Proposal Title: Whole Blood Resuscitation for Hemorrhagic Shock in Geriatric Trauma Patients: A Western Trauma Association Multicenter Trial

Co-PIs: Caitlin A. Fitzgerald, MD FACS, Mary Noory, MD
WTA Senior-PI/Member Sponsor: Martin Zielinski, MD FACS
Primary Site Institution: Baylor College of Medicine
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BACKGROUND AND SIGNIFICANCE

Trauma remains a leading cause of death in older adults, and the proportion of geriatric trauma patients (age ≥ 65) continues to rise as the population ages.[1] Compared with younger adults, older patients experience significantly higher mortality following traumatic hemorrhage. Age-related physiologic changes including reduced cardiovascular reserve, impaired oxygen delivery, and the increased usage of anticoagulant and antiplatelet agents all contribute to an elderly patient's vulnerability to hemorrhagic shock and traumatic coagulopathy.[2]

Hemorrhage remains one of the most preventable causes of early trauma death.[3-6] Traditionally, damage control resuscitation strategies emphasized component therapy (CT) via early balanced transfusion in a 1:1:1 ratio of packed red blood cells, plasma, and platelets.[7] More recently, low-titer group O whole blood (LTOWB) has emerged as a superior transfusion agent that has been shown to improve survival in trauma patients with hemorrhagic shock.[8-9] As a result, the use of LTOWB has rapidly expanded across both trauma centers and in the pre-hospital setting.

Despite the robust adoption of LTOWB transfusion protocols, most studies that have evaluated LTOWB when compared with CT have focused primarily on younger patients with severe hemorrhagic shock.[10-13] Thus, geriatric patients are often underrepresented in the literature which marks an important knowledge gap as older adults may derive a particular benefit from early LTOWB resuscitation. Previous work has shown that the use of LTOWB reduces the total transfusion volume and provides more rapid correction of coagulopathy,[14] two factors that may be especially important in elderly patients with limited physiologic reserve and underlying platelet and coagulation factor dysfunction.

At present, there are no multicenter trials in the literature that specifically evaluate the use of LTOWB resuscitation in geriatric trauma patients. As the number of elderly trauma patients continues to increase, there remains a critical knowledge gap in defining the optimal resuscitation strategies for this population. We aim to determine if LTOWB provides a similar mortality benefit in the geriatric trauma population. We hypothesize that a similar mortality benefit will be seen in trauma patients ≥ 65 years of age.

SPECIFIC AIMS

Aim 1: Determine whether initial resuscitation with LTOWB is associated with a mortality benefit in geriatric trauma patients when compared with CT.

Aim 2: Evaluate whether resuscitation with LTOWB decreases blood product utilization in geriatric trauma patients.

RESEARCH METHODS

Study Design and Population

This is a retrospective, multi-center study comparing early resuscitation with LTOWB to standard CT in elderly trauma patients with hemorrhage requiring transfusion. Patients meeting inclusion criteria will be divided into those who received any LTOWB and those who received only CT consisting of packed red blood cells, plasma, and platelets. Demographics, mechanism of injury, injury severity, treatment, and patient outcomes will be compared based on these groups.

The study population will include any adult trauma patient ≥ 65 years of age who required resuscitation with LTOWB or CT from January 1, 2017 through December 31, 2025. Patients will be excluded if they are < 65 years of age, are incarcerated, have a known do not resuscitate order in place, or die within 8 hours of admission.

Each participating center will obtain individual IRB approval to access to the electronic medical record of each patient who meets inclusion criteria from the trauma registry. Data will be collected according to a data collection tool which will be provided. Each center will upload de-identified data to a centralized REDCap database supported by Baylor College of Medicine. Data use agreements will be obtained should a participating institution require a DUA to share de-identified data. Data will then be collated for analysis.

As this is a retrospective study, no specific interventions are required, and patients will have been managed at the trauma surgeon's discretion. There will be no payments or cost to the subjects for participating in this study as it is a retrospective review. Given the minimal risks of this study, a waiver of consent will be requested.

Outcomes

The primary outcome will be survival to discharge in patients who received LTOWB versus those managed with CT only.

Secondary outcomes include 6-hour and 24-hour mortality, 6-hour and 24-hour blood product use, transfusion reactions, evidence of end organ dysfunction including acute respiratory failure, acute renal failure, sepsis, venous thromboembolic events, hospital and intensive care unit length of stay, and discharge disposition.

Variables

Once patients meeting the above inclusion criteria are identified, variables to be collected from both the trauma registry and the electronic medical record include:

1. Center specific data: American College of Surgeons Trauma Center Level, annual number of trauma admissions and activations, annual number of geriatric trauma admissions and activations.
2. Demographics: age, sex, race.
3. Baseline clinical characteristics: co-morbidities, ABO group, Rh D status, use of home anticoagulant or antiplatelet agents.
4. Admission information: mechanism of injury, ISS, AIS, admission vital signs including heart rate, systolic blood pressure, respiratory rate, temperature, GCS, admission labs including creatinine, PT, PTT, INR, Hgb, Hct, platelet count, arterial pH, base excess, lactate, all TEG (ACT, k-time, alpha, MA, LY-30) results in 1st 24-hours, all ROTEM (CT, MCF, α, L130), results in 1st 24-hours, reversal of anticoagulant/antiplatelet agent.
5. Blood product and fluid utilization (within 1st 6-hours and 24-hours of admission): units and volume of LTOWB, PRBCS, FFP, platelets cryoprecipitate transfused in both the field and in the hospital, volume of normal saline, lactated ringers, and albumin received, amount and dose of TXA received, total grams of calcium received.
6. Hospital course: hospital and ICU length of stay, ventilator days, operative procedures performed, discharge disposition, 6-hour mortality, 24-hour mortality, survival to discharge or 30-day mortality.
7. Complications: transfusion reactions, TRALI, TACO, sepsis, venous thromboembolic events, acute respiratory failure, acute renal failure, unplanned return to the operating room, unplanned intubation, unplanned intensive care unit admission.

Data Collection

Participating institutions will utilize the trauma registry to identify patients meeting the inclusion criteria described above. Each patient's medical record number will then be used to access the electronic medical record. Data collection will then be performed based on the data collection tool provided. Each participating institution will then upload each patient's data onto a REDCap database once a DUA has been obtained. Each patient will be de-identified and will be given a unique ID number within the study to limit the risk to loss of confidentiality. The REDCap database will be password protected and access will only be given to key personnel on each institution's research team. Once the REDCap database is complete, the PI at the host institution will download and collate the data on password protected computers. Data sharing will only take place between approved research team members through HIPAA compliant email.

Statistical Analysis

Continuous variables will be compared using student's t-test and the Mann Whitney U test. Categorical variables will be compared using Chi-squared tests. Descriptive statistics will be reported as the mean +/- standard deviation for continuous normally distributed data, skewed data will be reported using median [IQR], and as frequencies for categorical variables. Multivariate logistic regression will be used to evaluate the effect of candidate variables and type of blood products transfused on patient outcomes. Potential confounding factors including ISS

and admission vital signs will be adjusted for within the regression model. Statistical significance will be set at $p<0.05$.

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