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The Changing Pattern and Implications of Multiple Organ Failure (MOF) After Blunt Injury With Hemorrhagic Shock

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The Inflammation and the Host Response to Injury Collaborative Research Program

Abstract

Objective—To describe the incidence of post-injury multiple organ failure (MOF) and its relationship to nosocomial infection and mortality in trauma centers employing evidence-based standard operating procedures (SOPs).

Design—Prospective cohort study wherein SOPs were developed and implemented to optimize post-injury care.

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Setting—Seven U.S. Level I trauma centers.

Patients—Severely injured patients (> 16 years old) with a blunt mechanism, systolic hypotension (< 90 mmHg) and/or base deficit (> 6 meq/L), need for blood transfusion within the first 12 hrs, and an abbreviated injury score (AIS) ≥ two excluding brain injury were eligible for inclusion.

Measurements and Main Results—1,002 patients were enrolled and 916 met inclusion criteria. Daily markers of organ dysfunction were prospectively recorded for all patients while receiving intensive care. Overall, 29% of patients developed MOF. Development of MOF was early (median time of two days), short - lived, and predicted an increased incidence of NI, whereas, persistence of MOF predicted mortality. However, surprisingly, NI did not increase subsequent MOF and there was no evidence of a "second-hit" induced late onset MOF.

Conclusions—MOF remains common after severe injury. Contrary to current paradigms, the onset is only early, and not bimodal, nor is it associated with a "second-hit" induced late onset. MOF is associated with subsequent NI and increased mortality. SOP-driven interventions **may be** associated with a decrease in late MOF and morbidity.

Keywords

trauma; injury; standards of care; infection; multiple organ failure; mortality

INTRODUCTION

Multiple organ failure (MOF) was first described as a sequela to shock and infection over 30 years ago by Baue with the name first coined by Eiseman (1, 2). Modern resuscitation techniques developed in the 1960's led to improved immediate survival. However, late death increased as a result of the emergence of organ failure (3). MOF onset had a recognized bimodal temporal pattern frequently linked to a "second-hit" inciting event, such as nosocomial infection (NI). New treatment paradigms were directed at rapidly reversing physiologic abnormalities and reducing possible secondary insults. Among these were low tidal volume ventilation protocols to minimize the consequences of acute respiratory distress syndrome (ARDS), appropriate resuscitation guidelines to avoid overly aggressive crystalloid resuscitation, higher trigger (lower hemoglobin levels) prior to autologous red blood cell transfusion, as well as the use of glycemic control regimens to decrease post-operative infection rates (4-10). Although these standard operating procedures (SOPs) are associated with an improvement in mortality, the impact of these SOPs on MOF after severe injury is currently unknown (11).

The *'Inflammation and Host Response to Injury'* Large Scale Collaborative Project is a National Institute of General Medical Sciences (NIGMS)-funded collaborative study aimed at identifying the genomic and proteomic responses to injury associated with different clinical outcomes after trauma. As part of this multi-center clinical investigation, participating institutions developed and adopted standard operating procedures (SOP's) of best practices for the management of severely injured patients to optimize outcome and minimize differences in care between centers. This paper describes the incidence of MOF after severe blunt trauma and its relationship to nosocomial infection and mortality in trauma centers employing evidence-based standard operating procedures.

MATERIALS AND METHODS

This study is a primary analysis of data derived from an ongoing multi-center prospective cohort study. Standard operating procedures were developed and implemented across all

seven Level I Trauma centers to minimize variation in post-injury care, including early goal-directed resuscitation, glycemic control, venous thrombo-embolism prophylaxis, appropriate low tidal volume ventilation, ventilator-associated pneumonia management, and restrictive transfusion guidelines (4-10, 12). Patients admitted to one of the seven institutions over a four year period (November, 2003 through September, 2007) were included in the analysis. Cohort inclusion criteria included blunt mechanism of injury, presence of pre-hospital or emergency department systolic hypotension (< 90 mmHg) or an elevated base deficit (> 6 meq/L) within 30 minutes of arrival, a blood transfusion requirement within the first 12 hrs after injury, and any body region exclusive of the brain with an abbreviated injury score (AIS) ≥ 2, allowing exclusion of patients with isolated traumatic brain injury. Patients less than 16 or greater than 90 years of age, and those with cervical spinal cord injury, were also excluded. The study was approved by the Institutional Review Board (IRB) of each institution. In addition to local institutional oversight, the program was reviewed and approved by the IRB at Massachusetts General Hospital.

