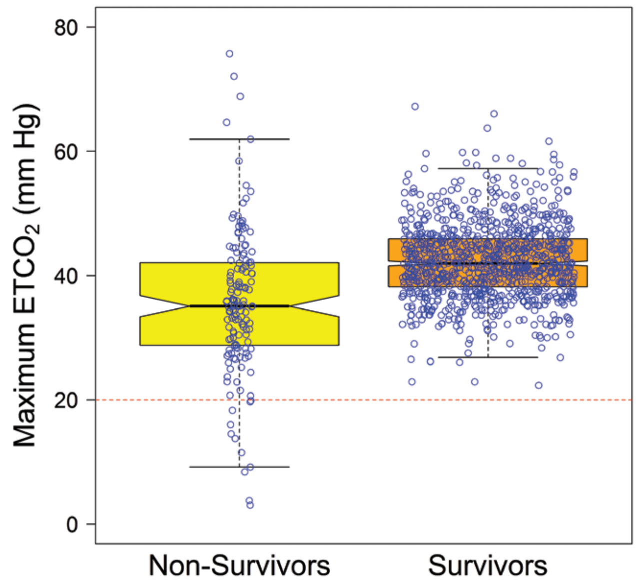

Figure 3. Maximum end-tidal carbon dioxide ($Etco_2$) within 10 minutes of the onset of mechanical ventilation in the operating room (OR). Box dot plot with data points overlaid. The hinges represent the first and third quartiles, the notches represent the 95% confidence interval (CI) of the median, and the whiskers extend to 1.5 × interquartile range. The red dotted line is at 20 mm Hg $Etco_2$. All patients who had a maximum $Etco_2$ ≤ 20 mm Hg within 10 minutes of the onset of mechanical ventilation in the OR expired. Maximum $Etco_2$ ≤ 20 mm Hg within 10 minutes of the onset of mechanical ventilation in the OR was associated with 100% mortality. All surviving patients had an $Etco_2$ >20 mm Hg within 10 minutes of starting mechanical ventilation in the OR. The difference between the means of the maximum $Etco_2$ was −6.3 mm Hg (95% CI, −7.5 to −5.0; $P < 10^{-6}$).

Table 2. Association of Hospital Outcome With the Maximum $Etco_2$ mm Hg Within 5 Min of the Onset of Mechanical Ventilation in the OR

	Hospital Outcome[b]	
$Etco_2$[a]	Died	Survived
≤20	21	0
>20	128	986

Abbreviations: $Etco_2$, end-tidal carbon dioxide; OR, operating room.
[a]Maximum $Etco_2$ mm Hg within 10 minutes of the onset of mechanical ventilation in the OR.
[b]P < .0001 by Fisher's exact test (2-tailed).

Table 3. Association of Hospital Outcome With the Maximum $Etco_2$ mm Hg Within 10 Min of the Onset of Mechanical Ventilation in the OR

	Hospital Outcome	
$Etco_2$[a]	Died[b]	Survived
≤20	11	0
>20	138	986

Abbreviations: $Etco_2$, end-tidal carbon dioxide; OR, operating room.
[a]Maximum $Etco_2$ mm Hg within 10 minutes of the onset of mechanical ventilation in the OR.
[b]P < .0001 by Fisher's exact test (2-tailed).

terminated early, because transfusion documentation frequently is entered into the record after the fact, thus precise timing could not be validated.

DISCUSSION

Our data indicate that an $Etco_2$ ≤20 mm Hg within 5 minutes of the onset of intraoperative mechanical ventilation after transfer of the patient from the resuscitation bay to the OR was associated with nonsurvival. There was a loss of sensitivity but no improvement in specificity when using a 10-minute interval for $Etco_2$ ≤20 mm Hg. A potential explanation for our findings is that a sustained significantly decreased level of $Etco_2$ that persists despite aggressive resuscitation may reflect a profound degree of circulatory and physiologic derangement precluding successful resuscitation. Over the 12 months since the data in the study were analyzed, among 403 patients similarly

Table 4. Days to Death in Patients With Maximum $Etco_2$ ≤20 mm Hg Within 5 Min of the Onset of Mechanical Ventilation in the OR

Number of Days to Death[a]	Number of Patients
0	12
1	6
2	2
3	1
>3	0

Abbreviations: $Etco_2$, end-tidal carbon dioxide; OR, operating room.
[a]Measured from OR arrival among the 21 patients with $Etco_2$ ≤20 mm Hg within 5 minutes of the start of mechanical ventilation in the OR.

presenting to the Ryder Trauma Center, none of the 345 survivors had an initial $Etco_2$ ≤20 mm Hg. However, our data are underpowered to generalize the accuracy of a threshold of 20 mm Hg or the precise interval to be considered as part of the decision-making process to terminate resuscitative efforts and will require confirmation at other centers before potential adoption. To have a binomial 95% upper confidence limit (UCL) of <1% for the misidentification of a trauma survivor based on $Etco_2$ ≤20 mm Hg within 5 minutes of the onset of mechanical ventilation in the OR, a sample size of 372 survivors would be needed at each hospital, assuming 0 survivors were misidentified in the sample (ie, with $Etco_2$ ≤20 mm Hg). If one wished to have a 99% UCL of <1%, 530 survivors would be required. If 1 survivor were allowed to be misidentified, the corresponding 95% and 99% UCL for misidentified survivors <1% would be 560 and 750 patients, respectively. These sample sizes can be used, in conjunction with the number of patients at a trauma center who go directly to the OR, along with the local hospital survival rate, to estimate the number of years of data required to participate in such a multicenter study.

