**Maine Medical Center**
**Department of Emergency Medicine**
**Journal Club Summary Template**

| **Date: 3/18/21** | **Presenter Name: Jacques Larochelle** |
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| **Article Citation: Guyette, F et al. "Tranexamic Acid During Prehospital Transport in Patients at Risk for Hemorrhage After Injury** |
| **Country(ies):** US |
| **Funding Source(s):** US Army Medical Research and Material Command ☐ None Stated |

| **Purpose** |
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| **Research Question(s):** ☐ None Stated |
| **Hypotheses:** Prehospital administration of TXA will infer improved 30 day mortality in eligible trauma patients. ☐ None Stated |
| **Study Purpose:** To identify if prehospital TXA in is safe and effective |

| **Methods** |
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| **Study Design:** Phase 3 multicenter double-blind, placebo controlled RCT |
| **Outcome(s)** ***[or Dependent Variable]:*** 30 day mortality |
| **Intervention** ***[or Independent Variable]:*** 1g prehospital TXA (all treatment arms)<br>Treatment A: no further TXA<br>Treatment B: in-hospital 1g infusion<br>Treatment C: in-hospital 1g bolus then 1g infusion |
| **Ethics Review:** X IRB Review ☐ IACUC Review ☐ Other: ☐ None Stated |
| **Research Setting:** Four level 1 US trauma centers |
| **Study Subjects:** injured patients from the field OR outside ED within 2 hours of incident and being transferred |
| **Inclusion Criteria:** either 1 episode of hypotension (SBP<90) or tachycardia (HR>100) |

**Exclusion Criteria:** Age>90 or <18, lack of IV/IO access, Isolated fall from standing, C spine injury, prisoner or pregnant patient, traumatic arrest lasting >5 minutes, penetrating brain injury, drowning or hanging, patient objection, patient wearing opt out bracelet

**Study Interventions:** 3 phases of intervention (A,B,C, with A being performed prehospital, B on arrival to hospital, C 8 hour infusion during admission)

**Study Groups:**
Control: A, B, C - saline administration
Treatment 1: A- 1g TXA, B-saline, C- saline
Treatment 2: A- 1g TXA, B- saline, C- 1g TXA infusion
Treatment 3: A- 1g TXA, B- 1g TXA bolus, C- 1g TXA infusion

**Instruments/Measures Used:**
Primary Outcome: 30 day mortality
Secondary Outcomes:

1) 24 hour inhospital mortality
2) Blood resuscitation at 6 and 24 hours
3) Incidence of multiorgan failure
4) ARDS
5) Nosocomial Infection
6) Early Seizures
7) PE/DVT
8) Crystalloid resuscitation after 24 hours
9) Incidence of coagulopathy

**Data Collection:**
Performed by research personnel with inhospital randomization by research staff. Investigational Drug Services at UPitt monitored the intervention for the trial (unblended to prehospital and in-hospital phase treatment assignment)

**Data Analysis:**

***A priori* sample size calculation?** X **Yes** ☐ No ☐ Not Described ☐ N/A
994 patients
**Statistical analyses used:**
Primary intention to treat analysis with 2 side Mantel-Haenszel test
2 sided Z test with pooled variance and 2 sided alpha = 0.05 to provide 90% power to detect difference of 7% in 30 day mortality
30 day survival curves using Cox proportional Hazards regression model
**Adjustment for potential confounders?** ☐ Yes ☐ No ☐ Not Described ☐ N/A
**If yes, list:** with expectation that effect would be modified by time to treatment from injury and qualifying shock severity, also adjusted for clustering by site

| Results |
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| **Study participants:** total of 927 patients enrolled with 460 in TXA arm and 467 in placebo with ultimately 447 in TXA and 456 in placebo after patient withdrawals or ineligibilities<br>Median Injury severity score 12 with all-cause mortality 9% |
| **Brief answers to research questions *[key findings]:***<br>-30d mortality in TXA 8.1% (36 deaths) vs 9.9% in placebo (45 deaths)→ not statistically significant difference<br>-Cox proportional hazards- no change in hazards of 30d mortality<br>-NO difference found in any of the secondary outcomes |
| **Additional findings:**<br>- Number of adverse events between groups was similar with no difference in the number of arterial thrombotic complications (stroke, MI)<br>- When stratifying TXA administration time after injury and qualifying shock index, post-hoc there was lower 30d mortality if TXA given within 1 hour of incident<br>- In the highest subgroup of severe shock: 18.5% mortality in TXA group vs 35% in placebo |
| **Limitations:**<br>- Overall low injury severity scores and transfusion requirements- introduces potential bias<br>-overall low mortality→ large inclusion criteria- casts wider patient net but includes many well patients<br>- Site differences: this study was performed at level 1 trauma centers, suggesting they are in cities with well-trained prehospital providers with a lot of trauma experience- this raises the question of generalizability to settings in less urban areas without significant trauma numbers<br>- Study was stopped early and did not hit full enrollment, thus it is under-powered, especially for the secondary outcomes |
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| Clinical Implications |
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| **Applicable?** Yes<br>**Feasible?** Yes<br>**Clinically relevant?** Yes<br>**Comments:** |
| **Level of evidence generated from this study** |
| ☐ Ia: evidence obtained from meta-analysis of randomized controlled trials<br>☐ **Ib: evidence obtained from at least one randomized controlled trial**<br>☐ IIa: evidence obtained from at least one well-designed, controlled study without randomization<br>☐ IIb: evidence obtained from at least one other type of well-designed quasi-experimental study<br>☐ III: evidence obtained from a well-designed, non-experimental study<br>☐ IV: expert committee reports; expert opinion; case study; case report |

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| Additional Comments/Discussion/Notes |
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