Clinical data were de-identified, entered and stored in a web-based data collection platform (TrialDB) by trained research nurses. Integrity of the data was maintained through ongoing curation and external data review by an independent chart abstractor. Patients were admitted to the intensive care units and daily markers of organ dysfunction were prospectively recorded. These included PaO_2/FiO_2 ratios for patients requiring ventilator support, serum creatinine levels (mg/dl), total bilirubin levels (mg/dl), pressure-adjusted heart rate, level of cardiac inotrope support, platelet count (platelets/ml 10^{-3}) and Glasgow Coma Score (GCS). These parameters allowed computation of the Marshall multiple organ dysfunction scores (MODS) for respiratory, renal, hepatic, cardiovascular, hematologic, and neurological systems to be determined up to 28 days while in the ICU (13). Using the Marshall scoring system, the diagnosis of MOF was defined as patients who had two or more consecutive days with a MODS score greater than or equal to six at least 48 hrs out from the time of injury. The score was calculated excluding the neurological component (as measured by GCS). The initial day of the two consecutive days with a score greater than or equal to six was considered as the onset day of MOF. Resolution was defined as two consecutive days with a score less than six. The initial day of the two consecutive days with a score less than six was considered the resolution day. Carrying forward the last observed value filled in intermittent missing data. On all days following the last observed MOF value, patients were assumed to be MOF-free and were assigned a score of zero. Patients could experience repeated episodes of MOF based upon the above definition.

The diagnosis of nosocomial infection required specific clinical criteria along with positive cultures. All time variables to the respective outcome event were determined from the day of initial injury, while the time to the first infection event was used in those patients with multiple infections. Diagnosis of ventilator-associated pneumonia (VAP) followed CDC criteria but also required a quantitative culture threshold of equal or greater than 10^4 CFU/ml for bronchoalveolar lavage specimens. Diagnosis of catheter-related blood stream infections required positive peripheral cultures with the identical organism obtained from either a positive semi quantitative culture (>15 CFU/segment), or positive quantitative culture (>10^3 CFU/segment) from a catheter segment specimen. Urinary tract infections required > 10^5 organisms/ml of urine. The day of first nosocomial infection was defined as the first day of any surgical site infection, pneumonia, urinary tract infection, blood stream infection, or catheter related blood stream infection occurring after study day two.

Patients who developed MOF were compared with those who did not develop MOF in a univariate fashion. Stepwise logistic regression modeling was then employed to determine independent risk factors for the development of MOF. Model covariates considered in the backward elimination process included selected patient demographics, early resuscitation

requirements, injury characteristics, shock parameters, comorbidities and early operative and ICU interventions. For this analysis, missing covariate values were mean imputed.

Cox proportional odds regression was used to model the effect of MOF on mortality and nosocomial infection. Mortality and nosocomial infection were treated as two distinct outcomes and were modeled separately. All patients who remained alive in the hospital on days three through 28 were considered to be at risk for death or nosocomial infection. The first two days were excluded to avoid acute resuscitation-induced organ dysfunction. Two summary measures of MOF were used as independent variables in the Cox model. First, the sum of the MOF scores on days two and three were used as a measure of baseline MOF intensity. Second, the cumulative sum of all MOF scores from day two through each study day, inclusive, were used as a measure of long term MOF exposure. On each of study days two to 28, these two scores were used to predict death or nosocomial infection on the following day. Baseline covariates included age, sex, ISS, APACHE, head AIS > three, 0-24 hour volume of PRBCs, 0-24 hour volume of crystalloids and surgical exposure were included as potential baseline confounders in multivariate models even though not statistically different because of their expected contribution to MOF development. Surgical exposure was treated as a time varying covariate that could increase the risk of nosocomial infection (particularly surgical site infections). The surgery score was initially assigned a value of zero. A value of one was assigned starting on the first day the patient had any procedure that did not violate the bowel or did not require damage control. A value of two was assigned on the first day the patient had a damage control procedure or a procedure that violated the bowel.

