Form "EAST Multicenter Study Proposal"
Details #129 (submitted 09/30/2021)

Study Title	Prospective Observational Trial Examining Nationwide Trends of Aggressive Resuscitation Protocols for Catastrophic Brain Injuries
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Are you a current member of EAST?	Yes
If you selected "No" above please identify a Sponsor that is an active EAST member:	
My Multicenter Study proposal is...	Prospective

Catastrophic brain injury is associated with significant morbidity and mortality as well as profound alterations to vascular regulation1, metabolism1, endocrine function2,3, and coagulopathy4. Currently, the optimal resuscitation practices in catastrophic brain injuries are not known. Individual trauma centers may have formulated protocols, but practices vary substantially between hospitals and individual surgeon intensivists. While there is no standardized protocol for civilian use, the military Joint Trauma System has established clinical practice guidelines for managing casualties of catastrophic brain injury, which includes early identification of such injuries, intensive care to achieve hemodynamic stability, and resuscitation with fluids, blood products, vasopressors, and consideration of hormone therapy in patients with refractory hemodynamic instability5.

There is no centralized platform for sharing current practice protocols and outcomes between trauma centers. To address this knowledge gap and non-uniformity of practice, we propose a multi-institutional study to describe current trends of aggressive resuscitation protocols for use in catastrophic brain injury currently instituted at trauma centers nationwide. Defining which practices are common in trauma centers will provide the necessary data for future studies examining which practices lead to better outcomes. Aggressive resuscitation has been shown to benefit outcomes including organ donation in patients presenting with massive brain trauma6-9. We hypothesize that centers with standardized protocols in place for patients arriving with catastrophic brain injury will have improved organ donation rates.

Use this area to briefly (1-2 paragraphs only) outline the burden of the problem to be examined

References

1.Smith M. Physiologic changes during brain stem death — lessons for management of the organ donor. J Heart Lung Transplant. 2004;23(9 Suppl):S217-222.

2.Chen EP BH, Kendall SW, Van Trigt Peter. Hormonal and hemodynamic changes in a validated animal model of brain death. Crit Care Med. 1996;24:8.

3.Powner J HA, Lagler RG, Ng RH, Madden RL. Hormonal Changes in Brain Dead Patients. Crit Care Med. 1990;18(7):4.

4.Stein SC SD. Coagulopathy in Traumatic Brain Injury. Neurocritical Care. 2004;1(4):10.

5.Neal CJ, Bell RS, Carmichael JJ, et al. Catastrophic Non-Survivable Brain Injury Care-Role 2/3. Mil Med. 2018;183(suppl_2):73-77.

6.Alarhayem AQ, Cohn SM, Muir MT, Myers JG, Fuqua J, Eastridge BJ. Organ Donation, an Unexpected Benefit of Aggressive Resuscitation of Trauma Patients Presenting Dead on Arrival. J Am Coll Surg. 2017;224(5):926-932.

7.Love KM, Brown JB, Harbrecht BG, et al. Organ donation as an outcome of traumatic cardiopulmonary arrest: A cost evaluation. J Trauma Acute Care Surg. 2016;80(5):792-798.

8.Salim A, Velmahos GC, Brown C, Belzberg H, Demetriades D. Aggressive organ donor management significantly increases the number of organs available for transplantation. J Trauma. 2005;58(5):991-994.

9.Joseph B, Aziz H, Sadoun M, et al. Fatal gunshot wound to the head: the impact of aggressive management. Am J Surg. 2014;207(1):89-94.

Primary aim	Describe variation in institutional practices for resuscitation of trauma patients with catastrophic brain injuries.
Secondary aims	Investigate the association of institutional protocols on organ donor conversion rates after catastrophic brain injury.
Inclusion Criteria	Patients =18 years old who present with catastrophic brain injury with vital signs in ED
Exclusion Criteria	Patients who are pregnant, minors (<18 years old), and prisoners
Therapeutic Interventions	None. Observational study
Primary Outcome	Rate of institutional aggressive resuscitation protocol implementation at participating centers
Secondary Outcomes	a. Components of individual institutional protocols b. Triggers for initiation of aggressive resuscitation protocols c. Patient outcomes

•Patient: age, gender, race/ethnicity, comorbidities

•Injury: mechanism (MVC, fall, etc.), intent (assault, self-inflicted, accident, etc.), injury severity score (ISS), abbreviated injury severity (AIS), other injuries.

