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

Hematoma Expansion and Clinical Outcomes Comparison in ICH: Clinical Trial Results Versus Real World Care

Announcer:
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Dr. Kreitzer:
Hi, my name is Natalie Kreitzer, and I'm an Associate Professor of Emergency Medicine in Neurocritical Care at the University of Cincinnati, and I'm also a member of the UC Stroke Team. I'm going to speak now about hematoma expansion and clinical outcome comparison in ICH, or intracerebral hemorrhage. And we'll talk about clinical trial results as well as real-world care.

Now, as an introduction, intracerebral hemorrhage is a minority of strokes, it's only 10 to 15% of all strokes, with ischemic strokes being the most common. That being said, the mortality is much higher than ischemic strokes with 30 to 50%. And 74% of patients are functionally dependent in some capacity at 12 months after ICH. Now the incidence is likely to double by the year 2050. And this is due to aging as well as patients being on more anticoagulants from atrial fibrillation, veno thromboembolic disease, or other reasons.

Now, there are several reasons that patients might be at a higher risk for hematoma expansion. We know that hematoma expansion affects clinical outcomes significantly. So this is a great endpoint to look at when we're talking about anticoagulation reversal or ICH in general. So there are a few things we can look at.

First, with imaging and the noncontrast head CT, it's hypothesized that certain shapes of hemorrhage are more likely to increase in size. And those patients who have a CT angiography that demonstrate the spot sign or active extravasation of a blood vessel will have higher risk of hematoma expansion. Secondly, in terms of demographics, men are more likely to have hematoma expansion compared to women. And there are certain lab values that we can look at that may indicate a higher risk of hematoma expansion, things like thrombocytopenia or abnormalities in PT/PTT that would reflect coagulopathy. And then lastly, medications, specifically anticoagulants, that would increase the risk of hematoma expansion significantly.

Traditionally, the definition of hematoma expansion is about 33% from comparing the first hematoma to the second hematoma on serial head CTs. Now this definition has been widely used because this is correlated with an impact in clinical outcome. That being said, as we'll talk a little bit later in the presentation, there are other definitions that have also been used to define hematoma expansion.

Now, hematoma expansion is not only important for research, it's also important for clinical outcomes. So as we look at this study, which was done by Davis in *Neurology* 2006, going into that second row, we see the percent and change in ICH volume at 24 hours, and this was looking at a 10% change in ICH volume. This had a hazard ratio of 1.05 that was statistically significant in terms of mortality. And then when we look at the Modified Rankin Score, that was impacted as well which is a reflection of clinical outcome or disability when we look at hematoma expansion.

Now as we're thinking about hematoma expansion, timing is critically important. And this is because most hematoma expansion occurs

within those first few hours after the start of ICH or from last seen well time. And we know that those first 6 hours is really when that hematoma expansion is most important and most likely to occur.

Now, when we think about vitamin K antagonists such as warfarin, there has been a significant amount of work that has shown that patients who have anticoagulation reversal, blood pressure management, within those first 4 hours have a significantly decreased rate of hematoma expansion.

Now, when we think about the most common anticoagulation right now in the United States, which is the anti Xa's, we can think about the reversal agent andexanet alfa. And as we look at participants in the ANNEXA-4 study, which was the study that was done in patients with acute major bleeding events, we can see that in that ICH subgroup, the percent with excellent or good hemostasis, who received andexanet alfa, was 80%.

Now if we translate some of this into real-world data, or retrospective studies that have been done outside of a clinical trial, we look towards some propensity matched real-world data, which means that participants are matched by their baseline criteria, and then some of them received andexanet alfa, some of them received usual care, which was generally four-factor PCCs. And in this study published by Costa in 2022, we can see that in that overall cohort, the trend was toward andexanet alfa having less hematoma expansion.

This was mirrored in a similar study that was published in *Stroke* in 2022. And this was an indirect comparison of participants with ICH who were enrolled in the ANNEXA-4 study, which was looking at patients who received andexanet alfa for reversal of their anti Xa, and the RETRACE-II study, which was largely looking at patients who had received four-factor PCCs. And you can see here that ICH expansion greater than 35% was significantly lower in those participants who received andexanet alfa at 13% compared to those in usual care, or PCCs of 36%. Now, this did not translate into a significant difference in in-hospital mortality, although it neared significance with a P-value of 0.6. That being said, in-hospital mortality is impacted by several factors, with the largest being withdrawal of care after ICH.

Now there is current ongoing work inside of a clinical trial. FASTEST study, for example, enrolls participants who are within 2 hours of last seen well or onset time of their ICH,. Those participants received placebo or recombinant factor VII for their ICH.

I hope you enjoyed this presentation. And thank you.

Announcer:
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