SAS 9·2 (SAS Institute Inc., Cary, NC) was used for all statistical calculations. All data were summarized as mean ± standard deviation, median [inter-quartile range], or percentage (%). Student-t or Mann-Whitney statistical tests were used to compare continuous variables, while Chi-Square or Fischer's Exact test were used for categorical variables.

RESULTS

Over the nearly four-year study period, 1,002 severely injured patients were enrolled. Eighty six patients died before post injury day two, leaving 916 patients who met the inclusion criteria. Table 1 provides demographics. The majority of patients were young, non-Hispanic, white males with a low incidence of comorbid disease processes. Median ISS was 29, median APACHE II was 30 and at least a third of the patients sustained an AIS > three grade injury in a major body compartment with an early mortality of 8·6% confirming severity of initial trauma (Table 2). Patients received a median of 10·5 L of crystalloid, approximately five units of packed cells and approximately three units of fresh frozen plasma (ratio of 1·7:1) (Table 3). Over 50% of the patients required mechanical ventilation on arrival to the emergency department, and nearly a quarter of patients were supported with vasopressor agents during the first 24 hrs.

Twenty nine percent of patients developed MOF. Patients who met MOF criteria were older, male, more severely injured, and had a higher proportion of comorbidities – particularly liver disease, than those who did not meet MOF criteria (Table 4). Patients diagnosed with MOF received greater resuscitation volumes of crystalloid, packed cells and fresh frozen plasma than those who did not meet criteria. Importantly, in this severely injured population, the physiologic parameters of shock, including base deficit and lactate, revealed that those with MOF had sustained greater depths of shock that lasted for a more prolonged period than those who did not have MOF. Of the 269 patients who developed MOF, 224 patients (83%) had one episode of MOF, 39 (15%) had two episodes and six (2%) had three episodes.

Multiple organ failure occurred early after injury [median day of first MOF diagnosis - [day two (Interquartile range (IQR): 2, 4)] and the number of new cases declined rapidly with increasing days post injury (Figure 1). Contrary to current paradigms, there was no late bimodal peak of organ failure identified. In addition, the first episode of MOF lasted a median of only four days (IQR: 2, 15). Interestingly, the median day of onset of nosocomial infection was seven (IQR: 5, 10), much later than the onset of MOF (Figure 1). While patients who developed MOF more commonly developed a subsequent nosocomial infection (75% vs. 39%, P<0·001 (Figure 2), in contrast to current belief, patients diagnosed with a nosocomial infection rarely developed subsequent MOF (Figure 2). As demonstrated in Figure 2, these findings are in contrast to the classical MOF paradigm implicating a secondary insult, such as nosocomial infection, as a contributor to MOF development.

Table 5 shows that predictors of MOF included male gender, pre-existing liver disease, greater injury severity, the use of early vasopressors, higher volumes of FFP and crystalloid resuscitation, as well as more severe depth of shock (lactate values in first 12 hrs) and duration of shock (worse base deficit values in hours 12 – 24 post injury). Red cell transfusion alone was not an independent predictor of MOF; however, transfusion was an entry requirement. Center contribution was also not evaluated as an independent predictor due to the standardization in care from the implementation of the SOPs. In fact, the rate of MOF, nosocomial infection, and MOF were similar between sites. Important predictors of nosocomial infection are shown in Table 6. Early severe and prolonged MOF was associated with the subsequent development of nosocomial infection. Independent predictors of mortality (Table 7) include the presence of increased age, higher severity of injury (APACHE II and ISS scores), and blood transfusion. The presence of MOF at baseline did not predict subsequent mortality, but persistence (or non-resolution) and higher cumulative exposure of MOF was a predictive of subsequent mortality.

DISCUSSION

The results of this study in severely injured blunt trauma patients identify several unique new trends in outcome. The development of MOF remains common, and is associated with higher rates of subsequent nosocomial infection, while persistence of MOF predicted increased mortality. Unlike the currently accepted paradigm, there was a single decreasing early peak in MOF incidence without evidence of the traditional secondary late-onset bimodal peak. Additionally, while MOF predicted the development of nosocomial infection, the development of infection, as a potential “second-hit” inciting event, surprisingly, was not temporarily associated with subsequent development of MOF. This may be partly explained by a stricter definitions in VAP based on BAL quantitative cultures compared to previous reports (2,14-15). However, the strict definitions used in this study was essential given the high incidence of SIRS and underlying chest injury which would have severely increased the number of false positive pneumonias detected (7).

