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4F-PCC Enables Faster VKA Reversal Before Urgent Orthopedic Surgery

Dr. Birnholz:

You're listening to *AudioAbstracts* on ReachMD, and this episode is brought to you by CSL Behring. I'm Dr. Matt Birnholz. Today, we will be examining a post hoc analysis published in *Advances in Therapy* that evaluated four-factor prothrombin complex concentrate, or 4F-PCC, versus plasma for reversal of vitamin K antagonists in patients who need urgent orthopedic surgery.

For patients on a vitamin K antagonist like warfarin who require urgent orthopedic procedures, delaying surgery is more than just an inconvenience. Hip fracture surgeries performed more than 48 hours after admission have been linked to longer hospital stays, higher complication rates, and increased mortality. So the question isn't just whether we can reverse anticoagulation—it's how fast we can do it.

Several guidelines favor prothrombin complex concentrates over plasma for rapid vitamin K antagonist reversal, but evidence specific to orthopedic surgery has been limited. This analysis helps address that gap.

Investigators drew on a multicenter, randomized, phase 3b trial that compared 4F-PCC with plasma for urgent vitamin K antagonist reversal. The post hoc analysis subgroup included 51 adults who needed urgent orthopedic surgery within 24 hours, with 30 patients receiving 4F-PCC and 21 receiving plasma. Most patients in both groups also received vitamin K according to local practice.

So what did the investigators find?

Well, both treatments performed similarly well in providing hemostatic efficacy. Excellent or good hemostasis was achieved in 83 percent of patients treated with 4F-PCC versus 71 percent of those receiving plasma—and this difference wasn't statistically significant.

But the story changes when looking at the speed of INR reduction. Over 40 percent of patients treated with 4F-PCC achieved an INR of 1.3 or below just 30 minutes after starting the infusion. And by one hour, that figure climbed to 60 percent. In the plasma group, not a single patient hit that mark at either time point. By three hours, about two-thirds of 4F-PCC patients had reached goal INR, compared with just one patient in the plasma group.

Patients receiving 4F-PCC also demonstrated substantially higher levels of vitamin K-dependent clotting factors during the first several hours after infusion.

But the most clinically relevant finding was the statistically significant difference in surgical timing. The median time from the start of infusion to the operating room was 5.8 hours with 4F-PCC, compared with 19.2 hours with plasma. That's over 13 hours faster, which could have meaningful implications for patient care, as well as hospital workflow.

In terms of safety, rates of thromboembolic events, renal complications, hepatobiliary adverse events, and mortality were similar between the two groups. Fluid overload events occurred less often with 4F-PCC than plasma, but this didn't reach statistical significance.

Now, it's important to interpret these findings in context. This was a post hoc subgroup analysis involving only 51 patients, so it wasn't powered to detect differences in all clinical outcomes. The INR threshold used here—1.3—is also more restrictive than the less-than-1.5 target more commonly used in current clinical practice. The authors also note that further prospective studies focused specifically on orthopedic patients are needed.

But even with these limitations, the data do reinforce our understanding of the use of 4F-PCC in patients on vitamin K antagonists who need urgent orthopedic surgery. Compared with plasma, 4F-PCC achieved faster anticoagulation reversal and allowed patients to head

into surgery much sooner, with similar hemostatic effectiveness and a comparable safety profile. Overall, these findings support 4F-PCC as a treatment strategy when surgical delays can adversely affect patient outcomes.

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Reference:

Kincaid M, Young AJ, Dybdahl D, Taylor BC. Effectiveness of four-factor prothrombin complex concentrate versus plasma in patients on vitamin k antagonists undergoing urgent orthopedic surgery: a post hoc analysis. *Adv Ther.* 2026;43(6):2783-2794. doi:10.1007/s12325-026-03561-z