EAST MULTICENTER STUDY
DATA COLLECTION TOOL

Multicenter Study: **Optimal resuscitation in pediatric trauma—an EAST multicenter study**

Enrolling Center: Cincinnati Children's Hospital Medical Center
Enrolling Co-investigator: Richard Falcone Jr. MD, MPH

Center: _____

Study ID (number patients consecutively): _____

Screening for Inclusion (patient must meet all four):

Trauma team activation ☐ yes ☐ no

Age <18 years ☐ yes ☐ no

Does patient have elevated age adjusted shock index? ☐ yes ☐ no

To calculate shock index:

Initial vitals in ED: HR _____ SBP _____

Shock index= HR/SBP= _____
Age ≤6 years elevated if > 1.2
Age 7-12 years elevated if > 1.0
Age ≥13 years elevated if > 0.9

If meets all four inclusion criteria, proceed to next section. If does not meet all inclusion criteria, stop here; no need to submit form.

Does the patient meet any of the following exclusion criteria?

☐ No EMS transport (police or personal vehicle drop off)
☐ Primary burn or asphyxiation injury mechanism
☐ If burn not primary mechanism but has >20% BSA
☐ Transferred from another facility (not transferred directly from scene)

If yes to any exclusion criteria, stop here and submit form. Otherwise continue to next page.

Demographics / Injury Variables

Date of birth _ _/_ _/_ _ _ _

Sex: ☐ Male ☐ Female

Type of injury: ☐ Blunt ☐ Penetrating

Mechanism of injury: ☐ MVC ☐ Motorcycle ☐ Pedestrian ☐ Fall ☐ Bicycle
☐ Other motor vehicle (ATV, snowmobile, etc.) ☐ Struck ☐ Crush ☐ GSW
☐ Stab ☐ Other (write in: _____)

Date of injury _ _/_ _/_ _ _ _ Time of injury _ _:_ _

Date of arrival _ _/_ _/_ _ _ _ Time of arrival _ _:_ _

Weight (estimated in ED): _____ kg

Mode of transport: ☐ ground EMS
☐ helicopter EMS
☐ private car/drop off
☐ other (write in) _____

Tier of activation: ☐ 1/highest ☐ 2/middle ☐ 3/lowest

Prehospital Information

Vitals in Field/Transport:

First HR: _____ SBP: _____ GCS: _____ ☐ not available
Last HR: _____ SBP: _____ GCS: _____ ☐ not available
Highest HR: _____ Lowest SBP: _____ Lowest GCS: _____ ☐ not available

Prehospital Fluids and Blood Products:
Crystalloid given: _____mL
Total blood products given: _____mL
RBC volume: _____mL
Plasma volume: _____mL
Platelet volume: _____mL
Cryoprecipitate volume: _____mL
Non-blood colloid given: _____mL

TXA given: ☐ yes ☐ no
If yes, was it started ☐ prehospital or ☐ in ED?

Emergency Department Resuscitation

Initial Vitals in ED:

HR: _____ SBP: _____ GCS: _____ Temperature: _____

Initial Laboratory Values:

Time drawn: _ _ : _ _

Hemoglobin		Platelets		INR	

Lactate		Base Deficit		pH		Creatinine	

TEG obtained in ED: ☐ yes ☐ no

If yes, initial r value: _____ MA value: _____

Fluid Resuscitation in ED:

Type of fluid (crystalloid, RBC, plasma, platelets, cryo, other colloid)	Volume Given (mL)	Start time (00:00)

ED Vital Signs (every 15 minutes up to 120 minutes):

Time (00:00)	HR	SBP

ED Disposition:

☐ Deceased
☐ Home
☐ Operating room/Interventional Radiology (If OR/IR, name procedure: _____)
☐ General care floor
☐ Intensive Care Unit
☐ Transfer to another hospital
☐ Other (write in: _____)

ED Fluid Totals:

