# Cardiopulmonary bypass

## Clinical studies in cardiac surgery patients

#### AKADEMISK AVHANDLING

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i hörsal Kammaren, Sahlgrenska Universitetssjukhuset, Göteborg, den 25 november, klockan 9.00 av

### MIKAEL BARBU Legitimerad Läkare

Fakultetsopponent: Professor Sören Berg Sektionen för thoraxanestesi, Thorax-Kärlkliniken, Universitetssjukhuset i Linköping

#### Avhandlingen baseras på följande delarbeten

- I. Barbu M, Kolsrud O, Ricksten SE, Dellgren G, Zetterberg H, Blennow K, Björk K, Thorén A, Hansson C, Jeppsson A.
  - Dextran- versus crystalloid-based prime in cardiac surgery: A prospective randomized pilot study *Ann Thorac Surg 2020;110:1541-48*
- II. Kolsrud O, Barbu M, Dellgren G, Björk K, Corderfeldt A, Thóren A, Jeppsson A, Ricksten SE. Dextran-based priming solutionduring cardiopulmonary bypass attenuates renal tubular injury A secondary analysis of randomized controlled trial in adult cardiac surgery patients Acta Anaesthesiol Scand 2022;66:40-47
- III. Barbu M, Kolsrud O, Radulovic V, Dellgren G, Björk K, Thóren A, Pivodic A, Ricksten SE, Jeppsson A. Hemostatic effects of a dextran-based priming solution for cardiopulmonary bypass: A secondary analysis of a randomized clinical trial Submitted
- IV. Barbu M, Jonsson K, Zetterberg H, Blennow K, Kolsrud O, Ricksten SE, Dellgren G, Björk K, Jeppsson A. Serum biomarkers of brain injury after uncomplicated cardiac surgery: Secondary analysis from a randomized trial Acta Anaesthesiol Scand 2022:66:447-3
- V. Barbu M, Hjärpe A, Martinsson A, Dellgren G, Ricksten SE, Lannemyr L, Pivodic A, Taha A, Jeppsson A. Associations between cardiopulmonary bypass variables and acute kidney injury in cardiac surgery patients Submitted

## SAHLGRENSKA AKADEMIN INSTITUTIONEN FÖR MEDICIN



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#### **Abstract**

**BACKGROUND:** Cardiopulmonary bypass (CPB) is necessary to facilitate most cardiac operations. Although the vast majority of patients tolerate CPB physiology in conjunction with cardiac surgery well, there is risks of adverse outcomes. Optimal CPB perfusion is not defined, and may vary according to operation and patient specific factors.

**AIMS:** The project aims to study different aspects of CPB management and risk in adult cardiac surgery. The first part of the project investigates the efficacy and safety of dextran 40 based prime compared to crystalloid prime. The second part aimed to describe the dynamics of brain injury markers in peripheral blood after routine cardiac surgery. Lastly, we aimed to identify manageable CPB variables associated to risk of acute kidney injury (AKI).

**METHODS:** We conducted a prospective, randomized, double-blinded, single-center study to compare dextran 40 based colloid prime with ringer acetate with added mannitol prime in elective adult cardiac surgery patients. Serum colloid osmotic pressure was measured before, during, and after CPB. Biochemical markers for organ injury, inflammation, hemolysis, hemostasis, pulmonary function, and brain injury markers were measured before and after CPB. Fluid balance, bleeding and transfusion requirements were recorded during and after operation. To analyze risk of AKI in relation to CPB management, we conducted a registry based study combining prospectively collected outcome data from the SWEDEHEART registry with our institutions automated CPB registry.

**RESULTS:** Dextran 40 based prime was better at maintaining serum colloid osmotic pressure during and shortly after CPB, and also improved total fluid balance compared to crystalloid prime. Although dextran treated patients had a measurable effect on laboratory and functional coagulation values, it did not increase the risk of bleeding or transfusion. Acute renal tubular injury and hemolysis was less pronounced in dextran prime patients, however, there were no difference in AKI rates. In adjusted observational data, we identified an association between risk of AKI and time on CPB, aortic clamp time, compromised flow, and nadir hematocrit during CPB, along with several patient specific risk factors. Markers of brain injury in serum and plasma were all significantly elevated in the first 24 hours after CPB compared to preoperative baseline values. The individual markers had different temporal distribution and large variability in magnitude and inter-individual differences. The increase was independent of blood-brain barrier damage, and levels were correlated with patient age, CPB duration, and/or hemolysis.

**CONCLUSION:** CPB prime with dextran 40 is safe and effective in adult cardiac surgery, and seems to attenuate CPB induced renal tubular injury and hemolysis. To reduce the risk of cardiac surgery associated AKI, it is important to keep the time on CPB and aortic cross clamp short, and to maintain hematocrit and pump flow during CPB. There is a release of brain injury biomarkers in peripheral blood after cardiac surgery that is not attributed to evident neurologic damage or bloodbrain barrier dysfunction.

**KEYWORDS:** Cardiopulmonary bypass, cardiac surgery, colloid, prime, acute kidney injury, brain injury marker, hemostasis