

## **Multicenter prospective observational study of trauma patients on antiplatelet agents**

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### **Specific Aims**

1. Discern any difference in bleeding severity of ticagrelor/prasugrel compared to clopidogrel with or without concomitant aspirin use (low dose vs. high dose).
2. Document effect of platelet transfusion on outcomes following injury in patients on antiplatelet agents including progression of traumatic brain injury, bleeding requiring surgery, angiography, or other intervention, re-bleeding following intervention, and death.
3. Document effect of Desmopressin (DDAVP) on outcomes following injury in patients on antiplatelet agents including progression of traumatic brain injury, bleeding requiring surgery, angiography, or other intervention, re-bleeding following intervention, and death.
4. Describe the variations between centers in the management and reversal strategies of antiplatelet agents in trauma patients along with monitoring of antiplatelet activity

Impact: With the increased use of more potent oral P2Y12 inhibitors such as ticagrelor and prasugrel, it is important trauma surgeons understand the effects of these medication on trauma patients. Optimal management of these agents is also needed to optimize trauma patient outcomes.

### **Research Strategy**

#### *Significance*

With the introduction of more potent P2Y12 inhibitors comes a new challenge to trauma surgeons when faced with patients taking these medications. These agents possess more reliable pharmacologic antiplatelet properties than clopidogrel. Which is favorable since clopidogrel has been shown to have <25% inhibition of platelet activity in up to 30% of patients.<sup>1</sup> Along with increased platelet inhibition comes increased bleeding events.<sup>2</sup>

With promising characteristics of decreased all-cause mortality and cardiovascular events, there has been an increase in these agents use compared to clopidogrel.<sup>1</sup> Little is known about the effect of these agents when a patients is injured.

Through examination of various antiplatelet agents, trauma surgeons will gain valuable knowledge when faced with patients taking these medications. Particular areas of information include; comparative bleeding events between agents, monitoring for progression of bleeding events and reversal strategy efficacy and risks. Successful completion of the study's aims will provide clinical evidence in the management of trauma patients taking antiplatelet agents.

### *Innovation*

As innovation of newer antiplatelet agents occurs, trauma surgeons must gain clinical evidence in the approach to these medications. Through this multicenter, prospective trial, valuable information will assist clinicians in the management of trauma patients taking newer P2Y12 inhibitors. To date, there are no studies examining these newer agents in trauma patients.

### *Approach*

We seek to ascertain information on the optimal management of trauma patients on newer antiplatelet agents through a multicenter, prospective trial. This will allow data analysis of various approaches to their trauma management as well as provide information on the bleeding significance when agents are compared.

Comparisons will be made on bleeding severity using transfusion requirements and AIS grades for patient on different agents. Additionally, reversal strategies and outcomes will be measured, if given; comparing those that receive attempts at reversal versus not. The endpoints listed above will then be compared between the different groups. The statistics performed will be t-tests and/or Mann-Whitney U and chi-square. Logistic regressions will also be used to evaluate for any end-data point with  $p < 0.2$  associated with increased severity or reversal.

After review of contemporary studies addressing antiplatelet agents in trauma patients, one study found 7.9% of trauma patients were taking antiplatelet agents.<sup>3</sup> It is estimated that 1,500 to 2,000 patients would need to be enrolled. With total centers enrolled needing to be approximately 15. This is based off Kobayashi et al's study looking at novel oral anticoagulants, as they also looked at aspirin and clopidogrel, other antiplatelet agents.<sup>4</sup>

The study will be carried out though a web-based portal data entry site. Each center will be able to enter their data in a secure data collection instrument; allowing study staff to monitor subjects. Communication via email (a study specific email will be created), telephone and monitoring the data collection instrument will provide exchange of

information and questions. The University of Florida College of Medicine- Jacksonville (UFCOM-J) Department of Surgery has an experienced research coordinator and research assistants to assist with this trial.

The UFCOM-J will be the studies primary IRB. Each institution participating will be asked to adhere to their institutions' IRB protocol's regarding multicenter trials. This is an observational study that will not alter institutional management protocols or patient care, as such enrollment in this study will pose no additional medical risk to participants. Thus, waiver of informed consent is requested. Data will be recorded on a web-based secure data sheet and transferred to a secured database that is devoid of patient identifiers. Thus, posing minimal risk of breach of confidentiality.

The results of this study will inform clinicians about the possible risks of increased bleeding events in trauma patient taking the newer P2Y12 compared to other antiplatelet agents. Additionally, data collected in this study will assist clinicians with management strategies to mitigate progression of bleeding events, should modalities show efficacy.

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3. Bonville DJ, Ata A, Jahraus CM, et al. Impact of preinjury warfarin and antiplatelet agents on outcomes of trauma patients. *Surgery.* 2011;150(4):861-868.
4. Kobayashi L, Barmparas G, Borsage P, et al. Novel oral anticoagulants and trauma: The results of a prospective American Association for the Surgery of Trauma Multi-Institutional Trial. *J Trauma Acute Care Surg.* 2017;82(5):827-835.