Crystalloid given: _____mL
Total blood products given: _____mL
PRBC volume: _____mL
Plasma volume: _____mL
Platelet volume: _____mL
Cryoprecipitate volume: _____mL
Whole blood volume _____mL
Non-blood colloid given: _____mL

Admission

Time of arrival to new unit (including OR; 00:00): _____

Vitals, Labs, and Fluid Totals after ED (leave blank if not obtained at that time point)

Time point (after arrival to new unit)	Vitals		Labs*						Fluid Totals (cumulative, mL)			
	HR	SBP	Hgb	PLT	INR	TEG r	TEG MA	pH	Crystalloid	RBCs	Plasma	PLT
1 hr												
3 hrs												
6 hrs												
12 hrs												
24 hrs												

*Round to within nearest 30 minutes, if no lab value within ±30 minutes, leave blank.

Outcomes

ICU length of stay in days (no ICU admission = 0): _____
Ventilator duration in days (no ventilator = 0): _____
Total length of stay in days: _____
Discharge disposition: ☐ alive ☐ deceased
If deceased, date (MM/DD/YEAR) and time (00:00) of death: _ _/_ _/_ _ _ _ _ _:_ _
If alive, GCS at discharge: _____

Complications and Date Occurred:

☐ Acute renal failure (date _ _ /_ _/ _ _ _ _)
☐ ALI/ARDS (date _ _ /_ _/ _ _ _ _)
☐ Catheter associated urinary tract infection (date _ _ /_ _/ _ _ _ _)
☐ Hospital acquired pneumonia (date _ _ /_ _/ _ _ _ _)
☐ Blood stream infection (date _ _ /_ _/ _ _ _ _)
☐ Sepsis (date _ _ /_ _/ _ _ _ _)
☐ DVT/PE (date _ _ /_ _/ _ _ _ _)
☐ None

Retrospective Registry Data

ISS		
AIS	Head	
	Chest	
	Abdomen	
	Spine	
	Upper Extremity	
	Lower Extremity	
	Face	
	Neck	
	External	

Injuries (insert all ICD-9/10 Diagnosis codes associated with admission from registry):

Procedures (insert all ICD-9/10 procedure codes associated with admission from registry):

Preexisting comorbidities: ☐ yes ☐ no

If yes, specify: _____

Name: Optimal resuscitation in pediatric trauma – an EAST multicenter study

I. ABSTRACT

There have been limited studies on the ideal resuscitation practices for children presenting in shock after injury concerning for hemorrhage. Adult trauma patients are recommended to receive one fluid bolus, with consideration for immediate transfusion if displaying signs of hemorrhage. While children who receive a massive transfusion, defined as greater than 40 cc/kg of blood, have mortality in excess of 10%, retrospective evaluation of pediatric trauma patients has shown mixed results with respect to the optimal crystalloid volume and ratio of products. Previous studies have found that high volume crystalloid resuscitation has been associated with increased length of stay, increased ICU stay, need for ventilator support and increased mortality. Retrospective data demonstrates that the chances of needing a transfusion are similar regardless if two or more fluid boluses are given, suggesting that response to crystalloid plateaus with the second bolus. This prospective, observational study aims to capture pediatric trauma patients presenting in shock at an earlier stage and focus on the initial administration of crystalloid, specifically the optimal volume and timing of transition to blood products.

II. PUPRPOSE OF STUDY

Hypothesis: The decreased use of crystalloid prior to transfusion in children presenting in shock following trauma is associated with improved outcomes.

Specific aims

Primary Aim

1. To determine the impact on primary outcomes of crystalloid administration volume and timing prior to blood products in children presenting in shock following trauma.

Secondary Aims

1. To determine patient factors that predict need for early transfusion of blood products in pediatric trauma patients presenting in shock.
2. To relate primary outcomes to ratio of blood products in pediatric trauma patients in shock who are transfused.
3. To define variability in pediatric trauma fluid and blood resuscitation practices between centers.

