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Increased Trauma Center Volume Is Associated With Improved Survival After Severe Injury: Results of a Resuscitation Outcomes Consortium Study

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Structured Abstract

OBJECTIVE—The Resuscitation Outcomes Consortium (ROC) is a network of 11 centers and 60 hospitals conducting emergency care research. For many procedures, high volume centers demonstrate superior outcomes versus low volume centers. This remains controversial for trauma center outcomes. This study investigated the relationship of trauma center volume on outcome.

METHODS—This study was a secondary analysis of prospectively collected data from the ROC multicenter out-of-hospital Hypertonic Saline Trial in patients with GCS 8 (traumatic brain injury [TBI]) or SBP 90 and pulse 110 (shock). Regression analyses evaluated associations between trauma volume and the following outcomes: 24 hour mortality, 28 day mortality,

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ventilator free days (VFD), Multiple Organ Dysfunction Scale (MODS) incidence, worst MODS score, and poor 6 month Glasgow outcome scale extended.

RESULTS—2070 patients were analyzed: 1251 in the TBI cohort and 819 in the shock cohort. Overall, 24-hour and 28-day mortality were 16% and 25%, respectively. For every increase of 500 trauma center admissions, there was a 7% decreased odds of both 24-hour and 28-day mortalities for all patients. As trauma center volume increased, non-organ dysfunction complications increased, VFD increased and worst MODS score decreased. The associations with higher trauma center volume were similar for the TBI cohort, including better neurologic outcomes at 6 months, but not for the shock cohort.

CONCLUSIONS—Increased trauma center volume was associated with increased survival, more ventilator free days and less severe organ failure. Trauma system planning and implementation should avoid unnecessary duplication of services.

INTRODUCTION

The American College of Surgeons Resources for Optimal Care of the Injured Patient requires that Level I trauma centers have at least 1200 yearly admissions.¹ This minimal volume criterion has been based on the argument that high volume trauma centers will have adequate resources and expertise to provide the highest quality patient care and have the best outcomes. This has been a source of debate regarding whether Level I centers have higher survival rates than Level II trauma centers. There have been many studies that both support²⁻⁵ and refute^{6, 7} this volume-outcome debate. Others suggest that it is not the volume of trauma admissions but a Level I designation of the trauma center that results in better outcomes.^{8, 9}

The Resuscitation Outcomes Consortium (ROC) was established to perform out-of-hospital resuscitation studies in cardiac arrest and severe trauma. Eleven centers from nine regions throughout North America make up the consortium. Two randomized controlled trials were performed to study out-of-hospital hypertonic saline resuscitation in severely injured patients; one study in patients with presumed hypovolemic shock¹⁰ and the other with severe traumatic brain injury.¹¹ Both studies were stopped for futility before enrollment was completed but not before 2222 patients were enrolled.

We sought to revisit the volume-outcome, designation level-outcome question. The aim of this study was to perform a secondary analysis of shock and TBI patients enrolled in the hypertonic saline trial to determine if there was an association between volume of trauma center admissions or level of designation and important health outcomes. We also sought to determine if there was an association between volume or designation level and rate of post injury complications. Our hypothesis was that higher trauma center admission volume or level I designation would confer a survival advantage over low volume or level II designated trauma centers.

METHODS

This study was a secondary analysis of 2 separate but associated prospective randomized trials of hypertonic saline in traumatic brain injury¹¹ and shock¹⁰ performed by the Resuscitation Outcomes Consortium (ROC). The ROC is a multicenter clinical trials network consisting of 11 regional clinical centers and one coordinating center in the United States and Canada. Local institutional or ethics review boards at all sites approved the original studies. The trial involved 114 emergency medical services agencies within the catchment areas served by the ROC. Two clinical trials were conducted simultaneously with the same intervention. The trials had two distinct patient cohorts, one for hypovolemic shock and the other for traumatic brain injury (TBI). This report is a secondary analysis of both cohorts. The primary studies were randomized, controlled, double-blinded, 3-arm clinical trials comparing a 250mL pre-hospital bolus of 7.5% saline (hypertonic saline, HS) versus 7.5% saline with 6% dextran 70 (HSD) versus 0.9% saline (NS) as the initial resuscitation fluid given to injured patients with hemorrhagic shock or traumatic brain injury in the out-of-hospital setting. Details of the initial study designs and primary outcomes have been previously published.¹⁰⁻¹²

