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Detailed Description of all Deaths in Both the Shock and Traumatic Brain Injury Hypertonic Saline Trials of the Resuscitation Outcomes Consortium

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Abstract

Objective—To identify causes and timing of mortality in trauma patients to determine targets for future studies.

Summary Background Data—In trials conducted by the Resuscitation Outcomes Consortium (ROC) in patients with traumatic hypovolemic shock (shock) or traumatic brain injury (TBI), hypertonic saline failed to improve survival. Selecting appropriate candidates is challenging.

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Methods—Retrospective review of patients enrolled in multicenter, randomized, trials performed 2006–2009. Inclusion criteria were: injured patients, age ≥ 15 years with hypovolemic shock (systolic blood pressure (SBP) ≤ 70 mm Hg or SBP 71–90 mm Hg with heart rate ≥ 108) or severe TBI [Glasgow Coma Score (GCS) ≤ 8]. Initial fluid administered was 250 mL of either 7.5% saline with 6% dextran 70, 7.5% saline or 0.9% saline.

Results—2061 subjects were enrolled (809 shock, 1252 TBI) and 571 (27.7%) died. Survivors were younger than non-survivors [30(IQR 23) vs 42(34)] and had a higher GCS, though similar hemodynamics. Most deaths occurred despite ongoing resuscitation. Forty six percent of deaths in the TBI cohort were within 24 hours, compared with 82% in the shock cohort and 72% in the cohort with both shock and TBI. Median time to death was 29 hours in the TBI cohort, 2 hours in the shock cohort, and 4 hours in patients with both. Sepsis and multiple organ dysfunction accounted for 2% of deaths.

Conclusions—Most deaths from trauma with shock or TBI occur within 24 hours of from hypovolemic shock or TBI. Novel resuscitation strategies should focus on early deaths, though prevention may have a greater impact.

INTRODUCTION

Traumatic injury remains the leading cause of death among North Americans aged 1–44 years, causing over one-third of deaths in 1–19 year olds.¹ These deaths, 11 per 100,000 population in the USA alone, are responsible for more years of potential life lost before age 65 than any other cause, including cancer and heart disease. The costs in terms of lost work and long-term morbidity are enormous. Common mechanisms of injury include: motor vehicle crashes, falls, and assault.

The most common causes of death are hemorrhagic shock and traumatic brain injury (TBI). In 1983, Trunkey described a trimodal distribution of death from trauma.² The earliest deaths include patients who rapidly exsanguinate or have irreparable injuries. These patients die within 60 minutes of injury from lacerations of the brain, brainstem, spinal cord, or major vessels. The second group includes patients who die over the ensuing several hours from hemorrhage and severe TBI. Late deaths, at 1–5 weeks, are from infection and multiple organ dysfunction syndrome (MODS). A great deal of research subsequently went into prevention and treatment of the systemic inflammatory response syndrome (SIRS), which was thought to cause these late deaths. As trauma systems and intensive care units have evolved, it seems that the number of patients in the latter group has decreased, despite the lack of mechanism-based therapies to prevent or treat SIRS and MODS.

Defining the timing and causes of death from trauma is critical for determining where to focus future research efforts. Focused, high-yield research is even more important as research budgets decrease with current public-sector financial constraints.

The Resuscitation Outcomes Consortium (ROC) was developed to conduct out-of-hospital and early hospitalization research to improve clinical outcomes in patients with cardiopulmonary arrest or severe traumatic injury. The first two interventional trauma trials simultaneously conducted by ROC tested the hypothesis that out-of-hospital administration

of hypertonic saline would improve outcome from severe hypovolemic (hemorrhagic) shock or from severe TBI, respectively. The hypothesis was that hypertonic fluids (7.5% saline with or without 6% dextran 70) could restore tissue perfusion with less fluid, improve cerebral perfusion with reduced intracranial pressure, and modulate the inflammatory response to decrease the risk of MODS.

Although both studies were discontinued for futility, the ROC investigators have utilized this unique, prospectively obtained dataset to better define the patient populations in order to optimize planning of future clinical trials.

This secondary analysis of the hypertonic saline studies presented herein includes all patient deaths. The hypothesis was that most deaths would be within 24 hours, with hemorrhagic shock and TBI being the most common causes. We further hypothesized that there would be few late deaths and that these deaths would be after life-sustaining care was withdrawn.