This study aims to capture pediatric trauma patients presenting in shock at an earlier stage and focus on the initial administration of crystalloid—specifically the optimal volume and timing of transition to blood products.

III. BACKGROUND AND SIGNIFICANCE

Resuscitation of adult trauma patients in hemorrhagic shock includes minimizing crystalloid and early transfusion of blood products in balanced ratios based on prospective observational and interventional studies (1); however, the ideal resuscitation practices for children presenting in shock after injury concerning for hemorrhage are unknown. The 10^{th} version of ATLS will continue to recommend pediatric trauma patients receive up to three 20 cc/kg crystalloid boluses, with consideration for blood products after the second bolus however recognizes a movement towards limiting crystalloid and damage control resuscitation in children following the first bolus (2). Adult trauma patients are

recommended to receive one fluid bolus, with consideration for immediate transfusion if displaying signs of hemorrhage. While children who receive a massive transfusion, defined as greater than 40 cc/kg of blood, have mortality in excess of 10%, retrospective evaluation of pediatric trauma patients has shown mixed results with respect to the optimal crystalloid volume and ratio of products (3).

Acker et al. found that high volume crystalloid resuscitation was not associated with increased risk of complications such as ARDS but was associated with greater duration of hospital stay and need for mechanical ventilation (4). Similarly, Department of Defense (DOD) data demonstrated greater ICU duration, ventilator duration, and length of stay in children who received >40 cc/kg of blood if they had received high volume crystalloid (5). In the same study, children who were transfused in balanced ratios of products had increased mortality. Retrospective data to be presented at the 2018 EAST Annual Assembly demonstrates that the chances of needing a transfusion are similar regardless if two or more fluid boluses are given, suggesting that response to crystalloid plateaus with the second bolus.

In summary, existing retrospective data has not facilitated consensus on the optimal timing and composition of resuscitation in hemorrhaging pediatric trauma patients and there continues to be variability in practice. Additionally, existing retrospective and prospective studies on pediatric resuscitation are centered on a volume-based definition of massive transfusion or activation of a massive transfusion protocol (5, 6). Patients who would have benefited from early transfusion or massive transfusion but received a crystalloid-heavy resuscitation may be missed if they do not meet inclusion criteria of a massive transfusion activation or minimum volume of transfused products.

IV. RESEARCH PLAN

1. Human Subjects

1. A. Type of Study
- Prospective multi-center observational study of injured children

1. B. Inclusion / Exclusion

Inclusion:
- Children ≤ 17 years of age
- Trauma team activation
- Transferred directly from scene
- Elevated age adjusted shock index (SIPA) (8)
    - Shock index = heart rate/systolic blood pressure on arrival
    - Ages ≤6 years elevated SIPA >1.22
    - Ages 7-12 elevated SIPA >1.0
    - Ages ≥13 elevated SIPA >0.9

Exclusion:
- >20% BSA burn
- Burn/inhalation only injury
- Asphyxiation injury
- Treated at another facility initially
- Transported by private vehicle or police

1. C. Sample size

- 475 patients are needed to detect a decrease in mortality between the published approximately 15% for children who require transfusion and 7.5%. Based on adult studies, this is the short-term survival benefit associated with optimal resuscitation (1). This sample size is a conservative estimate and will also ensure power to detect a difference in intensive care length of stay and hospital length of stay.

1. D. Data protection

- Each patient will receive a unique study number as will each participating institution.
- Data will be entered into a Redcap secure electronic database developed by the PI.
- All data will be maintained in a de-identified format. No patient identifiers will be stored or utilized in any data analysis.

2. Recruitment

Information regarding the study will be shared with the faculty, fellows, residents and nursing staff in the Emergency Departments and Pediatric Surgical Departments at participating institutions. Members of each of these groups are actively involved in the initial care of trauma patients.