Similar to previous studies, increasing age and male gender are associated with an increased incidence of MOF (14-16). It is unclear if the effect of age is the result of limited physiologic reserve, comorbid conditions that alter the response to injury, a modified response to injury associated with pre-injury medications or other unknown factors (17-19). In addition, being male was associated with greater than a two-fold increased risk of developing MOF. Sperry and colleagues have shown similar results, and also an association with higher IL-6 production in males post-injury as a marker of a plausible excessive pro-inflammatory mechanism in males after injury (20).

Expectedly, injury severity characteristics have been shown to be associated with the subsequent development of MOF (16, 21). Using univariate analysis, increasing injury

severity was associated with higher rates of MOF. Interestingly, however, in this severely injured cohort, physiologic markers of depth and duration of shock revealed that severe base deficit and higher lactates were even more significant predictors of MOF. Likewise, early elevated lactate levels and continued evidence of shock measured by elevated base deficit for 12 to 24 hours after injury were also independent predictors of MOF. As a potential partial explanation, these patients required more aggressive resuscitation as measured by crystalloid, blood and plasma transfusion volumes, which also correlated with MOF development, similar to prior studies (19, 22). However, since transfusion was an entry criterion for recruitment, only prolonged crystalloid resuscitation and FFP transfusion remained independent predictors of subsequent MOF.

Ciesla and colleagues previously showed that early organ dysfunction occurring within 48 hours of injury was infrequently sustained and resolved with completion of resuscitation (23). Similarly, there was an early peak in onset of MOF; with the majority of cases present on day two after injury but, unexpectedly, there followed a rapid deteriorating smooth slope of new onset cases with no late bimodal peak of new cases of MOF at six to eight days after injury, as historically described. Moore and colleagues described this second peak of MOF and attributed the second peak to deleterious pro-inflammatory consequences such as late infection; the commonly accepted “second-hit” phenomenon (24). The absence of a late peak of MOF in the current study may be due to the implementation of the SOP’s, and resolution of the underlying pathologic processes, which, while not preventing, enabled “tolerance” of subsequent infection without a secondary impact or increased mortality. As an example, increasing utilization of lung protective ventilation has been demonstrated to decrease activation of the immune system and incidence of MOF and is associated with decreased plasma inflammatory cytokine responses, and improved outcome in patients with acute lung injury or ARDS (23, 25, 26). Further support of this hypothesis is found by analyzing the relationship of organ failure and infection in this study. The incidence of nosocomial infection in this severely injured cohort approached 50%. However, while MOF was an identifiable risk factor for the development of nosocomial infection, nosocomial infection was not temporally associated with the development of MOF. It is entirely plausible that the late peak of MOF seen by Moore, while temporally associated with infection, was not caused by infection, but caused by management strategies that at the time were standard of care, but have since been shown to be injurious.

In contrast, persistence of sustained MOF is poorly tolerated and associated with a significantly increased mortality. The Canadian Critical Care Trials Group found that daily MODS scores provided additional prognostic value over the baseline score. Cabre and associates showed that a prolonged burden of MOF was associated with higher mortality, while Barie and associates found cumulative MODS scoring to be predictive of survival in an ICU setting (27-29). We accounted for two different measures of MOF; early severity of MOF was measured by the sum of the scores on days two and three after injury and the prolonged burden of MOF was measured as the cumulative (sum of) daily scores until the event in question. The two events analyzed were infection and death (after 48 hours post injury). Only cumulative MOF scores were associated with mortality in this study; the baseline MOF score was not an independent predictor of mortality as this score appeared related to physiologic factors associated with the initial injury severity.

While the results of this study are intriguing, there are limitations. First, this was an observational study and thus, only associations can be described and no cause and effect can be concluded. We implemented evidence-based SOPs in an effort to deliver and standardized best practice trauma care across centers. During the study period, SOP compliance was approximately 70% throughout the program and, compared to other benchmarks, was associated with an improvement in overall mortality.[(11)] However, this

observational study was not designed to test prospectively whether this intervention was responsible for the outcomes. Although there appears to be a need for prospective studies to determine the effect of SOPs on present day outcomes after severe blunt trauma, based on these and previous findings, prospective validation would be unethical.

