Acute kidney injury after cardiac surgery and heart transplantation
Monitoring, prevention and treatment

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hjärtats aula, Sahlgrenska universitetssjukhuset, den 4 november 2022, klockan 09.00

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Avhandlingen baseras på följande delarbeten

I. Tholén M, Ricksten S-E, Lannemyr L. *Renal near-infrared spectroscopy for assessment of renal oxygenation in adults undergoing cardiac surgery*, Journal of cardiothoracic and vascular anesthesia, 2020:34(12): 3300-3305

II. Tholén M, Ricksten S-E, Lannemyr L. *Effects of levosimendan on renal blood flow and glomerular filtration in patients with acute kidney injury after cardiac surgery: a double blind, randomized placebo-controlled study,* Critical care 2021:25:207

III. Tholén M, Kolsrud O, Dellgren G, Karason K, Lannemyr L, Ekelund J, Ricksten S-E. *Atrial natriuretic peptide (ANP) in the prevention of postoperative acute renal dysfunction and acute kidney injury in patients undergoing heart transplantation - a single-center randomized placebo-controlled blinded trial,* Manuscript

IV. Tholén M, Lannemyr L, Ricksten S-E. *The correlation, accuracy and agreement between estimated (eGFR) and measured glomerular filtration rate (mGFR) and the ability of eGFR to track changes in mGFR early after heart transplantation,* Manuscript

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Abstract

Background: Acute kidney injury (AKI) is a common and serious complication after cardiac surgery and heart transplantation, leading to increased morbidity and mortality. To date, there are neither proven clinical real-time kidney monitoring techniques, nor effective preventive measures or treatments of AKI for these patients.

Aims and methods: This thesis evaluated whether the non-invasive technique, near-infrared spectroscopy (NIRS), can accurately assess renal tissue oxygenation in patients during cardiac surgery. Renal vein oxygen saturation ($SrvO_2$) was compared to renal tissue oxygenation (rSO_2) by NIRS. Furthermore, the effects of the inodilator, levosimendan (0.1 µg/kg/min, n=16), on renal blood flow (RBF) and glomerular filtration rate (GFR) were compared to placebo (n=13) in patients with AKI post cardiac surgery. In addition, the renoprotective effect of the atrial natriuretic peptide (ANP) was studied in patients undergoing heart transplantation. Seventy patients undergoing heart transplantation were randomized to receive either ANP (50 ng/kg/min) (n=33) or placebo (n=37) starting after induction of anaesthesia and continued for 4 days after heart transplantation. The primary end-point was measured GFR (mGFR) at day 4, assessed by plasma clearance of ^{51}Cr-EDTA. Finally, the correlation, accuracy and agreement between estimated GFR (eGFR) and measured GFR (mGFR) were tested after heart transplantation.

Results: Renal rSO_2, as assessed by NIRS, was correlated to (r=0.61. p<0.001), and in agreement with invasively measured $SrvO_2$ with an acceptable error of 17.6%. In hemodynamically stable patients with AKI after cardiac surgery, levosimendan increased RBF (p=0.011), but had little or no effect on GFR (p=0.079). During ongoing ANP infusion, median (IQR) mGFR at day 4 postoperatively was 60.0 (57.0) and 50.1 (36.3) mL/min/1.73 m^2 (p=0.705) and the need for dialysis was 21.6% and 9.1% (p=0.197) for the placebo and ANP groups, respectively. The incidences of AKI for the placebo and the ANP groups were 76.5% and 63.6%, respectively (p=0.616). The accuracy of eGFR to assess mGFR was 51%. The bias was 11.2 ± 17.4 mL/min/1.73 m^2, indicating that eGFR underestimated renal function (mGFR). The limits of agreement were -23.0 to 45.4 mL/min/1.73 m^2 and the error 58%. The concordance rate between eGFR and mGFR was 72%

Conclusions: There is a good correlation and agreement between non-invasively measured renal tissue oxygenation and invasively measured renal vein oxygen saturation during cardiac surgery. In post cardiac surgery AKI, levosimendan induces a vasodilation of both afferent and efferent arterioles increasing renal blood flow with little or no effect on renal function. Prophylactic infusion of ANP during and after heart transplantation does not seem to attenuate postoperative renal dysfunction or decrease the incidence of AKI. eGFR underestimated mGFR and the agreement between eGFR and mGFR was poor. Furthermore, the ability of eGFR to assess changes in mGFR, postoperatively, was low. Thus, eGFR is not a good enough marker to assess renal function after heart transplantation.