All subjects will be recruited from the Trauma Service at one of the participating Trauma Centers. There will be no discrimination for recruitment based on race or ethnicity. Children that present to the Trauma Bay will be screened by the attending physician, trauma fellow, resident or Trauma Core Nurse to assess if the child meets established shock index criteria. Each morning, a research coordinator will review the previous 24 hour trauma service admits to verify children were not missed for this study.

3. Plan to Obtain Consent / Assent

Consent is not required for this study as this investigation is an evaluation of optimal volume and timing prior to the administration of blood products and not a clinical evaluation of the injured child that presents in shock. No study related interventions will be performed for this observational study. The risk to the patient is therefore considered minimal and is related only to the potential loss of confidentiality which should be minimal given de-identification plans for the data. In addition, due to the severity of the traumatic injuries being investigated, it would often not be appropriate to obtain consent from the parents or assent from the child as this would generate undue emotional distress as well as limit the ability to complete this important project.

We request a waiver of informed consent from the Institutional Review Board at CCHMC. The project meets the requirements of 45CFR Part 46 in that is presents no more than minimal risk to the participants and could not be practicably carried out without the waiver. The patients included in the medical record review are critically ill or injured patients and therefore it would not be feasible to obtain informed consent from each patient.

4. Vulnerable Populations

Children are considered a vulnerable population. In this study, selection of subjects, all of which are children, will be equitable and based on clinical presentation to the Emergency Department. As this is an observational study, childrens' care will be the same high-quality care whether or not they participate in this study.

5. Randomization

Randomization is not pertinent for this research.

6. Procedures

A data collection form (Appendix 1) will be started for each patient meeting inclusion criteria upon their arrival or within 24 hours. Data collection forms will be turned in to study coordinators/staff who will review the previous 24 hours' patients and complete the data collection form up to the section requiring retrospective review following discharge. This information will be abstracted from the trauma registry. Data points to be collected are in Appendix 1. All procedures are observational and involve recording of data, there is no intervention associated with this study. These data points will be used to achieve the aims and analysis plans below.

This will be a multicenter study with CCHMC as the coordinating center. Collaborating centers will be identified in the future and this protocol will be amended accordingly. All institutions will obtain their own IRB approval. A Redcap standardized data collection tool will be created for deposition of de-identified data on each patient. Each patient will receive a unique study number as will each participating institution. Data collections sheets can be submitted to the coordinating institution for data entry into Redcap or participating institutions may enter data directly into Redcap.

Aim 1: To determine the impact on primary outcomes of crystalloid administration volume and timing prior to blood products in children presenting in shock following trauma.

The primary outcomes of this study are mortality and return to normal age-adjusted shock index Secondary outcomes are intensive care days, ventilator days, complications, total blood products, and hospital length of stay in days. Weight based volumes of crystalloid and blood products at various time points will be determined and associated with the aforementioned outcomes using univariate and multivariable analyses. Cox logistic regression analysis will be used to evaluate the relationship with time-dependent, categorical outcomes such as 24 hour, 7 day, and 30 day survival. Patients discharged prior to the mortality cutoff will be right-censored as surviving. Adjusted survival curves will be generated to determine the impact of crystalloid volume on time to return of normal age adjusted shock index. Stratified analysis by age group may be performed. Since this is an observational study, adjustments will be made to account for clustering of patients at individual centers.

Aim 2: To determine patient factors that predict need for early transfusion of blood productions in pediatric trauma patients presenting in shock.

Additional univariate and time-dependent multivariable analyses will be performed with blood transfusion as the outcome to identify factors independently associated with transfusion.

Aim 3: To relate primary outcomes to ratio of blood products in pediatric trauma patients in shock who are transfused.

Among the subset of patients who are transfused, multivariable logistic regression will be used to determine the impact of blood product ratio on primary outcomes described above. Time-dependent analysis will be performed for the outcome of mortality.
Aim 4: To define variability in pediatric trauma fluid and blood resuscitation practices between centers.