Patient Population

Patients were included in the hypovolemic shock cohort if they had out-of-hospital systolic blood pressure (SBP) 70 mm Hg or less or 71 to 90 mm Hg with a concomitant heart rate (HR) 108 beats or more per minute. Patients were included in the TBI cohort if they had a blunt mechanism of injury and a GCS \geq 8 and didn't meet criteria for the shock cohort. Patients that met criteria for the shock cohort who also exhibited inclusion criteria for the TBI cohort, were included in the shock cohort. Exclusion criteria were the following: known or suspected pregnancy, age less than 15 years, out-of-hospital cardiopulmonary resuscitation, administration of more than 2000 mL crystalloid, colloid, or blood products before enrollment, severe hypothermia ($<28^{\circ}\text{C}$), drowning or asphyxia due to hanging, burns more than 20% total body surface area, isolated penetrating head injury, inability to obtain intravenous access, time of dispatch call received to study intervention more than 4 hours, and known prisoners. Interfacility transfers were also excluded. Once admitted, patient care was not proscribed, but investigators agreed to follow a set of standard operating procedures (SOPs) promulgated by the Inflammation and Host Response Injury Investigators. These SOPs included low tidal volume ventilation strategies for ARDS,¹³ strict hyperglycemia management¹⁴ and restrictive transfusion practices.¹⁵

The primary independent variables of interest were level of trauma center designation and the yearly volume of trauma center admissions. The local state (USA) or provincial (Canada) designating authorities determined Trauma Center designation level and only level I and II centers were included in the analysis. Trauma center volume was determined from local hospital registry data for patients that met trauma registry inclusion criteria and were admitted to the hospital or died in the ED during the timeframe of the parent studies.

The dependent variables analyzed were 24-hour and 28-day mortality, the rates of both infectious and non-infectious complications, the proportion of patients with 6-month Glasgow Outcome Scale-Extended (GOSE) \geq 4 (TBI cohort only), ventilator free days,

multiple organ dysfunction incidence defined as MODS score > 6 and worst MODS score. A GOSE 4 is considered severe disability (GOSE 3 or 4), vegetative state (GOSE 2) or death (GOSE 1).¹⁶ Both MOD incidence and worst MODS score were analyzed to evaluate both the odds of developing MOD as well as the severity of MOD.¹⁷ Non-infectious complications included fat embolism syndrome, cardiac arrest, myocardial infarction, cerebral infarction, deep venous thrombosis, pulmonary embolus, abdominal compartment syndrome and extremity compartment syndrome. Infectious complications included nosocomial pneumonia, bloodstream infections and surgical site infections. Nosocomial infection diagnoses had to meet CDC definitions. Complications were only analyzed in patients admitted to the hospital. Patients who either died in the ED or were discharged from the ED were not considered in the complication analysis.

Statistical Methods

The outcomes of interest were evaluated for both cohorts combined and the TBI and hemorrhagic shock cohorts independently. Patient characteristics, out of hospital care, and admission physiology were compared between trauma centers level I and II and trauma volume (increments of 1,000) using two-sided t test, ANOVA, or chi-square tests as appropriate. A $p < 0.05$ was considered significant. Primary and secondary outcomes were also described for the overall population stratified by trauma level and trauma volume.

Multivariable logistic regression accounting for within hospital correlation using generalized estimating equations (GEE) were used to evaluate the association between trauma volume, trauma level (separately and combined) for the following outcomes: 28-day mortality, 24-hour mortality, imputed 6 month GOSE (TBI only cohort), proportion of noninfectious complications and infectious complications and proportion developing multiple organ failure defined as MODS > 6 after adjusting for other factors. Linear regression accounting for within hospital correlation was used to evaluate the association with predictors after adjustment for other factors for the following outcomes: ventilator free days, and worst MODS score. Volume was analyzed as a linear continuous variable with results reported per incremental admission increase of 500 patients. Adjustment factors included age, gender, lowest pre-hospital SBP, pre-hospital GCS, mode of transportation, use of advanced airway, pre-hospital time, mechanism of injury, injury severity score (ISS), initial ED SBP, head Abbreviated Injury Scale (AIS) score, and site of enrollment (SAS, version 9.1.3, Cary, NC; Stata, version 11, College Station, TX).

RESULTS

A total of 2222 patients were enrolled in the 2 study cohorts. After exclusions, 2070 patients were analyzed: 1251 in the TBI cohort and 819 in the Shock cohort. One hundred fifty two enrolled patients were excluded from the primary analyses for the following reasons: hypertonic saline bag opened but not given (N=88), care rendered at more than 1 hospital (N=39), died before reaching hospital care (N=16) and missing hospital data (N=2). Table 1 describes the patient population studied. A higher proportion of patients were male and sustained blunt trauma. Approximately 80% of the patients were brought to a level I hospital, however these hospitals had annual hospital trauma admission volumes that varied

from low volume to high volume centers. Study patients had a relatively even admission distribution to low, medium and high volume trauma centers.

A higher proportion of patients were brought to level I or high volume centers after sustaining penetrating trauma or after treatment with a pre-hospital advanced airway. Patients with higher ISS scores were more likely to be taken to level I or high volume trauma centers. Patients brought to level I or high volume centers tended to receive more pre-hospital crystalloid resuscitation.

On hospital arrival, a greater proportion of TBI patients that went to level I or high volume centers tended to have lower arrival GCS scores and more frequent use of ICP monitoring. Similarly, a higher proportion of patients enrolled in the shock trial that were brought to level I or high volume centers were more likely to be acidotic, have early signs of coagulopathy denoted by higher admission INR and undergo an emergent hemorrhage control procedure. Overall, Table 1 provides evidence that pre-hospital triage patterns tended to bring more severely injured and metabolically deranged patients to level I trauma centers or higher volume trauma centers.

