COMMENTARY

Avoiding the 'H Bombs' in Traumatic Brain Injury

EPIC: 'Can't Get Back What's Lost in the Field'

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This transcript has been edited for clarity.

Robert D. Glatter, MD: Hello and welcome. I'm Dr Robert Glatter, advisor and editorial board member for Medscape Emergency Medicine. Today we will be discussing the results of the EPIC study—the Excellence in Prehospital Injury Care study—which was published last week in *JAMA Surgery* and demonstrated how simple interventions by EMS providers can increase survival in patients with a severe head injury.[1]

Joining us to discuss this important trial is the principal investigator and lead author of the EPIC study, Dr Daniel Spaite, professor and Virginia Piper endowed research chair of emergency medicine at the University of Arizona College of Medicine and associate director at the Arizona Emergency Medicine Research Center. Also joining us is Dr Peter Antevy, a pediatric emergency medicine physician at Joe DiMaggio Children's Hospital in Miami, Florida, and EMS director for Coral Springs Fire Department.

Revisiting the TBI Guidelines Published 12 Years Ago

Glatter: Dan, congratulations and thanks again for your landmark study and its contribution to prehospital care for patients with traumatic brain injury (TBI). It's really groundbreaking. Can you briefly go over the design of your study and then talk about the findings and some key take-away points for our audience?

Spaite: The first in-hospital TBI guidelines were published in 1996,[2] the first EMS guidelines for pediatrics were published in 2003,[3] and the first overall EMS guidelines were published in 2007.[4] It's been 12 years since those, but amazingly, there has been no large, controlled study looking at the potential impact of implementing the guidelines.

The 82 pages of guidelines for EMS boil down to implementing the aggressive prevention and treatment of the three H-bombs: hypoxia, hypotension, and if the patient's intubated, preventing hyperventilation.

We have this amazing setting in Arizona where we have over 130 EMS agencies covering more than 93% of the state's EMS response, and we have a relationship between the University of Arizona and the state health department where we're able to implement statewide, as we did with compression-only CPR. With EPIC we implemented, through two large grants from the National Institutes of Health, nearly 22,000 patients in a before/after controlled evaluation. In advance, we planned on looking at moderate, severe, and extremely critical TBI as three severity subgroups. In the severe group, we amazingly found a doubling in adjusted survival.

Glatter: For so many years, we've really been without true guidelines. To really move the needle, in that sense, to double survival to discharge in the severe group and then triple the survival in intubated patients, is remarkable. You're to be congratulated on showing efficacy in implementing these guidelines.

Spaite: As most people who are familiar with healthcare outcomes know, almost everything tends to improve with increments. You find a new antibiotic or a new treatment and you improve by 10%, so these odds ratios are amazing.

This is not the implementation of an expensive new drug or a new kind of technology. This literally is technology and treatments that we already know how to do (ie, how to put on high-flow oxygen, insert IVs, and how to intubate and use end-tidal CO2). The focus on that, with literally an initial 2-hour training and subsequent intermittent training, dramatically changed the final outcome.
One of the remarkable implications is that, in what is on average a 6-day hospitalization in the severe TBI group, remarkably, the first 20 minutes of care led to a gigantic quantum leap in the final outcome. Because the neuron dies so quickly, if you don't deliver a live brain, then the subsequent very sophisticated care, no matter how good it is, can't get back what's lost in the field.

Glatter: We talked previously about the golden hour of resuscitation, but that's certainly not the case here with the brain. That's something that really has an impact on all EMS providers and all of us in the continuum of care.

I want to get Peter's thoughts on this. Having the guideline, implementing it, and then operationalizing it is a whole different animal. You can have a guideline, but to actually make it work, to train and retrain, is really important.

In your experience, what have you found in terms of treating TBI? Have you had these guidelines?

Antevy: We have gone back and implemented, through the years, the ability to quantify exactly what we're doing. So we've known for years, thanks to Dr Spaite's work, that the end-tidal CO\textsubscript{2} number is important (a target of 40 mmHg with an acceptable range of 35-45). Interestingly, if you go to any of my EMS agencies—I work with 2000 paramedics here in south Florida—we use that number like it's the Bible. You can go to certain hospitals and they still don't have that number.

In EMS, we're way ahead of the game when it comes to focusing on procedures because we have protocols and we train very rigorously as opposed to what happens on the hospital side. The answer to your question is yes, we've implemented these guidelines, but it does take training, retraining, explaining the why, and then really going through this process of continuous quality improvement with every call.

As Dr Spaite will tell you, after you make that intervention, you have to go back and review every call to see if that intervention was done, and if not, why. And then you have to go back and retrain. It is a continuous process—it's not overnight—but this is very important and it is a great study.

Glatter: Dan, how would you react to that in terms of retraining? Are they using simulation at your center? How are you keeping prehospital providers engaged in this process?

