

# The use of fibrinogen in cardiac surgery patients

## Clinical and experimental studies

### AKADEMISK AVHANDLING

Som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademin, Göteborgs Universitet kommer att offentlig försvaras i Förmaket, Sahlgrenska Universitetssjukhuset, Göteborg, den 22 november 2019, klockan 09.00 av

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#### Avhandlingen baseras på följande delarbeten

- I. Waldén K, Jeppsson A, Nasic S, Backlund E, Karlsson M.  
Low preoperative plasma fibrinogen concentration is associated with excessive bleeding after cardiac surgery.  
Ann Thorac Surg 2014 Apr;97(4):1199-206.
- II. Jeppsson A, Waldén K, Roman-Emmanuel C, Thimour Bergström L, Karlsson M.  
Preoperative supplementation with fibrinogen concentrate in cardiac surgery: a randomized controlled study.  
Br J Anaesth 2016 Feb;116(2):208-14
- III. Waldén K, Jeppsson A, Nasic S, Karlsson M.  
Fibrinogen concentrate administration to cardiac surgery patients with ongoing bleeding does not increase the risk of thromboembolic complications or death. (Submitted manuscript)
- IV. Waldén K, Jeppsson A, Shams-Hakimi C, Karlsson M.  
Effects of fibrinogen supplementation on clot formation in blood samples from cardiac surgery patients before and after tranexamic acid administrations.  
Transfus Med 2019 May 22 10.1111/tme.12604 (Epub ahead of print).

**SAHLGRENKA AKADEMIN  
INSTITUTIONEN FÖR KLINISKA VETENSKAPER**



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**BACKGROUND** Cardiac surgery with cardiopulmonary bypass impairs hemostasis due to hemodilution and consumption of platelets and coagulation factors, such as fibrinogen. The aim of this thesis was to study the role of fibrinogen in bleeding complications in cardiac surgery patients.

**METHODOLOGY** Patients who underwent cardiac surgery at Sahlgrenska University Hospital from 2009 to 2017 were included in four studies. Study I assessed the importance of preoperative plasma fibrinogen concentration for excessive bleeding and the need for red blood cell transfusion in an observational study in 1954 patients. Study II was a double-blinded placebo-controlled study where 48 patients were randomized to prophylactic administration of fibrinogen concentrate or placebo. Primary endpoint was postoperative bleeding volume. Study III was an observational study in 5408 patients that assessed if patients who had received perioperative fibrinogen concentrate due to bleeding had a higher risk of thromboembolic complications or death. Study IV was an in vitro study where fibrinogen concentrate was added to blood samples from 15 patients to investigate if concomitant tranexamic acid and fibrinogen administration has additional effects on clot formation compared to fibrinogen alone.

**RESULTS** Preoperative plasma fibrinogen concentration correlated to increased postoperative bleeding but not to RBC transfusion. Prophylactic infusion of 2 g fibrinogen concentrate did not reduce postoperative bleeding volume. Patients who received fibrinogen concentrate due to perioperative bleeding did not have a higher risk of thromboembolic complications or death during the first year after surgery. The combination of tranexamic acid and fibrinogen did not have additional effects on platelet-independent clotting time or clot firmness than fibrinogen alone.

**CONCLUSION** Preoperative plasma fibrinogen concentration is associated with excessive bleeding after cardiac surgery. Preoperative supplementation with fibrinogen concentrate did not significantly influence postoperative bleeding in low risk patients undergoing coronary artery bypass grafting. Perioperative administration of fibrinogen concentrate in case of bleeding appears safe. The enhancing effects of fibrinogen concentrate on clot firmness in blood samples from cardiac surgery patients was not further increased in the presence of tranexamic acid.

**KEYWORDS** fibrinogen, cardiac surgery, bleeding, transfusion, thromboembolism, tranexamic acid