



American Association for the Surgery of Trauma

Multi-Institutional Trial Committee

New Proposal Application Form

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Title of Proposal: Hemorrhage control Interventions in Pelvic fractures Study (HIPS)

Hypothesis: The underlying hypothesis of this study is that amongst similarly injured patients with pelvic fractures, earlier timing of hemorrhage control intervention is a greater contributor to mortality reduction compared to type or number of interventions performed.

Type of Study: Prospective, Observational

Background-

Define the Knowledge Gap that Study Addresses:

The landmark 2015 AAST multicenter study by Constantini et. al laid the groundwork for our current understanding of the modern management of pelvic fractures(1). In this study, the authors found that there was no standardized approach to pelvic fracture management across trauma centers and reported a mortality rate of 32% amongst the 178 patients who were admitted with shock. Several other studies have reported a wide range of mortality rates in patients with pelvic fractures, likely due to the heterogeneity of associated injuries and the broad range of potential hemorrhage control interventions available. The Denver Health group has advocated the use of pre-peritoneal packing (PPP), and reported mortality rates as low as 21% in hypotensive patients with pelvic fractures with early use of this technique(2). A separate study from University of Southern California similarly low mortality rates at 21% using pelvic angioembolization (AE) for hemorrhage control (3). Others have similarly advocated for the benefit of AE in reducing mortality from pelvic fractures(4).

Within this context, Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) has emerged as yet another hemorrhage control adjunct in the management of hypotensive patients with pelvic fractures. A study using the Trauma Quality Improvement Program (TQIP) database found that patients undergoing REBOA placement fared better than those undergoing PPP, reporting an overall mortality of 42% amongst the cohort(5). This contrasts with another TQIP study that demonstrated worse outcomes with REBOA when compared to PPP(6). The use of REBOA in pelvic fracture management continues to grow; whereas only one center was using the technique in the AAST study published in 2015, there were 104 cases of REBOA use for pelvic fracture management reported in the 2017 TQIP registry.

There is a highly heterogenous approach across trauma centers in the use of hemorrhage control techniques for pelvic fracture management. A recent review of the AAST AORTA registry found that amongst patients undergoing Zone 3 REBOA placement for pelvic fracture, the majority then went on to undergo an additional hemorrhage control intervention, including AE and PPP(7). There is great uncertainty as to when to apply hemorrhage control adjuncts in hypotensive patients with pelvic fractures, and which interventions, if any, will lead to a survival benefit. The current evidence is conflicting on whether REBOA adds a survival benefit, and if it should be used as a bridge to other interventions. The use of PPP and its relationship to AE remains unclear, with some centers prioritizing one approach over the other. Compounding this issue is that to date there has not been a collaboration between various stakeholders of pelvic fracture management, leading to silos of knowledge amongst orthopedic surgeons, radiologists and trauma surgeons. There is a need for concerted effort and information sharing amongst all stakeholders to achieve mortality reduction in treatment of severe pelvic fractures.

Study Aim(s)-

Primary Aim: To determine optimum timing and combination of hemorrhage control interventions in pelvic fracture management to reduce mortality in patients presenting with pelvic fractures and shock to US trauma centers.

Secondary Aims: To identify modifiable factors that increase mortality in patients with pelvic fractures presenting in shock at US trauma centers

Proposed Study Population-

Inclusion Criteria:

Radiographic documentation of fracture involving the pelvic ring from blunt trauma with systolic blood pressure ≤ 90 mmHg documented within the first hour of admission and at least one of the following:

- 1)) Use of a pelvic hemorrhage control intervention: direct internal iliac artery ligation, angioembolization, Resuscitative Endovascular Occlusion of the Aorta (REBOA), or preperitoneal packing,
- 2) Transfusion requirement of ≥ 4 units of packed red blood cells or 2 units whole blood with the first 24 hours of arrival

Exclusion Criteria:

- 1) Isolated pubic rami or acetabular fractures
- 2) Arrival in cardiac arrest
- 3) Death in ED
- 4) Age < 18
- 5) Penetrating trauma

Outcome Measures-

Primary Outcome: In-hospital mortality

Secondary Outcome(s): 1) Length of stay, 2) ICU length of stay 3) complications (acute renal failure, need for dialysis, extremity ischemia) 4) transfusion requirements 5) time to hemorrhage control

Data Collection Variables:

See attached sheet.