Spaite: Well, one of the beauties of EPIC was, because of the nature of the 130 agencies involved statewide, this was not monolithic. The training included a 1-hour didactic session and 1 hour of hands-on lab using flow control bags, ventilation rate timers, and so forth. A few agencies did this completely virtually and online. We actually created an online, 20-minute refresher.

Because this is a vast number of agencies with a dramatic difference in available resources, we made sure that everyone knew that at least once a year they should be having some recurrence of training for the three H-bombs.

'Keep Your Eye On the Ball'

Spaite: If you read the paper, it's very interesting to note: Once you get past about the 1.5-year mark, the outcomes began to head back toward preintervention outcomes. It's very clear that there are dramatic changes, but if you take your eye off the ball, the distraction can be costly.

Glatter: Peter has alluded to the fact that, such as with high-performance CPR or RACE in terms of large-vessel occlusion for stroke, these are similar types of setups where we have to continue to retrain providers to remind them and to keep them engaged in the loop.

Spaite: Exactly right. The reality is that what we saw with compression-only CPR, in the same agencies in Arizona where we quadrupled cardiac arrest survival, interestingly enough, along comes Ebola. The federal government spends a billion dollars on Ebola preparedness, and everybody took their eye off the ball for cardiac arrest. In Arizona, we've still, to this day, never transported a single Ebola patient. It's just an example of that distraction that occurs if you don't keep your eye on the ball.

Glatter: How do you feel about that, Peter? Do you agree?

Antevy: Yes. In EMS, we have the big things that we're really responsible for: cardiac arrest, trauma, and stroke. Every EMS agency out there needs to have leadership in place so that those items that we're talking about today are
always at the top of the pyramid and we always are retraining.

We also now have a process where every single medic who sees a patient when they're transferred to the hospital, when they open up their "tough book" (their tablet) during their next shift, they get the outcome from the hospital right in front of them.

EMS is probably the worst specialty to get the feedback. If you think of an anesthesiologist, they turn the dial and they see the outcome. In EMS, it couldn't be further from that. If you have a medic who has a TBI patient, let's say, twice a year and they don't get the feedback on that exact patient very quickly, then not all that training we gave them really sticks.

It's that feedback loop, the continuous quality improvement, and it's keeping it at the top of mind. Every quarterly meeting I have, we talk about the big cases that we're responsible for, but we focus less on the minor injuries.

**Permissive Hypotension Is Inappropriate for TBI**

**Glatter:** How aggressive was the fluid management in your trial and in the real world, today, where things are changing and the pendulum is swinging to permissive hypotension and less fluid? Can you comment on some of those findings?

**Spaite:** One of the things that's very important is that the animal and human data that support the concept of permissive hypotension exclude TBI for very good reasons. The reality is that apoptosis (neuronal cell death) begins 4 or 5 minutes after low flow or low oxygen. The concept of permissive hypotension is really inappropriate for TBI.

**One prehospital hypotensive event of systolic pressure < 90 mm Hg, independently increases your odds of dying by 2.5.**

If you look at the 15,000 in the preintervention group, we found that if you ask what the optimal blood pressure is in adults (age 23 and above), the optimal blood pressure for outcome is a plateau between 135 and 185 mm Hg. [The pediatric study findings are embargoed for future publication.] The other thing that's remarkable is that there's no hint of an inflection point anywhere near 90 mm Hg when looking at outcomes. Between 40 and 135 mm Hg, you get improved outcomes.[5] That's not the same as saying we proved that this threshold should be much higher, but the reality is that it's probably way too low right now. This study does not answer the question of how high the treatment threshold should be. However, it definitely underscores how desperate the injured brain is to be perfused.[6]

**Antevy:** Dr Spaite, is that isolated head injury we're talking about?

**Spaite:** No. That's not isolated head injury. Actually, you find that two thirds of the TBI in EPIC is isolated, one third is multisystem trauma, and amazingly enough, in both groups you find identical curves.

Basically, the neuron dies so quickly that the brain trumps the other issues. You have this theoretical concern for giving too much fluid and popping a clot off. But the real concern, and what's now been clearly shown, is that a single hypotensive event in the EPIC data, one prehospital hypotensive event of systolic pressure below 90 mm Hg, independently increases your odds of dying by 2.5. A single hypoxic event in the prehospital setting triples your likelihood of dying.[7]

Again, it's observational, but I would suspect that the future randomized trials in this area probably will be testing 90, 100, 110, and maybe even 120 mm Hg as thresholds. Who would have ever thought?

**Fluid Resuscitation Battle: Normal Saline or Whole Blood?**

**Antevy:** This is just fascinating and it's advancing our field of medicine. What would you say to those folks who say that normal saline should never be used and that we should move to whole blood? I think we have to start to tease out what we're talking about.

**Spaite:** Well, the simple answer is that, of course, whole blood would be better. Everybody knows that. That's like testing whether or not to use parachutes when jumping out of a plane. We don't need to test them.

In Arizona, it was simple because we were not studying new drugs. We can't do that under a public health initiative. We have to do that through exception from informed consent. The only two options were saline and Ringer's, and
almost all of it was saline. That's what we had.