Despite a higher proportion of severely injured patients being brought to level I and high volume trauma centers, unadjusted 24-hour and 28-day mortality was not different between level I and level II centers or low volume and high volume centers (Table 2). Similarly, though a higher proportion of patients with lower GCS scores were brought to level I and high volume trauma centers, the proportion of patients with a 6 month GOSE 4 was also not different between level I and level II centers or low volume and high volume centers. ICU LOS, ventilator free days and severity of MODS were also not different. A higher proportion of patients developed both non-infectious and infectious complications in high volume centers. Thus, it appears that while a higher proportion of severely injured patients were brought to level I and higher volume centers their mortality was no higher than level II and lower volume centers. This may have come at the expense of higher complication rates.

To further explore the relationship between trauma center designation, volume and outcome, multivariable logistic regression was performed to adjust for differences in injury characteristics and determine their influence on outcome (Table 3). Data is reported in 500 patient admission increments for clarity of presentation. (However, if a significant finding were reported it would be present for any volume. The effect would be half as large for increments of 250 and twice as large for increments of 1000) As trauma center admission volume increased there were reduced odds in both all-patient 24-hour and 28-day mortality of 7% for every 500 trauma patient admission increase to a trauma center. This effect was maintained in the TBI cohort, but not in the shock cohort and persisted when both designation level and volume were adjusted for together. Additionally, there was a 55% relative decrease in 28-day mortality if a patient was in the shock cohort and brought to a level I trauma center versus a level II center. This level effect persisted when additionally adjusting for volume. While there was a trend towards improved survival for all patients brought to a level I center, this effect did not reach statistical significance. This analysis was repeated after excluding patients with ISS < 16 (data not shown). There were reduced odds in both all-patient 24 hour and 28-day mortality of 5% and 6% respectively for every 500

trauma patient admission increase to a trauma center. The results for the individual TBI and shock cohorts mirrored the results described above.

In the TBI cohort, increasing trauma center volume by every 500 admissions was associated with an 8% odds reduction in having a poor neurological outcome as measured by 6-month GOSE 4. There was no effect on 6-month GOSE outcomes based on trauma center designation. When additionally adjusting for center designation, admission to a high volume center was associated with better long-term neurological outcomes.

Secondary outcomes explored were both noninfectious and infectious complications (Table 4). As trauma admission volume increased there was an increase in all-patient risk of non-infectious complications. However, infectious complications were not increased in the all patient group. Similarly, as trauma center volume increased, there was an increased risk of non-infectious complications but not infectious complications in the shock cohort. This was not seen in the TBI cohort where there was no increased risk of either infectious or non-infectious complications. These findings persisted when volume and designation level were analyzed in the same model. Conversely, there was a higher risk of infectious complications in all patients brought to a level I trauma center. Non-infectious complications were not increased. Interestingly, the shock cohort had an increased risk of both infectious and non-infectious complications when patients were brought to a level I center. There was no effect on both infectious and non-infectious complications in the TBI only cohort when brought to a level I versus level II center. When volume and designation level were analyzed together, all differences in the all patient and shock cohorts were lost. These data taken together suggests that trauma center volume rather than designation level drove the effect on infectious and non-infectious complications.

To explore factors that may be in part responsible for outcome differences between level I and II designated centers and low and high volume trauma centers, multivariate logistic regression was performed to determine the odds of developing multiple organ dysfunction defined as a MODS score > 6 (Table 4). Despite more severely injured patients being admitted to high volume and Level I centers, there were no increased odds of patients developing MOD when either volume or designation level were analyzed separately. However, there were increased odds of developing MOD in the shock cohort as volume of patients increased when additionally adjusting for designation level. Conversely, there were decreased odds of developing MOD in the TBI cohort as volume increased and designation level was considered in the model. Finally, linear regression was performed to determine whether there were differences in ICU LOS, ventilator free days and severity of organ failure measured as worst MODS score (Table 4). As trauma admission volume increased there was an increase in all patient ventilator free days and a decrease in worst MODS score. There was a similar effect seen in the TBI only cohort, but not in the shock cohort. There was no effect on ventilator free days or worst MODS score between Level I and II designated centers. These effects were unchanged when volume and designation level were adjusted together. There was no effect of volume or designation level in any group on ICU LOS (data not shown). The interaction between volume and designation center was explored but no difference in effect was seen.

DISCUSSION

The debate centered on whether volume of trauma patients admitted or level of trauma center designation has any bearing on patient outcome has been active for decades. This study shows that as trauma center volume increases, the odds of both 24-hour and 28-day mortality decreases. This effect was maintained as volume increased to very high admission numbers of greater than 3000 trauma admissions per year. This effect was sustained when looking at the TBI study cohort alone but not the shock study cohort. Patients brought to a designated level I trauma center had half the odds of mortality than patients brought to a designated level II center in the shock cohort only.

