Impact of Time to Surgery on Mortality in Hypotensive Patients with Non-Compressible Torso Hemorrhage; a AAST Multicenter Prospective, Observational Study

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Title	AAST multicenter prospective, observational study on the impact of time to surgery on mortality in hypotensive patients with non-compressible torso hemorrhage
Running Title	Time to OR and mortality in noncompressible torso hemorrhage
Study methodology	Prospective, observational
Location of study	Multicenter
IRB of record	Institutionally dependent
Time frame of study	18 months from time of IRB approval
Location of study	Multi-center involving only accredited Level I and Level II trauma centers
Age range of subjects	15+ years
Objectives	To examine the effect of time to surgery on hypotensive patients who present with traumatic injuries to the torso
Primary inclusion criteria	Hemodynamically unstable adult (15+ years) trauma patients who present with traumatic injury to the torso
Study intervention or drug	Relevant study information will be observational and will involve no therapeutic intervention or deviations from standard care.

Study Summary:

This multicenter, prospective analysis will collect data on adult hypotensive trauma patients who present with noncompressible torso hemorrhage (which includes chest, abdomen or pelvic injuries). Time from initial emergency call to surgery (time of incision) will be collected as well as time spent in the Emergency Department (ED) and time to hemostasis. Demographics, admission vital signs, and injury details will be collected. Patients will be divided into 2 groups based on injury type (blunt vs penetrating). . Time to surgery and time to hemostasis will be examined in each group. Time will be examined as a continuous variable to determine if there is an inflection point for mortality in each of the groups. The groups will be compared to examine differences in incidence of all-cause, in-hospital mortality. The primary outcomes of interest are time to death and in-hospital mortality. Secondary outcomes of interest are hospital length of stay, ICU-free days, ventilator-free days, and number of packed red blood cells (PRBC), plasma, platelets and crystalloids received in the first 24 hours.

This is a non-interventional, observational emergency study. Data and outcomes are observational and involve no therapeutic interventions or deviations from standard care. The research will involve no investigational therapies, drugs, or devices. IRB-approved study members will enter de-identified data into a secure, password protected database.

We hypothesize that delays in time to surgery to gain control of hemorrhage increases all-cause mortality in adult hypotensive patients with noncompressible torso hemorrhage.

Background and Significance:

R. Adams Cowley's golden hour concept refers to the initial hour following a traumatic incident during which there is the likelihood that prompt medical treatment and rapid transport to definitive care will prevent death (1,2). This idea has guided the delivery of pre-hospital care in the US and has become the basis for much of the modern trauma system. Out-of-hospital care concepts such as scoop-and-run, aeromedical transport, and trauma center designations with trauma teams in place have been developed to hasten the transport and care of trauma patients (3)

Non-compressible torso hemorrhage (NCTH) is the leading cause of potentially preventable death in both military and civilian populations, accounting for 30 - 40% of trauma-related mortality (4-6). However, many of these deaths may be preventable with improved pre-hospital care and shorter times to definitive surgical care (8). Decreasing the time to definitive surgical care via operating room resuscitation has been shown to improve outcomes, especially in penetrating trauma patients (7,8). Clarke et al. reported that the extent of hypotension and length of time (up to 90 minutes) in the ED in hypotensive patients with isolated intra-abdominal injuries increased the probability of death by 1% for each additional 3 minutes in the ED (9). In a recent retrospective analysis of a large sample from an urban Level I trauma center, Meizoso et al. found that taking more than 10 minutes to get to the operating room was independently associated with mortality (8). This was the first study to examine and quantify how long is too long to spend in the trauma bay with a patient requiring an immediate operation. The proposed study seeks to expand on the findings of Meizoso et al by prospectively observing time to surgery and mortality among NCTH patients, including those injured by blunt as well as penetrating mechanisms. The primary outcomes of interest are time to death and in-hospital mortality. Secondary outcomes of interest are hospital length of stay, ICU-free days, ventilator-free days, and number of packed red blood cells (PRBC), plasma, platelets and crystalloids received in the first 24 hours.

Hypothesis

Delayed definitive surgical intervention will increase all-cause mortality in adult hypotensive patients with NCTH.

Objective

To examine the impact of time to surgery in adult hypotensive patients with NCTH.

Specific Aims

1) To examine the effect of time to surgical hemorrhage control on mortality in patients with noncompressible torso hemorrhage

2) To examine the effect of time to surgical hemorrhage control on the number of blood products received in first 24 hours

3) To examine the effect of time to surgical hemorrhage control on hospital length of stay, ICU-free days, and ventilator-free days

Study Design

Inclusion criteria

All of the following criteria and none of the exclusion criteria must be met for subjects to be included in this study:

15+ years of age

Penetrating traumatic injury to torso (chest, abdomen or pelvis) with Systolic blood pressure (SBP) ≤110 mmHg at time of presentation to ED

OR

Blunt traumatic injury to torso with SBP ≤ 110mmHg

Exclusion criteria

Subjects will be excluded if any 1 of the following criteria are present:

< 15 years of age

Transfer from outside facility

Presence of penetrating GSW to the head

Presence of extremity vascular injuries

CPR performed prior to or upon arrival

Receipt of resuscitative thoracotomy in Emergency Department

Time to OR > 12 hours

Informed consent

This is a prospective, observational emergency study that involves no therapeutic interventions or alterations from standard patient care. Patients will be identified in the emergency setting and assigned a unique patient identifier. Standard patient management will be conducted without interference from this study. Patients will receive exactly the same treatment as if no study existed. The risk to the welfare of the subjects are not greater in and of themselves than those ordinarily encountered during the performance of standard treatment, and their privacy will be protected by submitting only data devoid of identifying information to a secure database. Thus, a waiver of informed consent is requested. Data will be recorded on a data sheet and transferred to a secure database that is devoid of patient identifiers, thus posing minimal risk of breach of confidentiality.