Planned Duration of Study: 2 years

Center Participation Goal: 20 **Patient Recruitment Goal:** 2000

Power Analysis Performed: Yes No

Plan for Statistical Analysis: Patients who are enrolled into the study will be divided into groups based on the hemorrhage control interventions they undergo: REBOA, PPP, and AE, or none. In order to detect a mortality difference of 10% (which was reported in the most recent TQIP study comparing REBOA to PPP) with a power of 80% and alpha of 0.05, there will need to be approximately 356 patients in each group for a total of 1,424 patients. Outcomes will be compared amongst similar groups matched on injury severity, age, additional hemorrhage control procedures performed, severity of TBI, and degree of shock. For instances where patients undergo more than one pelvic hemorrhage control intervention, comparisons will be made while controlling for the additional hemorrhage control interventions. Post-match regression will be used to control for the additional hemorrhage control interventions performed to determine the mortality benefit provided by the primary intervention. Similarly, hemorrhage control interventions will be analyzed based on timing of intervention. Initial analysis will evaluate cutoff points for interventions, creating 3 evenly divided groups based on timing of intervention. Analyses will be performed looking at mortality differences based on timing of intervention, including all hemorrhage control interventions as one group, and then additionally evaluating outcomes using each individual intervention.

Define How Findings from this Multi-Center Study Will Serve as the Foundation for Future Studies or Future Funded Research:

This study will lay the groundwork for understanding the current approach to management of hypotensive patients with pelvic fractures in the US, the mortality attributable to the pelvic fracture itself, and whether any hemorrhage control intervention or combination thereof provides a mortality benefit. Obtaining initial estimates on the mortality benefit of each intervention will allow for a better understanding of whether there is a single approach, or combination thereof, that can reduce mortality in these patients. Evaluation of timing will determine optimum cutoff points for hemorrhage control interventions. This could lead to the design of a larger prospective study that can then test the hypothesis of whether a standardized approach to pelvic hemorrhage control and/or identifying best practices for time to hemorrhage control will lead to mortality reduction.

Does Study Require Informed Consent, Describe Rationale:

No informed consent will be required for this study, as all information gathered for this study will be routinely collected for medical care.

Database Development-

Do you have independent funding?: Yes No

Does your study require upload of imaging studies?: Yes No

If the cost of development of your database exceeds the allotted financial support from AAST, are you able/willing to fund the difference?: Yes No

Key References-

1. Costantini TW, Coimbra R, Holcomb JB, Podbielski JM, Catalano R, Blackburn A, et al. Current management of hemorrhage from severe pelvic fractures: Results of an American Association for the Surgery of Trauma multi-institutional trial. *J Trauma Acute Care Surg.* 2016 May;80(5):717–23; discussion 723-725.
2. Burlew CC, Moore EE, Stahel PF, Geddes AE, Wagenaar AE, Pieracci FM, et al. Preperitoneal pelvic packing reduces mortality in patients with life-threatening hemorrhage due to unstable pelvic fractures. *J Trauma Acute Care Surg.* 2017;82(2):233–42.
3. Matsushima K, Piccinini A, Schellenberg M, Cheng V, Heindel P, Strumwasser A, et al. Effect of door-to-angioembolization time on mortality in pelvic fracture: Every hour of delay counts. *J Trauma Acute Care Surg.* 2018 May;84(5):685–92.
4. Fu C-Y, Wang Y-C, Wu S-C, Chen R-J, Hsieh C-H, Huang H-C, et al. Angioembolization provides benefits in patients with concomitant unstable pelvic fracture and unstable hemodynamics. *Am J Emerg Med.* 2012 Jan;30(1):207–13.
5. Asmar S. Resuscitative Endovascular Balloon Occlusion of the Aorta vs Pre-Peritoneal Packing in Patients with Pelvic Fracture. *J Am Coll Surg.* 2021;232(1):12.
6. Mikdad S, van Erp IAM, Moheb ME, Fawley J, Saillant N, King DR, et al. Pre-peritoneal pelvic packing for early hemorrhage control reduces mortality compared to resuscitative endovascular balloon occlusion of the aorta in severe blunt pelvic trauma patients: A nationwide analysis. *Injury.* 2020 Jun;S0020138320304812.
7. Harfouche M, Inaba K, Cannon J, Seamon M, Moore E, Scalea T, et al. Patterns and Outcomes of Zone 3 REBOA use in the Management of Severe Pelvic Fractures: Results from the AAST Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery Database. *J Trauma Acute Care Surg.* 2020 Dec 31; Publish Ahead of Print.