METHODS

ROC Trial Overview

The ROC hypertonic saline trials involved 11 regional centers in the USA and Canada between 2006 and 2009.^{3,4} One hundred fourteen emergency medical services agencies were involved. The intervention involved administration of the study fluid (7.5% saline [hypertonic saline], 7.5% saline-6% dextran 70 [hypertonic saline-dextran], or 0.9% saline [normal saline]) in a randomized, double-blind fashion. With the exception of the study fluid, the management of the subjects was determined by the treating physicians based upon national guidelines for trauma care.⁵

The studies were conducted under the United States regulations for Exception from Informed Consent for Emergency Research (21 CFR 50.24) and the Canadian Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. The protocol was reviewed and approved by the US Food and Drug Administration and Health Canada. The protocol was also approved by all the institutional review boards (United States) and research ethics boards (Canada) in the communities in which the research was conducted. Consent was obtained from the subject or the subjects' legally authorized representative for continuation in the trial after hospital arrival.

Subjects

Subjects were to be included in the hypovolemic shock study if they had evidence of hypovolemic shock (systolic blood pressure <70 mm Hg or 71–90 mm Hg with heart rate >108 beats per minute). Subjects were to be included in the TBI study if they suffered blunt TBI with an early Glasgow Coma Scale (GCS) of <8, and did not have evidence of hypovolemic shock. The GCS we determined in the absence of neuromuscular blockade and before intubation. Subjects with both hypovolemic shock and TBI were to be included in the hypovolemic shock study. For the primary trial analyses, inclusion in either the hypovolemic shock or TBI study was determined based on the field medic's intent at the time a study bag was opened, regardless of whether the subject met inclusion criteria.

Exclusion criteria for both trials were: age < 15 years, ongoing prehospital cardiopulmonary resuscitation (CPR), administration of >2000ml crystalloid or any colloid or blood products prior to enrollment, severe hypothermia (<28°C), drowning, asphyxia due to hanging, burns > 20% total body surface area, isolated penetrating head injury, inability to obtain intravenous access, time of dispatch call received to study intervention >4 hours, known pregnancy, and known prisoners. Inter-facility transfers were also excluded.

Outcome Variables

For the hypovolemic shock study,⁴ the primary outcome variable was 28-day survival. For the TBI study,³ the primary outcome measure was 6-month neurologic outcome based on the Glasgow Outcome Scale Extended (GOSE), dichotomized to good outcome (GOSE >4) or poor outcome (GOSE <4).

Trial Outcome

Both trials were discontinued early by the Data Safety Monitoring Board for futility. Prior to study termination, 895 subjects were enrolled in the hypovolemic shock cohort and 1331 subjects in the TBI cohort. A total of 91 subjects were randomized but did not receive study fluid. A total of 853 subjects in the hypovolemic shock study and 1282 subjects in the TBI study were included in the final, primary analyses.

Data Analysis

This secondary analysis includes all subjects who died in either of the hypertonic saline trials. Subjects were divided into 3 cohorts: hypovolemic shock, TBI, and both hypovolemic shock and TBI, recognizing that the latter subjects would have been enrolled in the hypovolemic shock study. We excluded subjects who 1) had been enrolled in the original trials, but did not meet the inclusion criteria for those trials (n=71), regardless of the fact that they were included in the primary trial intention-to-treat analysis, 2) subjects who had a bag opened, but fluid was not given (n=87), and 3) subjects whose primary cause of death was not trauma (n=3).

For each subject, data obtained from the ROC database included the timing of death and the primary cause of death, which was designated as hypovolemic shock, sepsis, hypoxia, cardiac dysfunction, TBI, anoxic brain injury, multiple organ failure, pulmonary embolism, unknown, or other. The local investigators were instructed to utilize autopsy data (if available), death certificate, or death summary for determining the cause of death. If there were further questions, they were asked to consult with the treating physicians. There were 47 subjects for whom the cause of death listed as “cardiac dysfunction” and 56 subjects with a diagnosis of “other”. The case report forms for these subjects were reviewed in detail to determine if a more appropriate cause of death should be used for analysis. For example, if the cause of death was listed as “cardiac dysfunction”, but the subject received a massive transfusion, the presumption was that the appropriate cause of death was hypovolemic shock. The term “other” was maintained for subjects who died from an identified cause that was not on the case report form. The cause of death for all but 15 of these subjects was revised for the current analysis.

Data analysis was performed in S-PLUS (version 6.2.1), c (2003), Insightful Corporation, Seattle, WA.