CONCLUSION

MOF after severe blunt trauma remains a major complication. In this observational study, MOF occurred early after injury, without a secondary peak post injury as has been commonly defined. The development of MOF was associated with the subsequent development of nosocomial infection and persistence of MOF predicted death; however, the development of infection, though common, was not associated with subsequent development MOF. The data document the changes in MOF pattern and implications for modern day critical care management in the form of best-practice SOP's and requires further investigation.

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Classifications: organ dysfunction, nosocomial infection, inflammation, mortality, shock, trauma, intensivist, evidence-based medicine

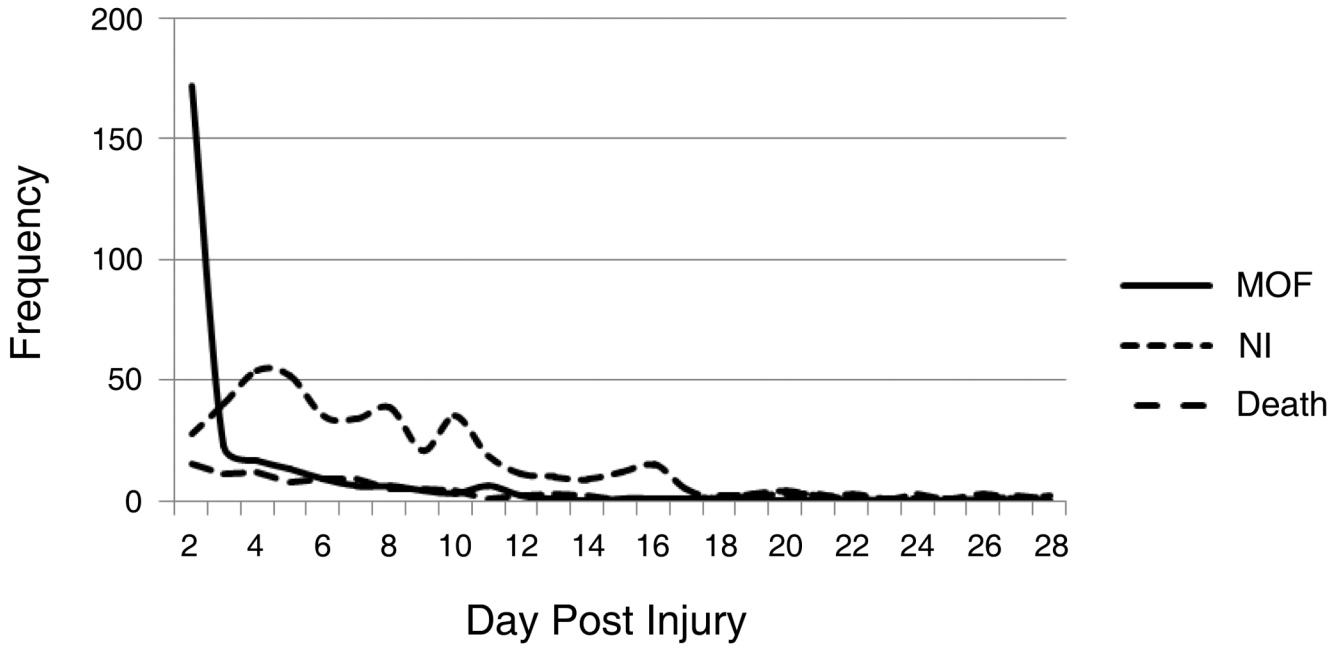

Figure 1.
Day of onset and frequency of multiple organ failure, nosocomial infection and death. MOF – multiple organ failure; NI – nosocomial infection.