A unique center ID will be assigned to each participating center so that patients from a single center can be identified. Differences in baseline characteristics and injury severity by center will be determined as well as variability in crystalloid volume and time to transfusion among those patients who were transfused.

7. <u>Previously Approved Research Studies</u>

None.

V. POTENTIAL BENEFITS

There are no direct benefits to the subject from taking part in this study. This study will help Trauma Service staff to capture pediatric trauma patients presenting in shock at an earlier stage and will focus on the initial administration of crystalloid – specifically the optimal volume and timing of transition to blood products.

VI. POTENTIAL RISKS, DISCOMFORTS, INCONVENIENCES AND PRECAUTIONS

There is no active intervention, so the risk to the study participant is minimal. The main risks are breach of confidentiality. Efforts to limit this risk are described above under 'Human Subjects'.

VII. RISK/BENEFIT ANALYSIS

This is a no greater than minimal risk study without direct benefit to the participant.

VIII. DATA AND SAFETY MONITORING PLAN

This is a prospective, data-collection only study which poses no greater than minimal risk. No active interventions other than normal procedural care will be done. The investigator will monitor the productivity of the study as well as expected and unexpected adverse events and unanticipated problems, and will follow institutional guidelines for reporting of such events /problems to IRB.

IX. CONFIDENTIALITY

Study participants will be assigned a unique identification number to protect their confidentiality. The research data will be stored in the Trauma Office at Cincinnati Children's Hospital and secured in a locked facility that will be accessible only to the principal investigator, co-investigators, and his / her

designees. The data from this study may be published, but subject's identify will not be disclosed. Subject identify will remain strictly confidential unless disclosure is required by law.

X. PERIOD OF TIME ESTIMATED TO COMPLETE THE PROJECT AS DESCRIBED

We anticipate enrolling approximately 475 patients total at all institutions. We anticipate CCHMC would contribute 50 patients per year based on review of our registry. Other centers will likely contribute equal or fewer number of patients; we estimate 25 patients per hospital per year. Depending on collaboration we expect data collection to take one to two years. If we have nine collaborating centers, it would take two years to accrue the target patients. If we had 19, it would take one year. We expect to complete data accrual, analysis, and reporting by July, 2020.

XI. FUNDING

No outside funding for this study will be required.

XII. PAYMENT FOR STUDIES

There will be no payment for enrollment in this study.

XIII. REFERENCES

1. Holcomb JB et al. The prospective, observational, multicenter, major trauma transfusion (PROMMTT) study: comparative effectiveness of a time-varying treatment with competing risks. JAMA Surg 2013; 148(2):127-30.
2. American College of Surgeons Committee on Trauma. Advanced Trauma Life Support Compendium of Changes. 2017.
3. Neff LP et al. Clearly defining pediatric massive transfusion: cutting through the fog and friction with combat data. J Trauma Acute Care Surg 2015; 78(1).
4. Acker SA et al. Injured children are resistant to the adverse effects of early high volume crystalloid resuscitation. J Pediatr Surg 2014; 49(12):1852-5.
5. Edwards MJ et al. The effects of balanced blood component resuscitation and crystalloid administration in pediatric trauma patients requiring transfusion in Afghanistan and Iraq 2002 to 2012. J Trauma Acute Care Surg 2015; 78(2): 330-5.
6. Spinella, PC. Massive transfusion In Children (MATIC) Study - Update. Washington University in St. Louis. http://www.bloodnetresearch.org/wp-content/uploads/2016/04/MATIC-Protocol-Review-Oct-8-2015.pdf.
7. Falcone RA Jr et al. A multicenter prospective analysis of pediatric trauma activation criteria routinely used in addition to the six criteria of the American College of Surgeons. J Trauma Acute Care Surg 2012; 73(2): 377-384.
8. Acker SA at al. Pediatric specific shock index accurately identifies severely injured children. J Pediatr Surg, 2015.

Appendix 1. Data Collection Form