Again, we did not prove that fluid, by itself, improved outcome because this implementation is bundled. We did not tease out hypotension versus hypoxia, but it appears that bundling together, including very aggressive treatment starting with 1 L in adults and giving all that you need to keep them above 90 mm Hg, is associated independently with improved outcomes. That's just normal saline. If you're in a setting where you could do whole blood or blood products, you probably would do much better.

Antevy: Are we then teasing out the patient who doesn't have TBI but has blunt trauma in the field? Do we treat them differently with permissive hypotension as opposed to a TBI-affiliated issue that you, again, go up to 120 mm Hg?

Spaite: Yes. I think what EPIC shows us is if the patient has any evidence of a severe brain injury, the risk to the injured brain is so significant when it gets hypoperfused, and so rapid, that you have to forget the constructs of permissive hypotension. On the other hand, there's growing evidence that permissive hypotension is helpful in non–brain-injured patients.

In TBI, for the time being, this gives us the best evidence we've ever had that you just don't let the brain be hypoperfused.

Glatter: Yes. This is interesting because, from a trauma perspective, we're always having that battle in the resuscitation room about fluids. Going forward, I think the studies that will evolve from EPIC will really be able to answer our questions. This is really remarkable.

Spaite: I have one comment, Rob, on the last issue. This is probably the worst-case scenario on fluids, meaning that we probably used the worst fluid you can use, but there's strong evidence within EPIC that that was still positive. I would say that, on arrival at the hospital, if you can immediately change to whole blood, then the likelihood is that outcomes will actually be much better than what we found in the early resuscitation and makes perfect sense as opposed to continuing to pour in fluids.

Glatter: Peter, at your shop, how do you manage it? Would you start blood immediately? How would you transition?

Antevy: After the Parkland issue, we recognize that there is a big push toward whole blood. We're about a month away from deploying whole blood here in Broward County, and then we're right behind in Palm Beach County. We would like to eventually have the whole blood on all of my captains' vehicles. Every unit would be ideal, but we just have too many to do that. That's the direction we're moving in.

We have moved to permissive hypotension, but based on what Dan is saying here today, I think we really have to take a look at the TBI patient and start to adjust our processes.

Spaite: Because this is simple, inexpensive, and most countries in the world now have at least these basic things, what's remarkable is that there is a potential for this to actually make a difference worldwide. That's a really fun part of the discovery in EMS. This is not just one EMS system that had one particular group of investigators who received a big grant to have some expensive widget. This is really implementable almost everywhere.

Antevy: I have one last question, Dan. I'm just curious: As far as the speed of that 1 L going in, is there a time commitment as far as whether it should be really fast? I know that in EMS, usually we have a bag and an 18- or 16-gauge needle, and we just let it drip in. Should we be implementing processes to push that fluid in quickly? What are your thoughts on this?

Spaite: We trained to get it in as quickly as possible. Even though we had the 36,000 patient care records from the 22,000 patients, there was no way to know, but we encouraged them to get as much in as they could.

When you look at the volume of boluses in the after group, and at every point under 110, 100, 90, or 80 mm Hg there was a 50% greater likelihood that you would get 1 L of fluid in a hypotensive patient by those different thresholds in the after versus the before group—it was clear that they were trying very hard to give true boluses, not just drips.

Antevy: I think that's what we have to work on in the field. There are new devices out there that will help us get it in quickly. The days of squeezing the bag or the pressure bag are in the past and must go away.
Guidelines for Pediatric Patients—Thoughts?

Glatter: How would this affect managing pediatric patients in terms of what you're looking at here? Would there be a change in terms of a head-injured patient without other systemic trauma and then the converse of that?

Spaite: The results for the pediatric portion are embargoed. What I think is safe to say and will not compromise our embargo is that the overall findings are very consistent in pediatrics, and if anything, are slightly stronger.

We have 3000 pediatric patients. It's so hard to get that large of a pediatric study. Because the findings are going to be consistent in pediatrics and adults, I believe that we will be able to have a very strong statement about pediatrics moving forward.

Antevy: That is music to my ears, Dan. I've been a very big proponent, and as a pediatric ER–trained person and now an EMS-boarded person, I will tell you that I think we need to treat kids like we treat adults and not opposite, like people have been saying for many years.

In cardiac arrest, we've made that change and we have seen a huge impact. It feels so good to know that, once again, kids are the same as adults when it comes to these types of things, such as cardiac arrest, TBI, and even stroke.

Glatter: This has been such a lively discussion and really has added to our knowledge about TBI. Thank you again for joining us.

What Are Your Thoughts?

Should patients with multisystem trauma, including TBI, be treated under the principles of permissive hypotension or should they be resuscitated to prevent hypotension?

Your Peers Chose:

- Permissive hypotension 33%
- Resuscitated to prevent hypotension 67%
- Not sure 0%
- Other (please leave your comments) 0%

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References


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