Notably, there was no difference in the transport time (approximately 30 minutes) from the scene of injury to the trauma center between survivors and nonsurvivors. Therefore, the low $Etco_2$ primarily points to profound cardiopulmonary derangement and severity of the injury, as opposed to reflecting delayed retrieval or long transport times. For health care systems with a less rapid delivery of trauma victims to facilities with the capability for immediate resuscitation and surgical intervention, a different $Etco_2$ threshold predictive of nonsurvival is possible, reflecting a longer interval during which the cardiac output was severely depressed.

The mean difference between the maximum $Etco_2$ levels within 5 minutes of the onset of intraoperative mechanical ventilation in nonsurvivors and survivors of trauma was substantial (−9 mm Hg), indicating an overall relationship between low $Etco_2$ and mortality (Figure 1). A recent study done on nonintubated trauma patients in an ED showed minimal difference in $Etco_2$ among various degrees of injury severity, but was underpowered for primary outcome and the patients studied had a significantly lower injury severity than our patient population.[12]

A study of blunt trauma patients intubated in the prehospital settings demonstrated that $Etco_2$ <25 mm Hg measured 20 minutes after intubation was associated with 95% in-hospital mortality.[9] Similar studies demonstrated an association of low $Etco_2$ values with mortality in various trauma groups, but none identified a threshold value below which resuscitative efforts may be futile.[8,10,12] More importantly, the previous investigations were performed in a prehospital setting or ED, rather than in an OR, as in our study. These environments are unlikely to have the treatment modalities, expertise, and man power available in the OR of dedicated trauma hospital.[13]

While previous studies have reported a correlation between low values of $Etco_2$ and the severity of injury,[8–10] our data suggest that capnography might be useful to guide decision-making regarding termination of aggressive resuscitative efforts in the OR.

Resuscitation of severely injured patients requires extensive human and material resources. We could not estimate overall hospital costs attributed to resuscitation of patients with $Etco_2$ <20 mm Hg who expired. In addition, we could not account for the opportunity cost of a trauma team working on these patients, wherein another patient could potentially could benefited from their care. Nonetheless, we were able to examine blood product utilization in nonsurvivors with low $Etco_2$, which was substantial. Sustainable transfusion practices in trauma patients are essential to maintain adequate stocks of blood products. In the initial stages of massive transfusion protocol, prethawed or never-frozen universal donor AB plasma is frequently used to ensure early and adequate hemostatic resuscitation. AB FFP has a limited donor pool of <4% of the US population, thus imposing strain to maintain an adequate supply for massive transfusion protocols in many hospitals.[14] Early and appropriately validated detection of nonsalvageable patients may reduce unnecessary use of resuscitative resources that are in limited supply.

Given our small sample size, it is premature to recommend clinical adoption of an $Etco_2$ ≤20 mm Hg within 5 minutes of the onset of intraoperative mechanical ventilation for early termination of resuscitative efforts in trauma patients. A multicenter study confirming our findings would be required before this kind of recommendation could be made. Meanwhile, if such patients present to the OR with severe traumatic injuries accompanied by low $Etco_2$, the potential for irreversible physiologic changes should be appreciated and current institutional practices followed.

There are several limitations to this study. First, it was performed at a single, freestanding urban academic trauma center with fellowship-trained trauma surgeons and a dedicated division of trauma anesthesiology. Advanced resuscitative techniques such as hemostatic resuscitation, massive transfusion protocols, resuscitative thoracotomy, damage control surgery, early central vascular access and monitoring, and viscoelastic coagulation testing are routinely used. Overall trauma mortality rate at our institution is approximately 7%, similar to other level 1 trauma centers accredited by American College of Surgeons.[15,16] Thus, the severity of the injuries experienced by our patients is likely comparable to other, similar trauma hospitals. A second limitation is that our local emergency transport system has relatively short retrieval times (approximately 30 minutes), even comparing to advanced emergency medicine services servicing other trauma centers, where median transport times up to 1 hour have been reported.[17] Thus, patients similar to the critically injured, moribund patients who arrive alive to our trauma resuscitation bay could die in transit elsewhere. This process of natural selection might result in higher overall survival in patients who survive the longer transport times. However, mortality might be increased in marginal patients who arrive alive but who had a prolonged course of hypovolemic shock, leading to irreversibility.[17]

CONCLUSIONS

$Etco_2$ level ≤20 mm Hg within 5 minutes of the onset of mechanical ventilation in the OR was associated with nonsurvival in trauma victims undergoing immediate surgery following resuscitation at a dedicated trauma hospital. Acceptance of this threshold for termination of resuscitation efforts should be deferred pending confirmation at other level 1 trauma centers in a sufficiently large sample to ensure statistical reliability.

DISCLOSURES

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