RESULTS

There were a total of 571 subjects from the combined hypertonic saline trials who died. (Table 1) This included 81 with shock, 335 with TBI, and 155 with both. Approximately three quarters of the subjects were male. The most common mechanism of injury was motor vehicle crash (29%). Thirteen percent had penetrating trauma. Across all cohorts, the survivors were younger [median 30 (IQR 23)] than non-survivors [median 42 (IQR 34)] and had a higher GCS [median 7 (IQR 8) vs 3 (2)]. For the TBI cohort, 85% had evidence of TBI on head computed tomography.

Table 2 details the timing of death by cohort. The majority of deaths in the shock cohort occurred within 24 hours (82.7%) compared to deaths in the TBI cohort (46.3%). Figure 1 plots the Kaplan-Meier survival curves for each cohort. Median time to death was 29 hours in the TBI cohort, 2 hours in the shock cohort, and 4 hours in patients with both. The most common causes of death for subjects in the hypovolemic shock and TBI cohorts were hypovolemic shock (72.0%) and TBI (75.9%) respectively (Table 4).

Across all 3 cohorts 96% of patients who died of hypovolemic shock died within 24 hours (Table 3 and Table 4). Half (52%) of the subjects who died of TBI died within 24 hours while 75% died within 72 hours. Overall, 73% of deaths occurred within 72 hours. The later deaths were mostly secondary to TBI (n=89). Other causes of late death included anoxic brain injury (n=17), sepsis (n=5) and MODS (n=5), as quantified by the Multiple Organ Dysfunction Score.⁶

Overall, 3% of the deaths occurred in the field and 22% in the ED. Of the subjects who died in the hospital after admission, 62% had life-sustaining care withdrawn prior to death while 38% died with ongoing resuscitative efforts. Six percent of patients died after discharge. (Table 5)

DISCUSSION

In this secondary analysis of a large, prospectively acquired research dataset the most common causes of death from trauma were hemorrhage and TBI. This is not a surprising finding since the primary trials were designed to enroll patients with either shock or TBI. What's more significant are the findings that the overwhelming majority of deaths from hemorrhage occurred within 24 hours, and those from TBI within 72 hours. Late deaths were rare. Sepsis and MODS caused only 2% of deaths. These findings challenge the trimodal distribution of deaths expounded by Trunkey² and have important implications for future trauma trials.

In 1977, Baker, et al, found that most trauma patients who died were under 50 years of age.⁷ The most common causes of injury were gunshot wounds or falls. Most of the deaths occurred at the scene. For those who survived to the hospital, most deaths in the first 2 days

were from TBI. Later deaths were mainly due to sepsis and MODS. This data led to the proposed trimodal timing of deaths from trauma described by Trunkey.²

Since our study excluded patients undergoing CPR, we excluded the patients who would have been in Trunkey's first group, who experienced immediate death with presumably irreparable injuries. The most meaningful way to decrease the risks for immediate death from trauma is through trauma prevention. Novel resuscitation strategies may have an impact in the future.

In Trunkey's paradigm, the vast majority of deaths in our study would have fallen into his second group, patients who die within the first hours or days post-injury with very few falling into the late death group. In contrast to this paradigm, we found that the late deaths from infection and MODS were rare. It seems that with maturation of emergency medical services and regional trauma systems, these late deaths are becoming more and more rare. In fact, the risk of MODS in all trauma patients seems to be decreasing.⁸

Sauaia, et al,⁹ examined all trauma-related deaths in Denver in 1992. They found that of 289 deaths, 34% were immediate, 53% in the first 48 hours, 13% after 48 hours and 9% of deaths after 7 days. The most frequent causes of death were TBI and hemorrhagic shock, though nearly two-thirds of the late deaths were from MODS, consistent with the Trunkey paradigm.

Meislin, et al,¹⁰ reviewed all deaths in a geographically diverse county in Arizona from 1991–93. They found that 52% of deaths occurred at the scene. Most of the remaining deaths occurred within 48 hours, but still about one quarter of the deaths occurred after 48 hours and 15% occurred after 1 week. The most common cause of death was TBI, followed by hemorrhage, even for the late deaths. The high number of out-of-hospital deaths is likely related to the rural environment and delay of care.