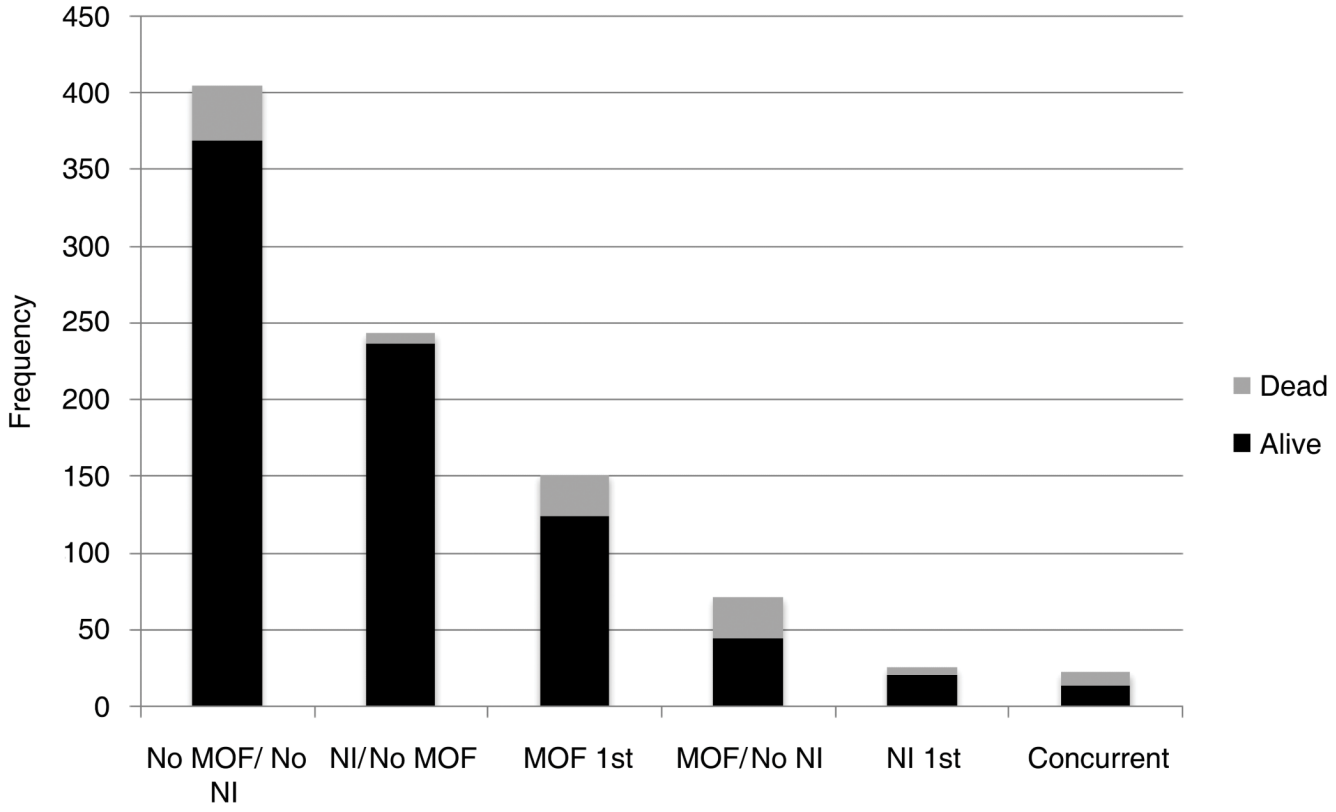

Figure 2.
Temporal relationship of nosocomial infection (NI), multiple organ dysfunction (MOF) and mortality. No MOF/No NI – patients who never experience either condition; NI/No MOF – patients who had nosocomial infection, never had MOF; MOF 1st – patients who had MOF before a diagnosis of nosocomial infection; MOF/No NI – patients who had MOF, never had nosocomial infection; NI 1st – patients who had nosocomial infection before a diagnosis of MOF; Concurrent – patients who had MOF and nosocomial infection diagnosed on the same day.