Multiple studies have looked at the effect of trauma center volume on outcome. Many of these studies rely on administrative datasets,^{5, 18, 19} statewide registries^{8, 20–22} or the National Trauma Data Bank (NTDB)^{2, 7, 9} where accuracy and validity of data has been questioned.^{23–25} An advantage of this study is that it is based on prospectively collected data with quality control and review and does not rely on administrative datasets or registry downloads. This is a major strength of the findings of this study.

Nathens⁵ showed that high volume trauma centers, defined as having greater than 650 admissions per year with an ISS > 15, had significant reductions in mortality only for the most severely injured patients with either isolated penetrating injuries with shock on admission or multi-system blunt trauma with coma on admission. Other studies have both supported^{2–4, 26} and refuted^{6, 7, 9} the premise that increased trauma center volume results in better outcomes. Our results showed a broad effect on survival in those with severe injuries. This may be due in part to the criteria required to be enrolled in this study included only those with evidence of severe injury in the pre-hospital setting.

Interestingly, our data showed a beneficial effect on 28-day survival in Level I centers only in the shock cohort. Others have shown that level I center designation and not volume provides a survival advantage for patients with severe injuries. Demetriades⁹ showed that in patients with major vascular or hepatic injuries as well as complex pelvic fractures that level I centers had lower odds of mortality than level II centers even when adjusted for trauma center volume. Cudnik,⁸ using the Ohio statewide registry data found that the odds of mortality at level I centers were lower than level II centers. Other authors have shown that in an analysis within level I centers only, a driving force that determines survival is volume and as trauma center volume increases the odds of mortality decrease.^{2, 19} A possible explanation for our data not showing a 24-hour survival advantage in level I designated centers may be related to findings in the original study. In the original study reported by Bulger¹⁰ there was a higher mortality in the hypertonic saline cohorts in the subgroup of patients who did not receive blood transfusions in the first 24 hours, compared to the control group receiving normal saline. Our data show that more severely injured patients were brought to high volume and level I centers. It is possible that this finding in the original study negated any potential benefit of being brought to a level I or high volume center.

In the original hypertonic saline trial, there was no outcome benefit to being treated with hypertonic saline as compared to normal saline in the TBI cohort.¹¹ However, in this study,

as trauma center volume increased the odds of mortality and poor neurological outcome in the TBI cohort decreased. Tepas et al., using Florida statewide administrative data of TBI patients found similar results. They showed that high volume centers had a lower risk of mortality as well as lower risk of discharge to a skilled nursing facility, suggesting better functional outcomes.¹⁹ Others have shown similar results.¹⁸ Our study showed that even with more severely injured TBI patients being brought to high volume centers, not only were the odds of survival increased, but the odds of meaningful survival as measured by 6-month GOSE were also increased versus lower volume centers.

Both infectious and non-infectious complications were evaluated in this study. As trauma center volume increased there was an increased risk of non-infectious complications but not infectious complications. This pattern was sustained for the shock cohort but not the TBI cohort where there was no relationship between trauma center volume and any complication. In a recent study from the Inflammation and Host Response to Injury investigators²⁷ analyzing a similar cohort of severely injured patients, multiple organ failure was associated with injury severity, depth and duration of shock and aggressive fluid resuscitation. In this study, higher volume trauma centers had a higher proportion of patients with these characteristics explaining in part this finding. Further, with the data showing that higher volume trauma centers had lower odds of mortality, more severely injured patients at higher volume trauma centers would be alive to get complications than at lower volume centers. A similar argument can be made for level I centers having a higher risk of developing infectious complications in the shock cohort but not in the TBI cohort when compared to level II centers. Similar to high volume centers, level I centers had a significantly decreased risk of mortality compared to level II centers in the shock cohort. A number of investigators have shown an increased risk of infection with higher ISS,^{28, 29} shock and acidosis,²⁹⁻³¹ and coagulopathy with transfusion,^{29, 32, 33} all factors that were in higher proportion in patients admitted to level I centers.

To explore potential explanations for our findings, we examined outcomes that were potentially associated with process and post injury management. Despite more severely injured patients being brought to high volume and Level I centers they had fewer days on the ventilator, no higher odds of developing MOD, and when patients at these centers did develop MOD it was less severe as evidenced by lower MODS scores. It is entirely plausible that high volume centers utilized standard operating procedures (SOP) associated with fewer days on the ventilator and faster recovery from organ failure that have been shown to improve outcomes in similar patient populations.³⁴ The ROC investigators agreed to institute similar SOPs; however, SOP compliance was not strictly measured in this study.