A decade later, Demetriades, et al,¹¹ studied trauma deaths in Los Angeles. They found that half the deaths occurred in the first hour. Eighteen percent of the deaths occurred between 1 and 6 hours after injury. Another 19% of deaths occurred before 72 hours. Thirteen percent of deaths occurred after 72 hours, 8% after 1 week. They noted a clear distinction between patients who suffered penetrating vs blunt injuries. Patients with penetrating injury were more likely to die within the first hour after injury and less likely to suffer a late death. During a similar timeframe, Stewart, et al,¹² found that 46% of patients who died underwent CPR in the field. Fifty two percent of deaths were within 12 hours of injury, 74% within 48 hours, and 86% within 7 days. The most common cause of death was central nervous system (CNS) trauma, followed by irreversible shock and combined shock and CNS injury. Multiple organ failure accounted for 9% of deaths. They recommended that the best approach to decreasing trauma deaths is injury prevention.

More recently, McGwin, et al,¹³ examined the timing of trauma deaths before and after the implementation of a regional trauma system. Even before the system was implemented, only 8% of deaths occurred after 1 week. This number decreased to 4% with the trauma system. At the same time, the number of immediate deaths increased from 51% to 56%. Before establishment of the trauma system, 10% of deaths occurred after 72 hours, compared to 7%

afterwards. Their data is confounded by changes in the patient demographics, including age, sex, race and mechanism of injury.

A review of military casualties between 2001 and 2011 found that 87% of deaths occurred before the individuals reached surgical care, with non-survivable injuries.¹⁴ Hemorrhage was the most common cause of death. The authors recommend, similar to Stewart, et al,¹² that prevention is the only way to significantly decrease the number of trauma deaths.

Although the ROC studies were different than these retrospective analyses in that subjects had to be alive upon arrival of EMS and have evidence of shock or TBI to be enrolled, potentially skewing the causes of death, it's worthwhile to consider comparisons. To do this, it is important to focus on patients who did not suffer immediate death in these studies as these patients were to be excluded from the ROC trials. Of patients who survived greater than 1 hour, Sauaia, et al,⁹ found that 19% of deaths occurred after 48 hours. Meislin, et al,¹⁰ found that 32% of deaths occurred after 48 hours. Demetriades, et al,¹¹ found that 26% of deaths occurred after 72 hours. McGwin, et al,¹³ found that 16% of deaths occurred after 72 hrs. In the ROC studies, we found that 17% of deaths in the shock or combined shock/TBI cohorts were after 72 hours compared to 33% in the TBI cohort. Some of the differences between studies could reflect the different distributions of blunt vs penetrating trauma, geography (urban vs rural), and maturation of the trauma system.

Trauma patients have also changed over time. For example, regarding mechanisms of injury, the rate of fatal falls, particularly in the elderly, is increasing, accounting for one fifth of the deaths in the hypertonic saline trials.¹⁵⁻¹⁸ In one study by Hu, et al,¹⁶ there were increased rates of death from motorcycle crashes and machinery, while deaths from motor vehicle occupant injuries have decreased. They also found significant differences amongst states.

Hospital mortality data does not paint the complete picture of death from trauma. Utilizing a statewide trauma registry, Davidson, et al,¹⁹ examined factors that influenced long-term survival. Discharge to a skilled nursing facility in patients over 30 years of age, severity of TBI, Injury Severity Score, Functional Independence Measure, and mechanism of injury being fall influenced mortality. Type of insurance also had an impact.

Another confounding issue in trauma outcome involves regional differences in the incidence and outcomes of severe traumatic injury, including both blunt and penetrating mechanisms. In a large, prospective, observational study conducted by the ROC investigators,²⁰ half of the deaths occurred at the scene, presumably from non-survivable injuries. The specific patient or center-related factors that cause this variability are yet to be elucidated. Suggested factors include prehospital and Emergency Department resuscitation protocols, timeliness of operative intervention, and ICU protocols. For those who survive to the hospital, these findings suggest that there is potential for increased survival from trauma at high-performing centers, with significant public health implications.

This study has limitations that should be considered. First, patients who were dead at the scene were not enrolled, thus excluding most of the patients in the immediate death group described by Trunkey.² Second, because the 2 hypertonic saline trials enrolled patients with hemorrhagic shock and TBI, we can't comment on the totality of potentially lethal trauma at

