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Released: 10/17/2022
Valid until: 10/17/2023
Time needed to complete: 1h 01m

**ReachMD**
www.reachmd.com
info@reachmd.com
(866) 423-7849

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# Life-Threatening Traumatic Bleeds and Anticoagulation – Reversal Approaches in the Emergency Department

**Announcer:**
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**Dr. Gibler:**
Our next presentation will be on management of trauma-related hemorrhage in patients on DOACs. And everyone in the audience who's an emergency physician takes care of trauma in some way, shape, or form, some at a level 1 trauma center, some in a community hospital, some in a critical access hospital. So, this is obviously important information. Dr. Babak Sarani is a surgeon, professor of surgery, and as I said before, emergency medicine, which I really feel collaboration and I understand from my colleagues at George Washington that he, like Dr. Cash, appreciates emergency medicine. And so, he is at George Washington University in Washington, DC and we really appreciate you being here. Dr. Sarani.

**Dr. Sarani:**
Well, good morning. Thank you, as always, Dr. Gibler. And thanks for everyone showing up so early. If there's ever an honorary title with no skills behind it, it's me being a Professor of Emergency Medicine. but it's something that I really do like to say to people. So, thank you. Let's just jump into the meat of the matter so we can have some time for conversation. I'm going to end with two case scenarios, each of which were my patients actually. So, we'll give you some real-life examples of things that we did.

Let's start with the concept of damage control. For those of you who may work in a level 1 or a level 2 trauma center, you'll hear the surgeons using these words regularly. This is a picture of the USS Cole after was bombed in the Port of Yemen by now, 15 to 17 or so years ago. The concept of damage control came from the United States Navy where you have a ship that's been severely damaged, is taking on water. This is kind of like a human who's now bleeding to death. We're not going to try to fix the ship because the people are going to come bomb us again, we need to get out of dodge so we're just going to plug the hole. And this is truly what the Navy does to get the ship out of hostile waters just someplace safe. The concept of damage control and the human bodies are very much the same thing is I cannot spend I should not spend all the time in the world in the operating room trying to fix every last thing to watch the person die, a physiologic collapse. What I need to do is just make the bleeding stop and then let the person kind of replete their physiologic stores. We'll go back and fix them again later on when the ship is in Norfolk, or the patient is in the ICU. So, it starts with hemorrhage control, and it goes to contamination control that we're not going to talk about. That's like poop coming out of you because you got gunshot to the colon. But this assumes that you have an inherently normal coagulation system or maybe you have trauma-induced coagulopathy which we can fix with a massive transfusion. It does not talk about what if I've got a pharmacologic inhibitor on board. What if the patient is on a DOAC?

This is a study that that is now somewhat dated but still very relevant from Denver. And they looked at patients who were not on DOACs. These are people who were very severely injured, and they measured the INR on arrival to the intensive care unit. So, on the X axis you have the INR on arrival to ICU. On the Y axis you have probability of death, and you can see, I mean it's rare in medicine to

see a linear relationship between anything but there's a distinct linear relationship between the INR on arrival to the unit and death following severe injury. So, it is imperative that we think of coagulopathy upfront and address it upfront which is really the basis for massive transfusion protocols that I think pretty much all of our hospitals to some degree have maybe not the critical access facilities. This is another study that was published by one of my former partners before we became my partner. Jim Dunn is one of the authors on this paper. This is our own soldiers wounded in the Iraq Afghanistan experience early in the war. And they, I see these are all young otherwise healthy Marines, Soldiers, Airmen, Sailors. And they looked and said, okay, look you've been severely injured whether it was an IED, or gunshot wound, what have you. How much plasma did you get for the amount of RBC? As that ratio closes and approaches a one-to-one resuscitation, you see a dramatic drop. A truly, I say to you, dramatic drop in hemorrhagic death about a 60% absolute risk reduction. You guys, if you don't give an aspirin here, I'm going to say things I don't even know anything about. I got a feeling if you don't give an aspirin chew and swallow for a STEMI like a cardiology guys were losing their mind and reports you. My friend, you have about a 2% mortality benefit when you do that. I'm talking about a 60% drop. So, this is crazy just by giving more yellow. But again, the point here is the person has an inherently normal coagulation system. They just need to be repleted. What if they don't? What if you have that elderly individual who is on rivaroxaban or apixaban something to that effect?