Our analysis was not able to address whether there was a ceiling to the volume effect in this study when volume overwhelmed resources and outcomes suffered. Arbabi looked at the effect of increasing patient volume on outcomes in times of patient surge when resources were fixed. In their single institution study in a high volume trauma center, they could find no differences in outcomes based on patient load when resources were strained.³⁵ Other studies have shown that there were no outcome differences between low volume and high volume surgeons managing trauma patients at the same institution.^{36, 37} These studies suggest that high volume centers have developed practices and procedures that extend

beyond the individual trauma surgeon. Perhaps the results of this trial are in part due to large volume centers having systems in place that not only account for volume with appropriate resources, but processes as well that allow for efficiency and earlier definitive care. Since there were only 4 centers in this study with annual trauma volumes greater than 3000 admissions per year, we are unable to determine whether there is a limit to the volume effect on outcome.

This study is the first to look at the continuum of trauma care from the out-of-hospital phase through the post admission phase of care and analyze outcomes and its relationship to trauma center volume. We have previously shown a large variation in outcomes of the various trauma systems that participate in the ROC.³⁸ Based on this known outcome variation within the study collaborators, it is plausible that large volume centers have worked with their EMS counterparts on protocols that deliver advanced trauma care earlier in the out-of-hospital phase of care. These out-of-hospital providers may better appreciate signs of injury severity, institute appropriate care and preferentially bring these patients to high volume centers.

This study has potential implications for trauma triage guidelines. The present CDC field triage guideline recommends that those with the potential for being most severely injured based on physiologic, anatomic or mechanistic criteria “be transported preferentially to the highest level of care within the defined trauma system.”³⁹ The results of this study suggest that these patients should be brought to the highest volume center within the trauma system. When there are multiple trauma centers within a system, should EMS bypass a closer low volume center to transport a severely injured patient to a higher volume center? The answer to that question is beyond the scope of this study’s findings. However, in another study from the Resuscitation Outcomes Consortium on a similar but separate trauma cohort, Newgard and colleagues⁴⁰ showed no difference in outcomes of severely injured trauma patients with out of hospital times up to 80 minutes compared with those with shorter out of hospital times. Taking the CDC guidelines together with the results of this study and the study by Newgard et al, it would be reasonable to suggest that severely injured patients be brought to the highest volume center when total out of hospital times can remain under 80 minutes. This decision would only be relevant when there are multiple centers in a trauma system that would allow transport within the 80 minute time frame. When out of hospital times would exceed this limit as in a rural setting with only a single trauma center, this issue becomes moot.

The American College of Surgeons Committee on Trauma presently sets the lower limit of admissions for a level I trauma center at 1200.¹ The results of this study do not define a new standard for trauma center volume. It does suggest that centers with higher volume have better survival than lower volume centers. Redundant trauma center proliferation in urban settings that only reduces existing trauma center admission volume without improving access to care should be scrutinized. Trauma systems should critically evaluate their triage guidelines and consider developing protocols that deliver the most severely injured consistently to the highest volume center.

There are limitations to this study. First, this is a secondary analysis of prospectively collected clinical trial data. The initial data set was not designed to answer these study questions and it is possible, despite attempts to account for confounding variables, we have not adequately accounted for all factors that needed to be considered. As an example, it is possible that counting trauma admissions was done differently at different trauma centers, reflecting different inclusion criteria between trauma registries.

Second, the results of this study can only suggest associations between improved outcomes and higher trauma center volume. The reason for this potential effect was not delineated by this analysis. The data suggest that high volume trauma centers may have systems in place that better prepare them to deliver definitive trauma care. This statement can only be inferred from the data and no cause and effect conclusions can be drawn.

Third, the results of this study may not be generalizable. The data collected for this analysis were in the context of a randomized trial of out-of-hospital use of hypertonic saline after severe injury with or without TBI. All personnel from out-of-hospital providers to accepting hospital providers were aware of this fact. It is possible that in all phases, care delivered was somehow different than if a patient were not enrolled in the parent study.

Finally, only total trauma center volume was used in this analysis. There was no account for volume of severe injuries admitted to any institution. It is possible that by only analyzing total trauma center volume important differences in the volume of severely injured trauma patients were missed. If a given trauma center had a high volume of total trauma admissions but a low volume of severely injured trauma admissions, the benefit of being a high volume center may not extend to the most severely injured. Conversely, if a low volume center had a high proportion of severely injured patients admitted to their center, they might be better able to manage more severely injured patients. These arguments are however counterintuitive to the results found and would have also tended to weaken the findings of this study.

CONCLUSIONS

The results of this study show that severely injured patients admitted to a higher volume trauma center have a lower odds of mortality than if they are brought to a lower volume trauma center. This survival benefit was associated with added complications, but high volume centers were able to mitigate the consequences of these events. This may be partly related to improved processes and protocols that lead to fewer days on the ventilator and less severe organ failure. High volume trauma centers likely have systems in place to deliver the highest quality efficient trauma care to the most severely injured patients brought to their centers. Thus, out-of-hospital triage guidelines should bring the most severely injured patients to the highest volume centers. Trauma center proliferation should be approached with caution due to the volume reduction effect resulting from wider distribution of the same number of patients to more trauma centers. Further study is warranted to define the factors that lead to improved outcomes at high volume centers.