these ROC sites. Third, although there were no statistically significant effects of the study fluids on outcomes, there is a chance that participation in the studies affected outcomes. In the shock study in particular, there was a trend toward increased early mortality in subjects who received hypertonic saline.⁴ Possible explanations include increased bleeding caused by more rapid increases in blood pressure in these groups. Another possibility is that the rapidly improved hemodynamics secondary to hypertonic saline led to a delay in the recognition of shock, which could have influenced the rapidity of interventions to obtain hemostasis. Fourth, the actual cause of death may not be clear in some patients, particularly those who died rapidly. Routine autopsy data would have been helpful, but we did use autopsy data when available. Fifth, most patients who died in the hospital did so after withdrawal of life-sustaining care. As these end-of-life decisions are affected by physician, patient and family biases, we can't be certain that the patients were destined to die. The decision to withdraw life-sustaining therapies carries the risk of creating a self-fulfilling prophecy. The fact that the practice of withdrawing life-sustaining care has evolved considerably since the time of Trunkey's original paper² could, in part, explain some of the differences we found in the timing of deaths. We suspect that this would not have changed the number or causes of death, but more work in this area is needed. We would encourage other researchers in this area to include more information on withdrawal of life-sustaining care rather than just reporting mortality.

The findings in this study are important for the development of future trials of trauma patients with hemorrhagic shock or TBI. Most deaths from trauma with shock or TBI occur within 24 hours from hypovolemic shock or TBI. Novel resuscitation strategies should focus on early deaths. Significant improvements in trauma mortality will come from prevention initiatives¹² and from interventions to prevent the early deaths from hemorrhage and TBI.

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The original trials are registered with clinicaltrials.gov as: NCT00316004 and NCT00316017.

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Figure 1. Survival by cohort

Table 1

Patient Characteristics by Vital Status

	TBI		Shock		TOTAL	
	Dead n = 335	Survived n = 917	Dead n = 236	Survived n = 573	Dead n = 571	Survived n = 1490
Median Age (IQR)	45 (36)	30 (23)	35 (28)	32 (21)	42 (34)	30 (23)
Race, n(%)						
White, n(%)	155 (46.3%)	461 (50.3%)	99 (41.9%)	209 (36.5%)	254 (44.5%)	670 (45.0%)
Minority, n(%)	31 (9.3%)	134 (14.6%)	46 (19.5%)	155 (27.1%)	77 (13.5%)	289 (19.4%)
Unknown n(%)	150 (44.8%)	322 (35.1%)	91 (38.6%)	210 (36.6%)	241 (42.2%)	532 (35.7%)
Gender, n(%)						
Male, n(%)	241 (71.9%)	711 (77.5%)	179 (75.8%)	450 (78.5%)	420 (73.6%)	1161 (77.9%)
Unknown, n(%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Injury Type, n(%)						
Blunt	323 (96.4%)	909 (99.1%)	172 (72.9%)	337 (58.8%)	495 (86.7%)	1246 (83.6%)
MVC, n(%)	95 (28.4%)	393 (42.9%)	73 (30.9%)	154 (26.9%)	168 (29.4%)	547 (36.7%)
Cyclist, n(%)	50 (14.9%)	119 (13.0%)	33 (14.0%)	57 (9.9%)	83 (14.5%)	176 (11.8%)
Pedestrian, n(%)	53 (15.8%)	92 (10.0%)	34 (14.4%)	28 (4.9%)	87 (15.2%)	120 (8.1%)
Fall, n(%)	97 (29.0%)	154 (16.8%)	20 (8.5%)	49 (8.6%)	117 (20.5%)	203 (13.6%)
Assault, n(%)	12 (3.6%)	89 (9.7%)	4 (1.7%)	24 (4.2%)	16 (2.8%)	113 (7.6%)
Penetrating, n(%)	12 (3.6%)	10 (1.1%)	63 (26.7%)	235 (41.0%)	75 (13.1%)	245 (16.4%)
Median Initial SBP (IQR)	139 (56)	129 (36)	74 (28)	80 (20)	120 (67)	113 (51)
Median Initial GCS (IQR)	3 (2)	6 (4)	3 (4)	14 (7)	3 (2)	7 (8)
Median Highest HR, (IQR)	101 (43)	104 (30)	120 (46)	120 (21)	110 (46)	110 (31)
Median Initial RR, (IQR)	16 (12)	16 (8)	12 (16)	20 (8)	14 (12)	18 (12)

Table 2

Timing of Death by Cohort.

