

Criteria for inclusion:

- Has infrastructure within hospital to evaluate and treat BIG 3 intracranial hemorrhages (does not have to transfer to another facility)
- Dedicated research staff or established processes to rapidly on-board foundation members (ex. credentialing for nurse coordinators, easy access/permissions to Electronic Health Record)
- Ability to submit periodic (approximately quarterly) updates for both grant manager and lead PI
- Completion of all required paperwork for grant manager
- Approval of site-specific protocol by local IRB
- Ability to enter complete data into RedCap
- Ability to contribute 1-2 years worth of data, all data to be submitted no later than 90 days after completion of enrollment (time to be determined)
- Inclusion criteria: patients with ICH as demonstrated on CT, on anti-thrombotics
- Ability to capture all data points within protocol
 - 4.5.4.1 Patient disposition from initial presentation
 - 4.5.4.1b Discharged from ED
 - 4.5.4.1c Admitted and discharged home within 24 hours without surgical intervention
 - 4.5.4.1d Admitted with hospital stay >24 hours
 - 4.5.4.2 Date of injury, Mechanism of injury
 - 4.5.4.3 Patient age and gender
 - 4.5.4.4 Use of AT agents (anticoagulants or antiplatelets) to include but not limited to:
 - 4.5.4.4a Anticoagulants: warfarin, oral direct thrombin inhibitor (dabigatran), oral Factor Xa inhibitor (rivaroxaban, apixaban, edoxaban), subcutaneous Factor Xa inhibitor (fondaparinux), therapeutic subcutaneous unfractionated heparin or low molecular weight heparin
 - 4.5.4.4b Antiplatelets: COX inhibitors (acetylsalicylic acid aka aspirin), non-steroidal anti-inflammatories (ibuprofen), P2Y12 inhibitors (clopidogrel, ticlopidine, prasugrel, ticagrelor, cangrelor), Aspirin and extended-release dipyridamole (Aggrenox), phosphodiesterase inhibitors (dipyridamole/ cilostazol)
 - 4.5.4.5 Admission diagnoses
 - 4.5.4.6 Injury pattern
 - 4.5.4.6a Glasgow Coma Scale on admission
 - 4.5.4.6b Reported loss of consciousness
 - 4.5.4.6c Neurologic exam (normal or abnormal): abnormal includes focal neurologic deficit, abnormal pupillary examination result, and GCS score of 12 or less.
 - 4.5.4.6d Presence or absence of intoxication
 - 4.5.4.6e Radiographic findings (including number and size of ICH)
 - - Presence of skull fracture
 - - Epidural hematoma (EDH)
 - - Subdural hematoma (SDH)
 - - Subarachnoid hemorrhage (SAH)
 - - Intraventricular hemorrhage (IVH)
 - - Intraparenchymal hemorrhage (IPH)
 - 4.5.4.6f Result of coagulation studies on admission

- - Viscoelastic hemostatic assays
- – Thrombo-elastography (TEG)- Reaction time (R-value), K time, alpha angle, maximum amplitude (MA), lysis at 30 minutes (LY-30)
- - Rotational thrombo-elastometry (ROTEM)- clotting time (CT), clot formation time (CFT), alpha angle, maximum clot firmness (MCF), clot lysis (CL)
- - International normalized ratio (INR)
- - Partial thromboplastin time (PTT)
- 4.5.4.6g Disposition from Emergency Department
- - Admission to ICU
- - Admission to non-ICU
- - Discharge from ED (after observation)
- 4.5.4.7 Incidence of TBI morbidity/ mortality
- 4.5.4.7a Deterioration in neurologic exam as demonstrated by severe or increasing headache; persistent vomiting; development of agitation or abnormal behavior; a sustained drop of 1 point in GCS score (at least 30 minutes); any drop of ≥ 3 points in the eye-opening or verbal response scores or ≥ 2 points in the motor response score; new or evolving neurological symptoms or signs such as pupil asymmetry or asymmetry of limb or facial movement(42)
- 4.5.4.7b Progression of ICH on repeat head CT, defined as an increase in the size of previous ICH or the development of a new ICH(43)
- 4.5.4.7c Need for neurosurgical intervention craniotomy, craniectomy, Burr holes, and/or extra-ventricular drain (EVD) placement.
- 4.5.4.8 Discharge diagnoses
- 4.5.4.9 Discharge disposition- death, home independently, home with prescribed assistance (physical therapy, nursing), acute rehabilitation, skilled nursing facility, hospice, transition to comfort care
- 4.5.4.10 Hospital length of stay, ICU length of stay