Data entry and Statistical analysis

All adult trauma patients who meet inclusion criteria and no exclusion criteria during the stated time period will be entered into the study database. Data and outcomes are observational and involve no therapeutic interventions from standard patient care. Patients will be divided into two groups based on injury type (blunt vs penetrating). Time to surgery and time to hemostasis will be examined in each group. Time will be examined to determine if there is an inflection point for mortality in each group.

The primary outcomes of interest are time to death and in-hospital mortality. Secondary outcomes of interest are hospital length of stay, ICU-free days, ventilator-free days, rate of damage control laparotomy (DCL), and number of packed red blood cells (PRBC), plasma, platelets and crystalloids received in the first 24 hours. Descriptive statistics will be used to describe the cohort. Values will be reported as number, frequency, ranges, mean, standard deviation, median, and interquartile ranges (IQR) where appropriate. Chi Square analysis, Fisher's exact test, Student's t-test, Mann Whitney U test, and the Kruskal-Wallis test will be used to compare groups where appropriate. Multivariate analysis will be performed using Cox regression models for time to death to calculate adjusted hazard ratios (aHRs) along with corresponding 95% confidence intervals (95% CIs). The level of significance will be set at $P < 0.05$.

Data elements to capture include:

Age at time of injury (years)
Gender (male%)
Race
Prehospital time [defined as the total time from activation of Emergency Medical Service (EMS) at scene to presentation of patient at ED) (minutes)]
ED time [Defined as Time from ED presentation to operating room (OR) (minutes)]
OR Prep time [Defined as Time from arrival in OR to time of skin incision (minutes)]
Injury details
- AIS score (chest, abdomen, pelvis)
- New Injury Severity Score (NISS)
- Penetrating Abdominal Trauma Index (PATI) (if applicable)
- Presence of CT-verified TBI
- Injury location (chest, abdomen, pelvis)

Admission vital signs
- Glasgow Coma Scale (GCS)
- Respiratory rate (RR; breaths per minute)
- Heart rate (HR; beats per minute)
- Systolic blood pressure (SPB; mmHg)
- Shock index (HR/SBP)

Fluid resuscitation therapy in ED, in OR, and 24 hour total
- Crystalloids (ml)
- Packed red blood cells (units)
- Fresh frozen plasma (units)
- Platelets (units)
- Cryoprecipitate

Admission labs (first values obtained at time of presentation)
- Hemoglobin
- Hematocrit
- Lactic acid
- Coagulation assays

- Fibrinogen
- Prothrombin time (PT)
- Partial thromboplastin time (PTT)
- International Normalized Ratio (INR)
- Platelet count

ABG values
- pH (arterial or venous blood gas)
- PaO2
- PaCO2
- HCO3
- Base deficit
- SaO2

TEG values from each TEG performed (if done)
- R value
- K value
- α – angle
- K-time
- Time to maximum amplitude (TMA)
- Maximum amplitude (MA) (millimeters)
- LY30 (percent)

Interventions performed prior to transferring patients to the OR (All Y/N responses)

Intubation

Foley catheter placement

Chest tube placement

Pelvic fracture stabilization

If yes (choose one):
- Pelvic binder
- Pelvic sheet wrap
- TPOD
- Other (specify)

Tourniquet placement

REBOA

If yes, report time from ED presentation to balloon inflation (in minutes)

Imaging studies
- Chest x-ray
- Pelvic x-ray
- Head CT
- Abdomen and pelvis CT
- Focused Assessment for the Sonography of Trauma (FAST)

If FAST was performed, were the findings positive or negative?

OR vital signs and labs

Heart rate (highest reading)

Systolic blood pressure (lowest reading)

Intraoperative injuries

Chest

Lung
Heart
Vascular structures

Abdomen
Diaphragm
Liver
Spleen
Pancreas
Gastrointestinal/mesentery
Vascular structures

Pelvis
Genitourinary
Vascular structures

Injured vascular structures:(Choose all that are applicable from drop box)

If venous:
Superior vena cava
Inferior vena cava
Subclavian
Axillary
Brachial
Renal
Portal
Iliacs
Femoral
Popliteal

If arterial:
Aorta
Carotids
Subclavian
Axillary
Brachial
Renal
Iliacs
Femoral
Popliteal
Superior mesenteric artery
Inferior mesenteric artery
Celiac trunk
Other

Time to correction of surgical bleeding (minutes)
Time to Wound VAC placement or wound closure (minutes)
Intraoperative cardiac arrest (Y/N)
Damage control laparotomy (Y/N)Time to abdominal closure
Type of OR utilized (hybrid OR vs regular OR)
Use of Resuscitative Endovascular Occlusion of the Aorta (REBOA) (Y/N)

Use of Tranexamic Acid (Y/N)
    Time to tranexamic acid from EMS call (as surrogate for time of injury)
    Location of TXA administration (ED vs OR)
    Dose of TXA given
    TXA infusion after initial bolus (Y/N)
Highest lactate in the first 24 hours after surgery
Highest base deficit in the first 24 hours after surgery
Mortality (Lived or died)
Time to mortality (in days)
Hospital length of stay (LOS)
ICU-free days (Calculated as days alive and monitored in a non-ICU setting until day 30. ICU-free days = 0 for subjects who die.)
Ventilator-free days (Calculated as the number of days alive and free from mechanical ventilation until day 30. VF days = 0 for subjects who die.)

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