FAQ: Use of prothrombin complex concentrates (PCCS) in cardiac surgery for postoperative coagulopathy

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This resource was created in July 2025 for the *Breakthroughs in blood: Advancements into action* webinar series and is available on Canadian Blood Services' professional education website, Profedu.ca.

It is intended for educational or informational purposes supporting implementation of the FARES-II study.

Karkouti K, Callum JL, Bartoszko J, et al. Prothrombin Complex Concentrate vs Frozen Plasma for Coagulopathic Bleeding in Cardiac Surgery: The FARES-II Multicenter Randomized Clinical Trial. *JAMA.* 2025;333(20):1781–1792. doi:10.1001/jama.2025.3501

1. What are prothrombin complex concentrates (PCCs) and how are they different from plasma?

Prothrombin complex concentrates (PCCs)	Plasma
• Human-derived blood product • Contains standardized concentrations of vitamin K-dependent clotting factors (i.e., II VII, IX, and X) • May also contain proteins C and S, anti-thrombin, and small amounts of heparin • Used to correct coagulopathy • Small volume product (80 mL; 25x more concentrated compared to plasma) • Pooled and pathogen-reduced to lower risk of blood borne pathogens and serious allergic reactions	• Human-derived blood component • Contains all coagulation and natural anticoagulants • Also contains all plasma proteins • Used to correct coagulopathy • Large volume product (1000 mL) • Depending on the type of plasma, it may be pooled and pathogen-reduced (i.e., Octaplasma) • It is provided ABO-compatible by a blood bank after a 20–30 minute thaw in a plasma thawing device

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2. Why are PCCs used after cardiac surgery?

After cardiac surgery, patients may develop coagulopathy due to the impacts of blood loss, the cardiopulmonary bypass circuit, and hemodilution from crystalloids. On average, there is a 50% reduction in thrombin generation observed from pre-bypass to after-bypass, though some patients have greater reductions. Additionally, after long durations of bypass or after certain cardiac procedures, the right ventricle has poor myocardial contractility. This can make it difficult for the patient to tolerate the large volume of plasma needed to correct the coagulopathy. As such, PCC is used to rapidly provide restoration of thrombin generation in a small volume, overcoming some of the limitations of frozen plasma.

3. How do PCCs compare to fresh frozen plasma (FFP)?

PCCs offer several advantages over FFP:

- infused faster
- greater amount of thrombin
- require smaller infusion volumes (reducing risk of fluid overload and hemodilution leading to red cell transfusions)
- more consistent factor concentrations
- do not require blood group matching or thawing
- can be stored at room temperature near a patient's location for rapid access
- rapidly restores deficient clotting factors to manage bleeding more efficiently and safely than plasma

The FARES-II study found that patients treated with PCCs were:

↓ less likely to experience hemostatic failure after treatment

↓ had less transfusions (i.e., red blood cells, platelets)

↓ less need for hemostatic rescue agents (recombinant factor VIIa)

↓ less bleeding (lower chest tube output at 24 hours)

↓ less serious adverse events

↓ less acute kidney injury.

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4. When should PCCs be considered post-cardiac surgery?

PCCs should be considered as the first-line therapy for coagulation factor replacement in patients with significant bleeding and lab evidence of coagulopathy (e.g., elevated INR, prolonged CT on ROTEM EXTEM).

5. What are the recommended dosing strategies for PCCs in a cardiac surgery setting?

The FARES-II study utilized the guideline recommended dose of 25 IU/kg. A flat dose of 1500 IU for patients under 60 kg and 2000 IU for patients over 60 kg. The study permitted a second dose (required in 8.9% of patients) if excessive bleeding continued in the setting of a coagulopathy. The use of doses higher than 2 doses of 25 IU/kg have not been studied. Other strategies for hemorrhage control need to be employed after 2 dose of 25 IU/kg, including ensuring adequate fibrinogen and functional platelet levels.

6. What are the potential risks of PCC use?

In the FARES-II study, patients in the PCC group experienced a similar rate of thromboembolic complication, as compared to plasma. In addition, they experienced less serious adverse events and acute kidney injury compared to those who received FFP.

PCCs should be used with caution in patients with:

- a history of heparin-induced thrombocytopenia
- thromboembolic events in the last 3 months (excluded from the FARES-II trial),
- prior serious reactions to PCC
- known IgA deficiency with anti-IgA.

These patients were not included in the FARES-II study.

7. Can PCCs be used with other hemostatic agents?

Yes. PCCs are often used in conjunction with fibrinogen concentrate, tranexamic acid, and platelet transfusions as part of a goal-directed hemostatic algorithm based on viscoelastic testing (e.g., TEG or ROTEM).

8. How is the effectiveness of PCC therapy monitored?

Effectiveness is monitored through the clinical assessment of bleeding and laboratory tests like INR, and viscoelastic tests (ROTEM/TEG) to guide further treatment, where serious bleeding persists.

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9. Are all PCC products the same?

No. PCCs come in 3-factor and 4-factor formulations. Only 4-factor PCCs (containing II, VII, IX, and X) have been evaluated in cardiac surgery for factor replacement.

10. What strategies can be used to improve the appropriateness of PCC use in cardiac surgery?

PCCs should be only be used in patients with at least moderate (grade 2) bleeding (See video 3 showing 5–10 mL/minute from Development and validation of an intraoperative bleeding severity scale for use in clinical studies of hemostatic agents) and elevated tests of coagulation (laboratory INR>1.5, point of care INR>1.5, or ROTEM CT EXTEM>80 seconds).

The use of components and manufactured blood products without knowledge of coagulation test results should only be considered with extreme hemorrhage where time does not permit testing. In all other situations, the use of all transfusion products should be informed and guided by near-patient testing and validated bleeding algorithms.

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