Form "EAST Multicenter Study Proposal"

Details #132 (submitted 09/30/2021)

Study Title A BIG update- Does Antithrombotic Use Matter?: An EAST Multicenter Trial

Primary investigator / Senior researcher LTC Julie A. Rizzo MD FACS
University of Texas Health Science Center at San Antonio
julie.a.rizzo.mil@health.mil

Email of Primary investigator / Senior researcher

Co-primary investigator

Are you a current member of EAST? No

If you selected "No" above please identify a Sponsor that is an active EAST member:

My Multicenter Study proposal is... Prospective

In 2014, the Brain Injury Guidelines (BIG) were developed to define which patients with TBI require admission, repeat imaging and/ or consultation with neurosurgery. Patients were risked stratified based on their use of antithrombotics. Any use of aspirin, coumadin, clopidogrel or even ibuprofen automatically mandates admission, repeat imaging and neurosurgical consult. As radiologic technology improves, increasingly subtle abnormalities are being detected, resulting in more patients diagnosed with ICH, more transfers, more admissions, more imaging and more neurosurgical consultation. This leads to increased resource utilization, increased workload, and increased cost. Recently, the necessity of admission, neurosurgical consult and repeat imaging on patients with minimal ICH and normal mental status has been challenged.

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

Secondary overtriage occurs when a patient is discharged to home <24 hours from transfer without surgical intervention. In 2018, a retrospective review of traumas seen at a single Level III trauma center evaluated the safety of utilizing the BIG criteria to develop management plans for TBI patients, specifically which patients need observation, discharge or transfer. They modified the original BIG criteria, eliminating antithrombotic use and including admission GCS. They noted no significant change in mortality, neurosurgical intervention or frequency of progressive of ICH on repeat imaging based on their modified criteria. More importantly, they noted that the modified criteria would have decreased transfers without leading to poorer patient outcomes. We hypothesize that secondary overtriage (discharge from the ED or discharged home within 24 hours without surgical intervention) can be decreased by eliminating antithrombotic use from the BIG criteria without worse clinical outcomes.

Primary aim

Our primary aim is to evaluate whether including antithrombotic usage as a criteria in the BIG classification intervention leads to unnecessary transfer, admission, repeat head CT, or neurosurgical consultation.

Our secondary aims include determining morbidity and mortality for patients classified as BIG 3 based solely on use of antithrombotics as well as morbidity and mortality for patients based on their BIG classification after excluding antithrombotic use from the criteria.

Secondary aims

[morbidity= deterioration in neurologic exam, progression on repeat head CT, need for neurosurgical intervention]

Adults patients (=18 years of age) who sustain blunt traumatic brain injury, demonstrate ICH on head CT and have a pre-existing use of antithrombotic agents (anti-coagulants and/ or anti-platelet agents).

Inclusion Criteria

Anti-coagulants: warfarin, oral direct thrombin inhibitor (dabigatran), oral Factor Xa inhibitor (rivaroxaban, apixaban, edoxaban), subcutaneous Factor Xa inhibitor (fondaparinux), subcutaneous unfractionated heparin or low molecular weight heparin

Anti-platelets: COX inhibitors (acetylsalicylic acid aka aspirin), non-steroidal anti-inflammatories (ibuprofen), P2Y12 inhibitors (clopidogrel, ticlopidine, prasugrel, ticagrelor, cangrelor), Aspirin and extended-release dipyridamole (Aggrenox), phosphodiesterase inhibitors (dipyrimadole/ cilostazol)

Exclusion Criteria

Pregnant patients, prisoners, penetrating mechanism of TBI, patients on hospice status, patients who die in the ED.

Therapeutic Interventions

Prospective observational study only. Patients will be managed according to surgeon's discretion.