Table 1

Cohort Demographics (N=1,002)

Age; median (IQR)	40 (26, 54)
Sex (% male)	65
Race (% of total)	
White	88.2
African-American	7.4
Asian	2.6
Other	1.8
Ethnicity (% of total)	
Non-Hispanic	84.6
Hispanic	12.2
Unknown	3.2
Pre-Existing Comorbidity (% of total)	
Hypertension	15
Alcohol use	13.4
Diabetes	7
Liver disease	4.4
COPD	3.5

IQR: Interquartile range; COPD: Chronic obstructive pulmonary disease

Table 2

Injury Characteristics (N=1,002)

Motor Vehicle Collision	86.1
Occupant	55.2
Motorcyclist	14.3
Pedestrian	13.9
Cyclist	2.7
Fall	8.4
Machinery	1.8
Assault	0.9
Other	2.9
Injury Severity	
AIS > 3 (% of total)	
Head	34.3
Abdomen	43.2
Thorax	62.5
Extremity	61.8
ISS; median (IQR)	29 (22, 41)
Admission Motor GCS; median (IQR)	3 (1, 6)
Admission APACHE II; median (IQR)	30 (25, 34)
Initial ED SBP; mean (+ SD)	111 (32)
Worst ED SBP; mean (+ SD)	84 (25)
Time: injury to arrival (hours); median (IQR)	1.3 (0.8, 1.6)

AIS: abbreviated injury scale; ISS: injury severity score; GCS: Glasgow coma scale; APACHE: acute physiology and chronic health evaluation; ED: emergency department; SBP: systolic blood pressure; SD: standard deviation; IQR: interquartile range

Table 3

Treatment Characteristics [N=1,002, all data: median (IQR) unless noted]

Resuscitation Parameters	
Crystalloid (liters)	
0 – 12 hours	10.5 (7.6, 15.0)
>12 - 24 hours	2.4 (1.6, 4.5)
PRBC (liters)	
0 – 12 hours	1.8 (1.0, 3.5)
FFP (milliliters)	
0 – 12 hours	700 (0, 1750)
Worst Base Deficit	
0 – 12 hours (n=988)	10 (7, 14)
>12 – 24 hours (n=825)	2 (0, 6)
Worst Lactate	
0 – 12 hours (n=877)	5.1 (3.6, 7.3)
>12 – 24 hours (n=616)	3.0 (2.0, 4.7)
ED Mechanical Ventilation (% of total)	56
Pressor use 0 – 24 hours (% of total)	24
Operative Procedures: 0 – 24 hours (% of total)	
Ortho	19
Abdominal	43
Thoracic	8
Outcome, [N (% of 916 that survived at least 48 hours)]	
Nosocomial Infection	452 (49.3)
Multiple Organ Failure	269 (29.4)
Mortality	104 (11.3)

IQR: interquartile range; PRBC: packed red blood cells; FFP: fresh frozen plasma; ED: emergency department

Table 4

Comparison of patients who developed MOF compared to those who never developed MOF

	MOF	No MOF	P
Demographics			
Patients N (% of total)	269 (29.4)	647 (70.6)	
Age: median (IQR)	46 (28, 59)	38 (25, 50)	<0.0001
Sex (% male)	77	59	<0.0001
Comorbidity (% of total)			
Hypertension	21.2	13.1	0.0022
Diabetes	11.5	5.6	0.0016
Liver disease	7.8	2.9	0.001
Alcohol use	15.2	13.9	0.60
COPD	5.2	2.9	0.09
Injury Characteristics			
AIS ≥ 3 (% of total)			
Head	36.8	33.1	0.28
Abdomen	45.7	40.8	0.17
Thorax	71.0	57.5	0.0001
Extremity	69.1	60.9	0.018
ISS: median (IQR)	41 (29, 50)	35 (27, 43)	<0.0001
Resuscitation Parameters			
Crystalloid 1st 12 hours, L	12.52 (8.76, 17.21)	9.73 (7.22, 13.20)	<0.0001
Crystalloid 12-24 hours, L	3.34 (1.80, 6.25)	2.20 (1.60, 4.00)	<0.0001
PRBC 1st 12 hours, L	2.80 (1.40, 4.95)	1.40 (0.70, 2.45)	<0.0001
FFP 1st 12 hours, L	1.2 (0.40, 2.54)	0.40 (0, 1.20)	<0.0001
Vasopressor use (% of total)	39.2	12.8	<0.0001
ED mechanical ventilation	59.9	50.9	0.013
Physiologic Parameters			
Worst BD 1st 12 hours	11 (15, 8.1)	9.1 (12, 7)	<0.0001
Worst BD 12-24 hours	3.7 (6.9, 1)	2.0 (5, 0)	<0.0001
Worst lactate 1st 12 hours	6.1 (4.4, 8.4)	4.6 (3.3, 6.1)	<0.0001
Worst lactate 12-24 hours	3.8 (2.4, 5.7)	2.6 (1.8, 3.9)	<0.0001