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Table 1

Demographics, Injury Severity, Out of Hospital Care and Admission Physiology

	Missing Data N=2070	All N=2070	Trauma Level			Trauma Volume					p-value
			Level I N=1649	Level II N=406	p-value	1000 N=284	1001-1999 N=504	2000-2999 N=438	3000 N=635		
Age, mean (SD), y	2 (0.1%)	38.1 (17.8)	37.7 (17.7)	39.6 (18.1)	0.0567	39.0 (18.7)	38.8 (18.3)	36.1 (16.4)	37.8 (17.4)	0.0645	
Male, N (%)	0 (0%)	1597 (77%)	1277 (77%)	312 (77%)	0.7984	216 (76%)	384 (76%)	355 (81%)	493 (78%)	0.2588	
Blunt, N (%)	0 (0%)	1737 (84%)	1368 (83%)	358 (88%)	0.0081	251 (88%)	390 (77%)	350 (80%)	564 (89%)	<0.001	
Penetrating, N (%)	0 (0%)	324 (16%)	275 (17%)	46 (11%)	0.006	31 (11%)	114 (23%)	86 (20%)	71 (11%)	<0.001	
ISS, mean (SD)	65 (3.1%)	25.1 (16.0)	25.8 (16.0)	22.4 (15.6)	0.0002	23.5 (14.5)	22.9 (16.4)	25.1 (15.6)	27.4 (16.1)	<0.001	
ISS imputed, mean (SD)	0 (0.0%)	25.5 (16.1)	26.2 (16.1)	23.0 (15.7)	0.0003	23.8 (14.6)	23.4 (16.6)	25.4 (15.6)	28.1 (16.4)	<0.001	
RTS, mean (SD)	129 (6.2%)	5.1 (1.6)	5.1 (1.6)	5.1 (1.7)	0.6807	5.3 (1.5)	5.1 (1.7)	5.1 (1.6)	5.0 (1.7)	0.1118	
TRISS Prob Outcome, mean (SD)	195 (9.4%)	0.7 (0.3)	0.7 (0.3)	0.7 (0.3)	0.353	0.7 (0.3)	0.7 (0.3)	0.7 (0.3)	0.7 (0.3)	0.0763	
Prehospital Advan Airway, N (%)	0 (0%)	1071 (52%)	889 (54%)	177 (44%)	0.0002	92 (32%)	166 (33%)	181 (41%)	535 (84%)	<0.001	
Air Transport, N (%)	0 (0%)	715 (35%)	541 (33%)	174 (43%)	0.0002	89 (31%)	140 (28%)	179 (41%)	237 (37%)	<0.001	
Prehospital time, mean (SD)	1 (0.05%)	54.5 (28.3)	55.4 (29.3)	50.9 (24.0)	0.0011	57.8 (33.6)	50.0 (25.4)	51.4 (27.8)	56.2 (22.9)	<0.001	
Prehospital fluids (L), mean (SD)	0 (0.0%)	1.0 (0.8)	1.1 (0.8)	0.8 (0.6)	<0.001	0.6 (0.5)	0.9 (0.6)	1.0 (0.7)	1.4 (1.1)	<0.001	
TBI Only cohort, N	0 (0%)	1251 (60%)	996 (60%)	247 (61%)	0.8717	187 (66%)	280 (56%)	260 (59%)	399 (63%)	0.0166	
Admission GCS, mean(SD)	6 (0.5%)	5.4 (3.7)	5.2 (3.6)	5.8 (4.2)	0.0408	6.3 (4.2)	6.1 (4.0)	5.9 (4.2)	4.0 (2.4)	<0.001	
ICP Monitor, N	0 (0%)	348 (28%)	290 (29%)	57 (23%)	0.0546	34 (18%)	73 (26%)	68 (26%)	139 (35%)	<0.001	
Highest ICP, 1st 24°, mean(SD)	907 (72.5%)	28.7 (20.8)	28.4 (21.2)	30.4 (18.5)	0.4693	31.2 (20.1)	29.7 (23.6)	27.1 (19.8)	27.5 (19.7)	0.6982	
GOSE 4 (6 months) - no imputations	189 (15%)	611 (58%)	501 (58%)	106 (57%)	0.9556	90 (61%)	141 (63%)	125 (56%)	178 (50%)	0.0174	
GOSE (6 months), mean (SD) - no imps	189 (15.1%)	4.2 (2.7)	4.2 (2.7)	4.0 (2.7)	0.5156	3.8 (2.7)	4.0 (2.7)	4.2 (2.8)	4.6 (2.7)	0.005	
Shock cohort, N	0 (0%)	819 (40%)	653 (40%)	159 (39%)	0.8717	97 (34%)	224 (44%)	178 (41%)	236 (37%)	0.0166	
Admission SBP, mean (SD)	14 (1.7%)	105.7 (43.0)	106.7 (43.1)	102.3 (43.0)	0.2547	110.1 (33.5)	103.9 (45.0)	99.2 (44.5)	111.6 (44.0)	0.02	
Admission hemoglobin (g/dl), mean (SD)	51 (6.2%)	10.6 (2.6)	10.4 (2.6)	11.5 (2.4)	<0.001	11.5 (2.3)	11.0 (2.2)	10.6 (2.7)	10.0 (2.7)	<0.001	
Admission metabolic acidosis, N (%)	441 (53.9%)	332 (88%)	317 (89%)	15 (65%)	0.0033	24 (77%)	19 (73%)	68 (83%)	186 (94%)	0.001	
Admission INR, mean (SD)	130 (15.9%)	1.5 (1.1)	1.6 (1.2)	1.3 (0.5)	<0.001	1.4 (0.6)	1.3 (0.5)	1.5 (1.1)	1.8 (1.5)	<0.001	
Required emergent hemorrhage control, N (%)	2 (0.2%)	281 (34%)	243 (37%)	38 (24%)	0.0012	13 (13%)	86 (38%)	63 (35%)	97 (41%)	<0.001	