Well, do I need to reverse this person? And these are the questions that you need to ask. And this is what, how we approach it. Are they on a drug, yes or no? What drug are they on? And then most importantly perhaps when was the last time they took the drug? If the drug was taken more than about 15 or so hours ago it probably is not as relevant to us in the trauma community as you would think. But certainly, if it's less than 15 hours less than 12 hours, absolutely less than 10 hours we are going to want to know that and perhaps act on that. Second one is what's the metabolism of the drug? Is this person showing up with AKI? Remember generally speaking these are elderly patients with comorbid conditions. They show up with a creatinine of 2.5. I'm going to make the assumption that the half-life of that drug just extend much more so. And so that 10, 15-hour rule may not apply. The problem is it becomes qualitative medicine really quickly because there's no way to measure what's actually happening. And then Natalie kind of talked a little bit about the location of severity, the bleed. And I totally agree with that. It bleed in the brain. A little subdural, little subarachnoid, very different animal than someone who's bleeding extracorporealy or maybe from their extremity. I can put up a tourniquet and stop the bleeding easily. I might be able to write out a hepatic bleed. Intracranial bleed doesn't give me much room to negotiate. And so, she's totally right. So where is the bleed located? How severe is the bleed? These are the factors you have to take into account. And then I think we can talk about this in the Q and A, which is, okay, well what do I do about it? If you're in a level one trauma center and you have Andexanet alfa and you have Kcentra and you have all the good stuff, yes, we should do what Dr. Cash mentioned in that evidence-based approach. Give the antidote. But if you don't have that drug now, what do you do? And I think we can talk about some of that.

Some guidelines we can kind of try to go by. The first one just reiterates what I just said. Where is the bleed? How severe is the bleed? And then the third point is, what drug do I give? At least in this consensus guideline, they recommended Andexanet alfa for 10A reversal. But they gave us the option of four-factor PCC if you do not have Andexanet alfa or if because of your own protocol, you're not supposed to use it. As an example, at George Washington, if someone has taken a 10A inhibitor more than 15 hours out they will not get Andexanet reversal, period. They will however get PCC because we don't want to just stand there and look at them. And we want to talk to you in two seconds here about is that a good idea?

And here you go, here's your two seconds. This is hot off the press. So, this is, you guys are going to get some inside information that others don't know. This was presented in abstract form about a year and a half ago. It's currently undergoing the publication process through the Journal of Trauma and Acute Care Surgery. This is the biggest study of its kind. This was a multi-center retrospective study looking to ask is PCC, four-factor PCC specifically, it's four-factor PCC non-inferior to Andexanet alfa for reversal of 10As in patients who took that drug within 12 hours. So, they have drug onboard and are either in hemorrhagic shock or have a severe intracranial bleed due to trauma. So, this was like a very specific question we asked, and we got appropriate powered, it's appropriately powered it meets all the endpoints.

273 patients, 77 got a four-factor PCC, 186 got Andexanet. And the bottom line is it appears that four-factor PCC is non-inferior to Andexanet. Specifically, this study does not say that PCC is superior, does not say that. It just says it's non-inferior. So, what I take away from this study is look if you don't have Andexanet alfa or if your protocol says this person is too many hours out and I'm not going to give you Andexanet alfa at least give them the four-factor PCC at worst it can't hurt, at best it may help. That's what this study says. Do not just stand there and look at these people. You do have options. So, questions, can I use PCC in lieu of Andexanet alfa? We just talked about that. Is the dark rebound after the infusion is stopped? I think Dr. Kreitzer showed you that graph that shows that drug comes back. The anti-10A activity goes up once you stop the infusion. Now does that matter? I think you need to watch the patient carefully to look for signs of re-bleed. The studies would say it does not matter that if you were to give Andexanet once you reverse, the clot forms, clot will not dissolve and go away. You should be okay. But please be aware of the fact that there is this concern about drug rebound. Do I wait and see what happens? I think we all also don't do that. By the time the train has left the yard the train has left the

yard and I think we're better off stopping the bleed stopping the ongoing hematoma expansion than staying and seeing what happens. And it's VTE risk higher than PCC than a because PCC presumably is factor. Whereas AA, Andexanet alfa not really a procoagulant it's an anti-anticoagulant if you will? My personal gestalt is I don't think that's true, especially if you restart the anticoagulation in a timely fashion. But you know jury remains out on those questions.

**Announcer:**
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