IQR-Interquartile range, AIS–Abbreviated Injury Score, ISS–Injury Severity Score, PRBC–packed red blood cells, FFP–fresh frozen plasma, BD–base deficit, L–liters. Unless noted, all Resuscitation and Physiologic Parameter data expressed as median (IQR)

Table 5

Multivariate model of predictors of multiple organ failure

	Hazard Ratio	95% C.I.	P
Demographics			
Male gender	2.19	1.51 – 3.18	<0.0001
Comorbidity			
Hypertension	2.10	1.34 – 3.29	0.0011
Liver disease	2.29	1.08 – 4.845	0.03
Injury Characteristics			
AIS ≥3			
Thorax	1.67	1.13 – 2.46	0.01
Extremity	1.72	1.19 – 2.48	0.004
APACHE II (per point)	1.06	1.03 – 1.09	0.0002
ISS	1.01	0.99 – 1.03	0.075
Resuscitation Parameters			
Crystalloid 12-24 hours, L (per liter)	1.09	1.03 – 1.15	0.003
FFP 1st 12 hours, L (per liter)	1.31	1.15 – 1.51	<0.0001
Vasopressor use	2.09	1.51 – 3.18	0.0004
Physiologic Parameters			
Worst BD 12-24 hours	0.95	0.91 – 0.99	0.02
Worst lactate 1st 12 hours	1.07	1.01 – 1.14	0.04

AIS: Abbreviated injury score; FFP: Fresh frozen plasma; BD: base deficit; CI: confidence interval; APACHE: Acute physiology and chronic health evaluation

Table 6

Multivariate model of predictors of nosocomial infection after injury

	Hazard Ratio	95% C.I.	P
Demographics			
Age (per year)	1.00	0.99 – 1.01	0.86
Gender; Female	0.89	0.72 – 1.09	0.26
Injury Characteristics			
AIS ≥3			
Head	0.82	0.66 – 1.01	0.07
APACHE II (per point)	1.01	0.99 – 1.03	0.32
ISS (per point)	1.01	1.00 – 1.02	0.003
Surgery score	0.95	0.79 – 1.15	0.60
Resuscitation Parameters			
RBC 1st 24 hours (per liter)	1.035	0.997 - 1.075	0.0748
Crystalloid 1st 24 hours (per liter)	0.999	0.985 - 1.104	0.9359
Outcome			
Baseline MOF (per point)	1.05	1.01 – 1.08	0.006
Cumulative MOF (per point)	1.01	1.00 – 1.02	<0.001

AIS: Abbreviated injury scale score; APACHE: Acute physiology and chronic health evaluation score; ISS: Injury severity scale score; RBC: Red blood cell transfusion; MOF: Multiple organ failure score; CI: confidence interval

Table 7

Multivariate model of predictors of mortality after injury

	Hazard Ratio	95% C.I.	P
Demographics			
Age (per year)	1.02	1.00 – 1.03	0.014
Gender; Female	1.35	0.83 – 2.19	0.233
Injury Characteristics			
AIS ≥3			
Head	1.48	0.94 – 2.35	0.092
APACHE II (per point)	1.09	1.04 – 1.15	<0.001
ISS (per point)	1.03	1.01 – 1.05	0.002
Surgery score	0.60	0.42 – 0.86	0.006
Resuscitation Parameters			
RBC 1st 24 hours (per liter)	1.09	1.02 – 1.16	0.008
Crystalloid 1st 24 hours (per liter)	0.989	0.966 - 1.1012	0.3544
Outcome			
Baseline MOF (per point)	1.03	0.97 – 1.10	0.32
Cumulative MOF (per point)	1.03	1.02 – 1.04	<0.0001

AIS: Abbreviated injury scale score; APACHE: Acute physiology and chronic health evaluation score; ISS: Injury severity scale score; RBC: Red blood cell transfusion; MOF: Multiple organ failure score; CI: confidence interval