

# Plasma coagulation in cardiac surgery

Akademisk avhandling

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Avhandlingen baseras på följande arbeten:

- I) Ternström L, Radulovic V, Karlsson M, Baghaei F, Hyllner M, Bylock A, Hansson KM, Jeppsson A.  
**Plasma activity of individual coagulation factors, hemodilution and blood loss after cardiac surgery: a prospective observational study**  
*Thromb Res 2010; 126: e128-e133*
- II) Radulovic V, Hyllner M, Ternström L, Karlsson M, Bylock A, Hansson KM, Baghaei F, Jeppsson A.  
**Sustained heparin effect contributes to reduced plasma thrombin generation capacity early after cardiac surgery**  
*Thromb Res 2012; 130(5): 769-74*
- III) Radulovic V, Laffin A, Hansson KM, Backlund E, Baghaei F, Jeppsson A.  
**Heparin and protamine titration does not improve thrombin generation capacity after cardiac surgery: a prospective randomized study**  
*Manuscript*
- IV) Radulovic V, Baghaei F, Fagerberg Blixter I, Samuelsson S, Jeppsson A .  
**Comparable effect of recombinant and plasma-derived human fibrinogen concentrate on ex vivo clot formation after cardiac surgery**  
*J Thromb Hemost 2012; 10(8): 1696-8*

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## Plasma coagulation in cardiac surgery

**Background** Cardiac surgery using cardiopulmonary bypass is a complex procedure, sometimes accompanied with excessive bleeding. The nature and pathophysiology of this bleeding is multifactorial and not completely understood. Fibrinogen is a final step in the coagulation cascade and its substitution can alter postoperative hemorrhage.

**Aim** To investigate different aspects of plasma coagulation in cardiac surgery. Firstly, to assess potential changes in coagulation factor levels during surgery and its relation to bleeding. Secondly, to study plasma's potential to generate thrombin after cardiac surgery. Thirdly, to compare two different protocols to dose the anticoagulant heparin in regard to thrombin generation capacity. Fourthly, to investigate effects of recombinant human fibrinogen *ex vivo*.

**Material and methods** In study I, coagulation factor activities were measured before and after surgery in a cohort of 57 patients undergoing first time elective coronary artery bypass grafting (CABG). Study II comprises the same cohort, now measuring thrombin generation potential using calibrated automated thrombography (CAT). Study III is a prospective trial, randomizing 60 elective CABG or valve replacement patients to either anticoagulation with weight-based heparin dosing or using heparin and protamine titration with a bedside device. In study IV, plasma of 10 cardiac surgery patients was spiked with various concentrations of human plasma derived fibrinogen or recombinant human fibrinogen. *Ex vivo* clot formation was assessed by rotational thromboelastometry.

**Results** There was pronounced variation in level of individual coagulation factors after surgery. Concentration of fibrinogen and FXIII showed a weak correlation to bleeding volume 12 hours after surgery. Pronounced deterioration of thrombin generation capacity was found, possibly caused by persistent heparin effect and/or heparin rebound. Different heparin dosing protocols had no effect on pre- and postoperative plasma's thrombin generation capacity or on bleeding volume. *Ex vivo*, there was no difference between the new recombinant human fibrinogen concentrate and the one plasma derived regarding clot formation ability.

**Conclusions** Postoperative decline (or rise) of individual coagulation factors does not seem to affect the postoperative bleeding volume, with reservation for fibrinogen and FXIII. Heparin effect is still present at 2 and 4 hours after surgery, affecting thrombin generation. More precise heparin and protamin dosing protocol does not influence this phenomenon. Recently manufactured recombinant human fibrinogen concentrate is able to generate a clot of similar viscoelastic properties as plasma derived.

### Keywords

Plasma coagulation, cardiac surgery, bleeding, cardiopulmonary bypass, heparin, protamine, fibrinogen

