# Bleeding news

## Prothrombin Complex Concentrate vs Frozen Plasma for Coagulopathic Bleeding in Cardiac Surgery: The FARES-II Multicenter Randomized Clinical Trial

*Keyvan Karkouti, Jeannie L Callum, Justyna Bartoszko, Kenichi A Tanaka, Sigurd Knaub, Sukhpal Brar, Kamrouz Ghadimi, Antoine Rochon, Darren Mullane, Etienne J Couture, Yulia Lin, Christopher Harle, Michelle Zeller, Diem T T Tran, Cristina Solomon, Vivek Rao, Michael Law, Amir L Butt, Edward P Chen, Maria Rosal Martins, Tarit Saha, Andrew W Shih, Marie-Claude Vézina, Fuad Moussa, Raffael Pereira Cezar Zamper, Summer Syed, Hakan Buyukdere, Sylvia Werner, Deep Grewal, Daniel Wong, Kofi B Vandyck, Robert Tanzola, Bevan Hughes, Olivier Royer, Sophia Wong, Jerrold H Levy; FARES-II Study Group*

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**Author of the comment:** *Dra. Pilar Marcos.* *Intensive Medicine. Hospital Germans Trias i Pujol, Badalona, Barcelona.*

Up to 15% of patients undergoing **heart surgery** may present **excessive perioperative bleeding,** which entails an increase in their morbidity and mortality. In order to improve the outcomes of these patients, an **unblinded multi-centre (12 hospitals in Canada and the US) randomized clinical trial (RCT)** was conducted, which we comment here.

The **main endpoint** of the RCT was to prove that treating perioperative bleeding in heart surgery with the administration of **prothrombin complex concentrate (PCC) was not inferior to treating it with fresh frozen plasma (FFP),** as measured by the haemostatic response. This **haemostatic response** was defined as the need for reoperation between 60 min and 24 hours after the administration of the treatment.

**Inclusion criteria.**

- Age ≥ 18.
- Informed consent, pre-surgery in the US and post-surgery in Canada.
- Heart surgery of any kind, except for heart transplant and type-A aortic dissection.
- Scheduled elective surgery.
- Preferably, an INR ≥ 1.5 was required for randomization, but cases where the bleeding was so critical that there was no time to find out the INR were also accepted. Some centres used the viscoelastic test, but the inclusion criterion was still INR ≥ 1.5.
- Moderate and/or major bleeding in the operation room (before closing) defined by the Lewis et al [1] scale, which is highly surgery-focused.

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| Degree | Visual presentation | Anatomic appearance | Visual estimated bleeding ratio (mL/min) | Qualitative description |
|---|---|---|---|---|
| 0 | No bleeding | No bleeding | ≤ 1 | No bleeding |
| 1 | Oozing or Intermittent bleeding | Capillary-type bleeding | >1-5 | Mild |
| 2 | Continuous bleeding | Venule or arteriole bleeding | >5-10 | Moderate |
| 3 | Controllable jet and/or uncontainable bleeding | Non-central venous o arterial bleeding | >10-50 | Severe |
| 4 | Unidentified or inaccessible jet | Central venous o arterial bleeding | >50 | Critical |

Table 1. Lewis et al scale to measure operative bleeding [1]

**Intervention.** PCC or FFP, based on weight, summarized in Figure 1.

**Results.** As we can see in Figure 1, the groups were comparable, and in the PCC group, the effective haemostatic response was significantly higher, significant savings in transfusions were observed, and the development of acute kidney failure was significantly lower.

Post-CEC moderate/severe bleeding in heart surgery
11/30/2022 – 5/28/2024

| | PCC ≤ 60 Kg: 1500 UI >60 Kg: 2000 UI (n=213) | FFP ≤ 60 Kg: 3 U > 60 Kg: 4 U (n=207) | |
|---|---|---|---|
| Complex surgery | 67.6% | 73.4% | pns |
| Emergency surgery | 16.9% | 21.3% | pns |
| CEC time (min) | 171 DS 76.4 | 176 DS 80.5 | pns |
| Tranexamic acid dose (g) | 3.4 DS 1.6 | 3.6 DS 4 | pns |
| Heparin dose (UI) | 50 343 DS 20 288 | 51 114 DS 21 474 | pns |
| Protamine dose (mg) | 381 DS 116 | 390 DS 152 | pns |
| Received fibrinogen | 42.7% | 46.9% | pns |
| Effective haemostatic response | 77.9% | 60.4% | p<0.001 |
| Total dose of transfused blood products (Units) | 6.6 (5.9-7.5) | 13.8 (12.3-15.5) | p<0.001 |
| Thromboembolic events | 8.5% | 7.2% | pns |
| Acute kidney failure | 10.3% | 18.8% | p=0.02 |

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**Comments**

- **Informed consent** was obtained before surgery in the US and after surgery in Canada. In Spain, it would be virtually unthinkable to perform an operation with no previous consent. A total of 46 patients, after having been randomized and treated, were excluded from the analysis because they subsequently revoked their consent. Those 46 non-analysed yet treated patients may already account for a significant bias.
- The fact that there was no **common transfusion protocol** to all sites may introduce a very significant bias, even though the amount of tranexamic acid, heparin, and protamine, as well as the number of patients receiving fibrinogen, was similar in both groups. It must also be noted that we have no information on the amount of fibrinogen received by each group. An adequate replacement of fibrinogen may often lead to a lesser need to administer PCC.
- The use of a viscoelastic test was valid in this RCT, but if it was used, an INR ≥ 1.5 was still necessary for patient inclusion. I believe it is currently unthinkable to assess the administration of PCC or FFP in heart surgery without following the transfusion algorithms of a viscoelastic test, as recommended by European guidelines EACTAIC (European Association of Cardiothoracic Anaesthesiology and Intensive Care), EACTS (European Association for Cardio-Thoracic Surgery), and EBCP (European Board of Cardiovascular Perfusion), with a 1A evidence level [2]. Taking into account this is an American-Canadian study, upon review of the latest International Consensus Statement, with a strong participation by the US, we can see that this RCT would not make much sense, because this Consensus recommends guiding transfusion using algorithms based on viscoelastic tests because they may reduce bleeding, transfusion, and reoperation, since they can help identifying the underlying cause for the bleeding [3]. I believe there is enough evidence as to administer PCC at the time indicated by the viscoelastic test algorithm.

**Conclusion.** I believe we should administer PCC instead of FFP in cases of bleeding in heart surgery, since the haemostatic action of PCC is superior to that of FFP, and for the first time, an RCT proves that it does not increase the risk of thrombosis. However, the time of administration should be guided by the viscoelastic test.

# Bleeding news

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