ISS= Injury Severity Score; RTS=Revised Trauma Score; TRISS=Trauma Injury Severity Score; TBI=Traumatic Brain Injury; GCS=Glasgow Coma Scale; ICP=Intracranial Pressure; GOSE=Glasgow Outcome Scale-Extended; INR=International Normalized Range;

Table 2

Primary and Secondary Outcomes of Total Study Population

	Missing Data		Trauma Level					Trauma Volume				p-value
	N=2070	All N=2070	ACS I N=1649	ACS II N=406	1000 N=284	1001-1999 N=504	2000-2999 N=438	3000 N=635				
28-day mortality, N (%)	9 (0.4%)	504 (25%)	397 (24%)	102 (25%)	69 (24%)	116 (23%)	105 (24%)	149 (24%)	0.9828			
24-hour mortality, N (%)	8 (0.4%)	321 (16%)	254 (16%)	64 (16%)	41 (14%)	74 (15%)	71 (16%)	96 (15%)	0.8996			
6-month GOSE<=4 imputed, N(%) -- TBI Only N=1251	0 (0%)	678 (53%)	532 (53%)	123 (50%)	103 (55%)	155 (55%)	134 (52%)	188 (47%)	0.1503			
ICU LOS, mean (SD)	221 (10.7%)	7.9 (12.5)	7.9 (12.5)	8.3 (12.4)	7.5 (9.6)	8.4 (18.3)	8.6 (11.1)	7.5 (9.0)	0.3826			
Vent free days, mean (SD)	16 (0.8%)	17.6 (11.8)	17.6 (11.8)	17.6 (12.1)	18.1 (12.0)	18.3 (11.8)	16.8 (11.8)	18.0 (11.5)	0.1937			
Infectious comp. N (%)	221 (10.7%)	528 (29%)	446 (30%)	81 (23%)	67 (27%)	111 (25%)	104 (26%)	191 (32%)	0.0459			
Nosocomial pneumonia, N (%)	221 (10.7%)	353 (19%)	295 (20%)	58 (17%)	48 (20%)	68 (15%)	74 (19%)	127 (21%)	0.0848			
Bloodstream infections, N (%)	221 (10.7%)	117 (6%)	101 (7%)	16 (5%)	21 (9%)	15 (3%)	26 (7%)	37 (6%)	0.0259			
Non-infectious comp. N (%)	220 (10.6%)	247 (13%)	206 (14%)	39 (11%)	25 (10%)	43 (10%)	60 (15%)	98 (17%)	0.0026			
Worst MODS, mean (SD)	53 (2.6%)	8.7 (9.5)	8.7 (9.4)	8.5 (9.7)	8.2 (9.6)	8.1 (9.5)	8.7 (9.4)	8.8 (9.2)	0.6324			

ICU-LOS=Intensive Care Unit Length of Stay; MODS=Multiple Organ Dysfunction Scale

Table 3

Primary Study Outcomes

	28 Day Mortality OR (95% CI) p-value *	24 Hour Mortality OR (95% CI) p-value *	6 Month GOSE <=4 OR (95% CI) p-value *
Volume (per 500 people increase)			
All Patients	0.93 (0.89, 0.97) 0.002	0.93 (0.88, 0.99) 0.027	
Shock Cohort	0.94 (0.88, 1.01) 0.100	0.94 (0.88, 1.02) 0.132	
TBI only Cohort	0.93 (0.89, 0.98) 0.003	0.94 (0.88, 1.01) 0.068	0.92 (0.87, 0.98) 0.011
Trauma Level (I versus II)			
All patients	0.77 (0.54, 1.10) 0.148	0.75 (0.47, 1.21) 0.241	
Shock Cohort	0.45 (0.23, 0.89) 0.023	0.55 (0.27, 1.13) 0.104	
TBI only Cohort	1.04 (0.70, 1.56) 0.837	0.55 (0.22, 1.37) 0.199	1.31 (0.90, 1.91) 0.162
Volume and Designation Level in same Model			
All Patients: Volume	0.93 (0.88, 0.98) 0.004	0.93 (0.87, 0.99) 0.030	
All Patients: Trauma Level I	0.97 (0.64, 1.46) 0.870	1.01 (0.63, 1.62) 0.974	
Shock Cohort: Volume	0.98 (0.92, 1.04) 0.551	0.96 (0.90, 1.04) 0.310	
Shock Cohort: Trauma Level I	0.46 (0.23, 0.94) 0.032	0.67 (0.31, 1.43) 0.297	
TBI only Cohort: Volume	0.91 (0.87, 0.96) 0.001	0.92 (0.87, 0.98) 0.013	0.89 (0.84, 0.95) <0.001
TBI only Cohort: Trauma Level I	1.40 (0.88, 2.22) 0.152	1.46 (0.76, 2.80) 0.262	1.87 (1.16, 3.02) 0.010