Primary Outcome

Progression of ICH on repeat head CT

Need for neurosurgical intervention

Secondary Outcomes

Deterioration in neurologic exam

Mortality

- Date of injury
- Mechanism of injury
- Patient age
- Patient gender
- BIG criteria:
- Use of anti-thrombotics (see below)
- Reported loss of consciousness, intoxication, GCS
- Radiographic findings
- Intracranial hemorrhage (size, location, multifocality)
- Skull fracture (none, non-displaced, displaced)
- Results of TEG, INR, PTT on admission
- Disposition
- Transfer to higher level of care with subsequent admission
- Transfer to higher level of care with subsequent discharge from ED
- Transfer to higher level of care, subsequent admission/ discharge in =24 hrs
- Admission to presenting hospital (non-ICU status)
- Admission to presenting hospital (ICU status)
- Discharge from ED at presenting hospital
- Management
- Repeat head CT performed
- Neurosurgical consult obtained
- Outcomes
- Mortality
- Progression of ICH on repeat head CT

List specific variables to be collected & analyzed

- Neurosurgical procedural intervention
- Intracranial pressure monitor
- External ventricular drain
- Craniotomy
- Burr holes
- Discharge
- Mortality or hospice
- Rehabilitation
- Home

- Anti-coagulants: warfarin, oral direct thrombin inhibitor (dabigatran), oral Factor Xa inhibitor (rivaroxaban, apixaban, edoxaban), subcutaneous Factor Xa inhibitor (fondaparinux), subcutaneous unfractionated heparin or low molecular weight heparin
- Anti-platelets: COX inhibitors (acetylsalicylic acid aka aspirin), non-steroidal anti-inflammatories (ibuprofen), P2Y12 inhibitors (clopidogrel, ticlopidine, prasugrel, ticagrelor, cangrelor), Aspirin and extended-release dipyridamole (Aggrenox), phosphodiesterase inhibitors (dipyrimadole/ cilostazol)
- Admission to presenting hospital

This is a prospective, observational trial. Collected variables will include those listed in the data dictionary, and the data points will be entered into the data collection form on the central data collection tool.

Outline the data collection plan and statistical analysis plan succinctly

For the statistical analysis we are proposing to perform univariate analysis for rates of the collected variables for patients with in each group of BIG criteria (ie BIG 1, BIG 2, BIG 3). We will identify the individual radiographic criteria, GCS, use of antithrombotics, and presence or absence of intoxication to determine which criteria lead to the BIG categorization for each patient. We will repeat the analysis after eliminating antithrombotic usage from the criteria and reclassifying each patient respectively. Other secondary outcome measures include change in neurologic exam, progression of ICH on repeat head CT, need for neurosurgical intervention and mortality.

Include the Target Number of Centers:

20

Include the Target Number of Patients:

2000, 100 patients per year at each center

What is the anticipated time to complete this study?

1 year

If applicable, include a Data Power Analysis:

Outline consent procedures here, if applicable

This is a prospective observational study, designed to prospectively record data on patients who are managed according to institutional patient management protocols. Thus, waiver of informed consent is requested. Data will be recorded on a data sheet and transferred to a secured database that is devoid of patient identifiers.

Succinctly outline a risk/benefit analysis

This is a purely observational trial. PII will be deidentified. There are no individual patient benefits from this trial. The predicted benefit would be changes in clinical management, and avoiding unnecessary transfers, admissions, repeat imaging and neurosurgical consultation.

Joseph B, Friese RS, Sadoun M, Aziz H, Kulvatunyou N, Pandit V, et al. The BIG (brain injury guidelines) project: defining the management of traumatic brain injury by acute care surgeons. *J Trauma Acute Care Surg.* 2014;76(4):965-9.

Include a brief listing of key references

Capron GK, Voights MB, Moore HR, 3rd, Wall DB. Not every trauma patient with a radiographic head injury requires transfer for neurosurgical evaluation: Application of the brain injury guidelines to patients transferred to a level 1 trauma center. *Am J Surg.* 2017;214(6):1182-5.

Martin GE, Carroll CP, Plummer ZJ, Millar DA, Pritts TA, Makley AT, et al. Safety and efficacy of brain injury guidelines at a Level III trauma center. *J Trauma Acute Care Surg.* 2018;84(3):483-9.