	TBI n = 335	Shock n = 81	Both n = 155
<24h, n(%)	155 (46.3%)	67 (82.7%)	112 (72.3%)
<72h, n(%)	219 (65.4%)	67 (82.7%)	129 (83.2%)
<28d, n(%)	303 (90.4%)	77 (95.1%)	144 (92.9%)
<180d, n(%)	331 (98.8%)	81 (100.0%)	153 (98.7%)

Table 3

Primary Cause of Death by Timing of Death.

n	<24h n = 334	24–72h n = 81	72h–28d n = 109	TOTAL n = 571
Hypovolemic Shock, n(%)	129 (38.6%)	2 (2.5%)	3 (2.8%)	134 (23.5%)
Hypoxia, n(%)	3 (0.9%)	0 (0.0%)	3 (2.8%)	8 (1.4%)
Cardiac Dysfunction, n(%)	3 (0.9%)	0 (0.0%)	0 (0.0%)	4 (0.7%)
TBI, n(%)	164 (49.1%)	71 (87.7%)	71 (65.1%)	314 (55.0%)
Anoxic Brain Injury, n(%)	10 (3.0%)	6 (7.4%)	16 (14.7%)	33 (5.8%)
Pulmonary Embolism, n(%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)
Sepsis, n(%)	0 (0.0%)	0 (0.0%)	5 (4.6%)	5 (0.9%)
Multiple Organ Failure, n(%)	1 (0.3%)	0 (0.0%)	4 (3.7%)	7 (1.2%)
Other, n(%)	3 (0.9%)	1 (1.2%)	1 (0.9%)	6 (1.1%)
Unknown, n(%)	19 (5.7%)	0 (0.0%)	0 (0.0%)	21 (3.7%)
Spinal Cord Injury, n(%)	2 (0.6%)	1 (1.2%)	1 (0.9%)	4 (0.7%)
Missing, n(%)	0 (0.0%)	0 (0.0%)	5 (1.0%)	34 (6.0%)

Table 4

Primary Cause of Death by Cohort and Timing of Death

	<24h TBI n = 155	Total TBI n = 335	<24h Shock n = 67	Total Shock n = 81	<24h Both n = 112	Total Both n = 155
Hypovolemic Shock, n(%)	19 (12.3%)	22 (6.6%)	58 (86.6%)	59 (72.8%)	52 (46.4%)	53 (34.2%)
Hypoxia, n(%)	0 (0.0%)	3 (0.9%)	2 (3.0%)	4 (4.9%)	1 (0.9%)	1 (0.6%)
Cardiac Dysfunction, n(%)	1 (0.6%)	1 (0.3%)	1 (1.5%)	1 (1.2%)	1 (0.9%)	2 (1.3%)
TBI, n(%)	123 (79.4%)	249 (74.3%)	5 (7.5%)	5 (6.2%)	36 (32.1%)	60 (38.7%)
Anoxic Brain Injury, n(%)	6 (3.9%)	19 (5.7%)	0 (0.0%)	2 (2.5%)	4 (3.6%)	12 (7.7%)
Pulmonary Embolism, n(%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sepsis, n(%)	0 (0.0%)	2 (0.6%)	0 (0.0%)	2 (2.5%)	0 (0.0%)	1 (0.6%)
Multiple Organ Failure, n(%)	0 (0.0%)	4 (1.2%)	0 (0.0%)	2 (2.5%)	1 (0.9%)	1 (0.6%)
Other, n(%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	2 (2.5%)	3 (2.7%)	3 (1.9%)
Unknown, n(%)	6 (3.9%)	7 (2.1%)	1 (1.5%)	1 (1.2%)	12 (10.7%)	13 (8.4%)
Spinal Cord Injury, n(%)	0 (0.0%)	2 (0.6%)	0 (0.0%)	0 (0.0%)	2 (1.8%)	2 (1.3%)
Missing, n(%)	0 (0.0%)	24 (7.2%)	0 (0.0%)	3 (3.7%)	0 (0.0%)	7 (4.5%)

Table 5

Life-sustaining Care Withdrawn by Cohort

	TBI n = 335	Shock n = 81	Both n = 155	Total n = 571
Died in Field, n(%)	4 (1.2%)	4 (4.9%)	8 (5.2%)	16 (2.8%)
Died in ED, n(%)	50 (14.9%)	26 (32.1%)	51 (32.9%)	127 (22.2%)
Died in Hospital with Life-sustaining Care, n(%)	73 (21.8%)	34 (42.0%)	43 (27.7%)	150 (26.3%)
Died in Hospital with Life-Sustaining Care Withdrawn, n(%)	184 (54.9%)	14 (17.3%)	46 (29.7%)	244 (42.7%)
Died after Hospital Discharge, n(%)	24 (7.2%)	3 (3.7%)	7 (4.5%)	34 (6.0%)