•Initial in-hospital neurocognitive exam: Glasgow Coma Score (GCS), GCS-eye (GCS-E), GCS-verbal (GCS-V), GCS-motor (GCS-M), CT brain findings (Marshall classification)

•Initial in-hospital vital signs: systolic/diastolic blood pressure (SBP/DBP), mean arterial pressure (MAP), respiratory rate (RR), heart rate (HR), temperature

•ED interventions

•Hospital course: neurosurgical interventions (craniotomy, craniectomy, etc.), other surgeries, hospital LOS, ICU LOS, ventilator duration, tracheostomy placement, feeding tube placement

•Institution or ICU protocol for catastrophic brain injury in place? (y/n)

•Institution or ICU protocol for catastrophic brain injury initiated? (y/n)

•If catastrophic brain protocol exists and not initiated, reason(s) for it non-initiation (ex. injury severity, patient age, advance directive/DNR in place, etc.)

List specific variables to be collected & analyzed

•Patient status triggering initiation of aggressive resuscitation

•Therapy (if applicable):

•Fluids administered during resuscitation? (y/n)

•Volume of fluids administered during resuscitation

•Whole blood, PRBCs, platelets, fresh frozen plasma and cryoprecipitate administered during resuscitation? (y/n)

•Number of whole blood, PRBCs, platelets, fresh frozen plasma and cryoprecipitate units during resuscitation

•Hormone replacement therapy agents administered (including methylprednisone, vasopressin, insulin, T3, T4, dopamine) during resuscitation? (y/n)

•Dosages of hormone replacement therapy agents administered during resuscitation

•Fluid balance in OR

•Damage control indicators present during operation? (coagulopathy, acidosis, hypothermia?)

•Post-operative course (fluid requirements in first 12 hrs post-op, 24 hrs post-op, antibiotics given?)

•Mechanical ventilation? (y/n)

•Ventilation mode

•Maximum peak airway pressure observed

•Number of hours on vent

•Biomarker levels (creatinine, troponin, bilirubin, lipase, ALT, AST, ejection fraction, PaO2 and FiO2) at peak levels and time of donation or death without donation

•Advance directive pre- and post- admission? (y/n)

•Withdrawal of care? (y/n)

•DNR status (pre- and post-admission)

•Outcomes:

•Brain death? (y/n)

•Cardiopulmonary arrest? (y/n)

•Time from admission to death

•Organs donated? (y/n)

•If no organ donation, reason for non-donation (medically unstable, no next-of-kin consent, etc.)

•List of organs donated

•Adverse events/complications:

•Medication specific: cardiac arrhythmia, hypertension, tachycardia, seizure, other

•In-hospital events: acute kidney injury (AKI), cardiopulmonary arrest, myocardial infarction (MI), pneumonia, respiratory failure, acute respiratory distress syndrome (ARDS), sepsis, unplanned operative intervention, venous thromboembolic event (VTE), other

Institutional protocols for aggressive resuscitation after catastrophic brain injury will be collected from centers with such guidelines. For centers without standardized protocols, we will examine variation in practices between institutions and intensivists.

Outline the data collection plan and statistical analysis plan succinctly

Data will be entered into a secure REDCap database using information from chart review from participating individual institutions. Descriptive statistics will be calculated for categorical and continuous variables. Continuous variables will be examined using Student's t-test, and categorical variables will be examined with chi-squared test. Multivariable logistic regression will be used to identify any predictors of secondary outcomes. As the goal of this study is descriptive (Aim 1), this will obviate the need of power analysis. Previous studies with similar goals include Alarhayem et. al 6 and Love et. al 7, both of which were descriptive.

Alarhayem AQ, Cohn SM, Muir MT, Myers JG, Fuqua J, Eastridge BJ. Organ Donation, an Unexpected Benefit of Aggressive Resuscitation of Trauma Patients Presenting Dead on Arrival. J Am Coll Surg. 2017;224(5):926-932.

7.Love KM, Brown JB, Harbrecht BG, et al. Organ donation as an outcome of traumatic cardiopulmonary arrest: A cost evaluation. J Trauma Acute Care Surg. 2016;80(5):792-798.

Include the Target Number of Centers:

12

Include the Target Number of Patients:

250

What is the anticipated time to complete this study?

Two

If applicable, include a Data Power Analysis:

NA

Outline consent procedures here, if applicable

This prospective observational study is designed to record data on patients who will be managed according to a critical care team's best clinical judgment. IRB approval will be obtained at all participating sites and Data Transfer Agreements will be completed when applicable. Waiver of informed consent will be requested, as the data obtained will originate from existing information in the medical record and will involve no patient contact. Data will be collected by each participating site, will be de-identified, and entered into a secure REDCap database.

