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Targeting resuscitation to normalization of coagulating status: Hyper and hypocoagulability after severe injury are both associated with increased mortality

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Discussant

DR. BRYAN C. MORSE: I would like to take this opportunity to thank the members of the Southwestern Surgical Congress for the opportunity to discuss this paper and congratulate the authors on their submission as part of the Jack Barney Award.

This two-center trial examines the phenotype of post-injury coagulopathy. This is a timely study and is the first study to evaluate the entire TEG profile in assessing the coagulation status of trauma victims. The study highlights that hypercoagulability is the most common TEG profile after trauma, especially after blunt mechanism, but that mixed and hypocoagulable states are also present which further muddies the water. Furthermore, all of these abnormal profiles increase mortality. This study forms the framework for what we know, but also how we study the coagulation cascade moving forward.

Similar to what we know, based on what Dr. Moore just said, normal is probably good, and, as pointed out, physiology seeks homeostasis. So as a disruptive force is applied to the coagulation cascade, the body reacts to maintain equilibrium. Unfortunately, we don't really fully understand the magnitude, timing and vectors of these forces.

To this end, I have a couple of questions for Dr. Moore.

1. Regarding the construct of your study, can you detail how TEG is utilized at your institution to direct resuscitation? This may help your external validity as I suspect this is different than it is in other trauma centers.

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2. Based on your data, how does the coagulopathy profile correspond to non-compressible hemorrhage and compressible hemorrhage which may actually just be surrogates for time?
3. Can you explain why there is a difference between penetrating and blunt coagulation profiles?

I think this really gets to the clinical bottom line, when we can predict coagulable states in the trauma bay, without a TEG, and predict which patients should get a heparin drip instead of a massive transfusion protocol.

Again, I would like to thank the Congress for the opportunity to discuss this manuscript, and offer congratulations to the authors.

Closing discussant

DR. HUNTER MOORE: Thank you, Dr. Morse. When we started out with our TEG-based resuscitation, when someone arrives at the emergency department, obviously you are going to be a little bit behind in terms of getting your TEG measurements. So at Denver Health, we start out with a ratio of one unit of plasma, two units of red cells, and then when your TEG starts returns, you can start transfusing based off of the specific deficiencies. An ACT associated with a deficiency in your coagulation proteases, so a prolonged ACT triggers an initial plasma transfusion. If you have a lower angle, this is reflective of fibrinogen deficiencies so that precipitates transfusion, and the lower maze is reflective of your overall platelet function, so that triggers a platelet transfusion, and, finally, when the tails start to coalesce together, that's in your measurement of fibrinolysis, your LY30. If your LY30 is over a certain amount, that's an indication for using tranexamic acid.

At Houston, they use a pretty similar methodology but they go with a 1-to-1 ratio when they start, but then they start with a goal-directed resuscitation as those indices come back.

When we talk about non-compressible hemorrhage, it's really hard to differentiate phenotypes, and if they are bleeding because they are dying, or dying because they are bleeding.

In terms of a certain phenotype that has increased risk for coagulopathy, we do know that penetrating injuries are associated with hypocoagulability. So if you have someone that hasn't had control of their bleeding, such as a non-truncal vascular injury, bleeding into their chest or their abdomen, you would expect they would be more hypocoagulable compared to a person who has compressible hemorrhage where a tourniquet can be placed and not lose as much blood, but with our data set, because we didn't prospectively measure that, so I can't tell you definitively.

Your next question on blunt versus penetrating injury, what we know from our animal models, as I described, that hemorrhage is associated with hypocoagulability, and Dr. Cohen is in the room, also showed this as well, but you aren't getting hypocoagulability without some degree of hemorrhagic shock in animals.

When we separated hemorrhagic shock versus tissue injury, we actually saw that the two have opposing effects on each other, so with hemorrhagic shock you become more fibrinolytic. If you increase tissue injury but don't have as much shock you go into fibrinolysis shutdown. With the combination of the two, it's hard to really delineate because you can't quantify tissue injury, hemorrhage shock in trauma patients. What we try to do is not a real good marker of how much tissue injury got crushed, and so it's hard to figure out what specifically is driving one versus the other in a mixed situation, but it's probably a balance between tissue injury versus shock as to whether you are hypocoagulable or hypercoagulable, which supports why blunt trauma is more prone to be hypercoagulable.

Finally, can we predict hypercoagulability without a TEG, and what is the clinical relevance of this? Well, probably not. If you are using a PTT or an INR, these are designed to look for protease deficiencies and not hypercoagulability. It's pretty rare to get a really low measurement in these. I can't remember how many times I have seen an INR that's less than 0.8, which is our lower cut-off. Unfortunately, I don't think without viscoelastic testing, you are not going to be able to detect who is hypercoagulable early after injury.

In terms of treatment, obviously when someone hits the door, you are not going to be putting them on a heparin drip, but soon after injury, the majority of the patients are going to transition to a hypercoagulable state. We have prospective data over time that shows that in about four hours almost every patient is in fibrinolysis shutdown. Some of these people recover by 24 hours. We know with Dr. Pieracci's data, that I believe he presented here about three years ago, that almost everyone by 48 hours is hypercoagulable with all the other indices. So the timing of treating someone with heparin or some other anticoagulant or pro-fibrinolytic is probably around 24–48 hours, which is great for us because it gives us a therapeutic target.

Discussant

DR. JUSTIN REGNER (Temple, TX): Great presentation. In your abstract, you mentioned that we should be moving more towards goal-directed TEG response. And specifically, you said going away from 1-to-1 ratios. When you look at FFP, it has similar concentrations of protein C in the FFP component as blood. Are you really suggesting that we are now going past 1-to-1 and more to the goal-directed where we can get fibrinogen or activated protein C in the future, are we at that point yet?

Closing discussant

DR. HUNTER MOORE: That's a great point. The nice thing about plasma, plasma is more of a buffer in your coagulation system. It's not going to push you hyper or hypo. Even though there's some data that says retrospectively that the more plasma you get, the more hypercoagulation you get and the more PEs and lung injury. That's probably reflective of your endothelium, but that's a very astute point that we have more multiple mechanisms to make that push you back to the homeostatic levels. So potentially replacing people with protein C or actually antithrombin III has been proposed in Japan for people with this sort of

DIC phenotype that they are classifying because they haven't paired coagulation due to AP3 deficiency.

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