OR=Odds Ratio; CI=Confidence Interval

Adjustment Factors: age, sex, lowest PH SBP, PH GCS, transportation mode, use of advanced airway, PH time, mechanism of injury, ISS, initial ED SBP, head AIS

Table 4

Secondary study outcomes

	Infectious Complications OR (95% CI) p-value [^]	Non-infectious Complications OR (95% CI) p-value *	MODS>6 OR (95% CI) p-value *	Ventilator Free Days Coef. (95% CI) p-value *	Worst MODS Coef. (95% CI) p-value *
Volume (per 500 people increase)					
All Patients	1.02 (0.98, 1.06) 0.387	1.07 (1.02, 1.12) 0.003	0.99 (0.95, 1.03) 0.511	0.29 (0.14, 0.44) <0.001	-0.15 (-0.27, -0.04) 0.012
Shock Cohort	1.06 (0.98, 1.14) 0.157	1.12 (1.05, 1.21) 0.002	1.05 (0.99, 1.11) 0.124	0.04 (-0.14, 0.22) 0.658	-0.03 (-0.17, 0.12) 0.713
TBI only Cohort	1.00 (0.94, 1.08) 0.910	1.05 (1.00, 1.10) 0.070	0.95 (0.89, 1.01) 0.077	0.44 (0.21, 0.67) <0.001	-0.23 (-0.40, -0.06) 0.009
Trauma Level (I versus II)					
All patients	1.57 (1.03, 2.41) 0.037	1.42 (0.71, 2.83) 0.325	0.99 (0.67, 1.48) 0.969	0.56 (-0.83, 1.95) 0.425	-0.39 (-1.38, 0.61) 0.440
Shock Cohort	1.88 (1.10, 3.19) 0.020	2.39 (1.17, 4.88) 0.016	1.01 (0.60, 1.69) 0.981	0.93 (-0.75, 2.62) 0.268	-0.98 (-2.24, 0.28) 0.124
TBI only Cohort	0.94 (0.68, 1.28) 0.679	1.01 (0.47, 2.18) 0.972	0.97 (0.57, 1.66) 0.925	0.44 (-1.50, 2.38) 0.650	-0.03 (-1.40, 1.34) 0.966
Volume and Designation Level in same Model					
All Patients: Volume	1.00 (0.95, 1.05) 0.889	1.07 (1.02, 1.11) 0.006	0.98 (0.94, 1.03) 0.503	0.31 (0.15, 0.47) <0.001	-0.16 (-0.28, -0.03) 0.014
All Patients: Trauma Level I	1.57 (0.97, 2.54) 0.068	1.10 (0.51, 2.39) 0.803	1.03 (0.66, 1.61) 0.907	-0.33 (-1.89, 1.22) 0.664	0.08 (-1.01, 1.18) 0.878
Shock Cohort: Volume	1.03 (0.96, 1.11) 0.391	1.10 (1.02, 1.19) 0.012	1.06 (1.01, 1.12) 0.025	-0.03 (-0.22, 0.16) 0.770	0.05 (-0.09, 0.12) 0.460
Shock Cohort: Trauma Level I	1.52 (0.88, 2.61) 0.130	1.58 (0.71, 3.52) 0.261	0.75 (0.43, 1.34) 0.335	1.14 (-0.78, 3.07) 0.231	-1.29 (-2.69, 0.10) 0.067
TBI only Cohort: Volume	0.98 (0.91, 1.05) 0.589	1.05 (1.00, 1.11) 0.059	0.94 (0.88, 0.99) 0.033	0.50 (0.29, 0.71) <0.001	-0.27 (-0.43, -0.11) 0.002
TBI only Cohort: Trauma Level I	1.60 (0.80, 3.18) 0.183	0.88 (0.38, 2.09) 0.779	1.24 (0.69, 2.21) 0.476	-1.10 (-3.18, 0.97) 0.284	0.85 (-0.61, 2.30) 0.244

Adjustment Factors:

* age, sex, lowest PH SBP, PH GCS, transportation mode, use of advanced airway, PH time, mechanism of injury, ISS, initial ED SBP, head AIS

[^] age, sex, lowest PH SBP, PH GCS, transportation mode, use of advanced airway, PH time, mechanism of injury, ISS, initial ED SBP, head AIS, chest AIS, surgery Coef=Coefficient