Succinctly outline a risk/benefit analysis

The risk ascribed to this study is no greater than that of the current standard of care in which patients may or may not receive aggressive resuscitation based on a clinician's best judgment. However, if aggressive resuscitation is identified as advantageous for patients with catastrophic brain injuries in terms of survival, or ability to donate organs in the case of death, then significant benefit could result in future standard, evidence-based protocols.

Include a brief listing of key references

1.Smith M. Physiologic changes during brain stem death — lessons for management of the organ donor. J Heart Lung Transplant. 2004;23(9 Suppl):S217-222.

2.Chen EP BH, Kendall SW, Van Trigt Peter. Hormonal and hemodynamic changes in a validated animal model of brain death. Crit Care Med. 1996;24:8.

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EAST Multicenter Study Proposal: Prospective Observational Trial Examining Nationwide Trends of Aggressive Resuscitation Protocols for Catastrophic Brain Injuries

Background

Catastrophic brain injury is associated with significant morbidity and mortality as well as profound alterations to vascular regulation[1], metabolism[1], endocrine function[2,3], and coagulopathy[4]. Currently, the optimal resuscitation practices in catastrophic brain injuries are not known. Individual trauma centers may have formulated protocols, but practices vary substantially between hospitals and individual surgeon intensivists. While there is no standardized protocol for civilian use, the military Joint Trauma System has established clinical practice guidelines for managing casualties of catastrophic brain injury, which includes early identification of such injuries, intensive care to achieve hemodynamic stability, and resuscitation with fluids, blood products, vasopressors, and consideration of hormone therapy in patients with refractory hemodynamic instability[5].

There is no centralized platform for sharing current practice protocols and outcomes between trauma centers. To address this knowledge gap and non-uniformity of practice, we propose a multi-institutional study to describe current trends of aggressive resuscitation protocols for use in catastrophic brain injury currently instituted at trauma centers nationwide. Defining which practices are common in trauma centers will provide the necessary data for future studies examining which practices lead to better outcomes. Aggressive resuscitation has been shown to benefit outcomes including organ donation in patients presenting with massive brain trauma[6-9]. We hypothesize that centers with standardized protocols in place for patients arriving with catastrophic brain injury will have improved organ donation rates.

Specific Aims

Primary aim: Describe variation in institutional practices for resuscitation of trauma patients with catastrophic brain injuries.

Secondary aim: Investigate the association of institutional protocols on organ donor conversion rates after catastrophic brain injury.

Experimental Design/Methods

We will perform a prospective, observational study investigating the current state of treatment and aggressive resuscitation protocols for use in catastrophic brain injury patients. We will describe the use of catastrophic brain injury protocols as well as variation in practice between different institutions and different intensivists.

We define a standardized protocol in this study as a written document in place at an institution for guidance of trauma patient care that is followed by a majority of the practitioners. Some protocols may be in the format of an order set. In line with the Joint Trauma System Clinical Practice Guideline, catastrophic brain injury is defined here as any brain injury that is expected (by the trauma surgeon, neurosurgeon, or other care team members) after imaging evaluation and /or clinical exam to result in the permanent loss of all brain function above the brain stem level [5].

We will determine the variability of institutional practices nationwide in resuscitation strategies such as, but not limited to, the use of vasopressors, blood products, steroids, and hormone replacement therapy. In addition, we will determine if the presence of a standardized catastrophic brain injury protocol is associated with increased organ donation.

Inclusion Criteria:

Patients ≥18 years old who present with catastrophic brain injury with vital signs in ED

Exclusion Criteria:

Patients who are pregnant, minors (<18 years old), and prisoners

Outcomes Measures

A) ***Primary Outcomes:***

Rate of institutional aggressive resuscitation protocol implementation at participating centers

B) ***Secondary Outcomes:***

a. Components of individual institutional protocols
b. Triggers for initiation of aggressive resuscitation protocols
c. Patient outcomes

Variables

- Patient: age, gender, race/ethnicity, comorbidities
- Injury: mechanism (MVC, fall, etc.), intent (assault, self-inflicted, accident, etc.), injury severity score (ISS), abbreviated injury severity (AIS), other injuries.
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    - Volume of fluids administered during resuscitation

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    - Number of whole blood, PRBCs, platelets, fresh frozen plasma and cryoprecipitate units during resuscitation
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- Advance directive pre- and post- admission? (y/n)
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- DNR status (pre- and post-admission)
- Outcomes:
    - Brain death? (y/n)
    - Cardiopulmonary arrest? (y/n)
    - Time from admission to death
    - Organs donated? (y/n)
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References

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