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Defining oliguria during cardiopulmonary bypass and its relationship with cardiac surgery–associated acute kidney injury

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Abstract

Background. While urine flow rate $\leq$0.5 ml kg^{-1} h^{-1} is believed to define oliguria during cardiopulmonary bypass (CPB), it is unclear whether this definition identifies risk for acute kidney injury (AKI) . The purpose of this retrospective study was to evaluate if urine flow rate during CPB is associated with AKI.

Methods. Urine flow rate was calculated in 503 patients during CPB. AKI in the first 48 h after surgery was defined by the Kidney Disease: Improving Global Outcomes classification. Adjusted risk factors associated with AKI and urine flow rate were assessed.

Results. Patients with AKI [n=149 (29.5%)] had lower urine flow rate than those without AKI (P<0.001). The relationship between urine flow and AKI risk was non-linear, with an inflection point at 1.5 ml kg^{-1} h^{-1}. Among patients with urine flow <1.5 ml kg^{-1} h^{-1}, every 0.5 ml kg^{-1} h^{-1} higher urine flow reduced the adjusted risk of AKI by 26% (95% CI 13–37; P<0.001). Urine flow rate during CPB was independently associated with the risk for AKI. Age up to 80 years and preoperative diuretic use were inversely associated with urine flow rate; mean arterial pressure on CPB (when <87 mmHg) and CPB flow were positively associated with urine flow rate.

Conclusions. Urine flow rate during CPB <1.5 ml kg^{-1} h^{-1} identifies patients at risk for cardiac surgery–associated AKI. Careful monitoring of urine flow rate and optimizing mean arterial pressure and CPB flow might be a means to ensure renal perfusion during CPB.

Clinical trial registration. ClinicalTrials.gov NCT00769691 and NCT00981474.

Key words: cardiac surgery; cardiopulmonary bypass; acute kidney injury; oliguria

Between 5 and 30% of patients who undergo cardiac surgery are at risk for developing postoperative acute kidney injury (AKI), a complication that increases their risk for in-hospital and long-term mortality.[1] The diagnosis of cardiac surgery–associated

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Editor's key points

- Acute kidney injury (AKI) is common after cardiopulmonary bypass but it is unclear whether urine output during bypass predicts subsequent AKI.
- In this retrospective analysis of prospectively collected data, there was an independent linear association between low urine output $<1.5\,ml\,kg^{-1}\,h^{-1}$ and AKI.
- This challenges previous assumptions that a urine output of $0.5\,ml\,kg^{-1}\,h^{-1}$ is adequate during cardiac surgery.
- The association of oliguria and AKI was stronger when mean arterial pressure was below the individual lower limit for cerebral autoregulation.
- Maintaining mean arterial pressure above an individual's lower limit of cerebral autoregulation might reduce the risk of acute kidney injury.

AKI is delayed after the initial renal insult in part because of reliance on insensitive methods for diagnosis (e.g., serum creatinine concentrations).[2] Changes in urine flow rate may occur earlier after kidney injury than changes in serum creatinine concentrations and therefore might provide early evidence of renal injury in a time frame that might allow preventative interventions. Consensus guidelines suggest a urine flow rate $<0.5\,ml\,kg^{-1}\,h^{-1}$indicates an early stage of AKI when lasting >6 h.[3–4] This cut-off is also widely viewed as the lowest acceptable value for urine flow rate in surgical and critical care settings.[5] Whether a urine flow rate $<0.5\,ml\,kg^{-1}\,h^{-1}$ during cardiopulmonary bypass (CPB), or any rate, portends risk for AKI is unclear. Moreover, potentially modifiable risk factors or effective interventions for oliguria during CPB are not clearly defined.

Renal hypoperfusion resulting from hypotension is a potentially modifiable risk factor for AKI.[6] Similar to the brain, blood flow to the kidney is autoregulated to ensure perfusion over a range of blood pressures (BPs).[7] Our group has evaluated whether monitoring of cerebral blood flow (CBF) autoregulation provides a more precise approach for determining mean arterial pressure (MAP) targets during CPB than empirical targets.[8–11] We have found that the lower limits of CBF autoregulation vary widely between individuals and that the magnitude that MAP is below the lower limits of autoregulation influences the risk for AKI.[8–10,12] These findings indicate that the target MAP during CPB across individuals cannot necessarily be generalized and accurately empirically determined. Rather, an individualized definition of the lowest tolerable MAP based on physiologic end points, such as those derived from cerebral autoregulation monitoring, may better ensure organ perfusion during CPB, including that to the kidney. Whether MAP during CPB in relation to CBF autoregulation end points influences urine flow rate is unknown.

In this study we hypothesize that patients who subsequently developed AKI had a lower urine flow rate during CPB than patients without this complication. A secondary aim was to identify potentially modifiable variables associated with urine flow rate.

Methods

From April 2008 to January 2015, we enrolled 579 patients undergoing cardiac surgery in prospective studies to assess CBF autoregulation during CPB, as described in prior publications.[8–11] Patients were eligible for enrolment if they were judged to be at high risk for stroke, as we have previously described.[8–11] Patients were excluded if they did not speak English, if they had visual impairment, or if there were contraindications to magnetic resonance imaging. The relationship between urine flow rate and MAP values below the lower limit of CBF autoregulation using this database has not been reported. The current study was a retrospective analysis of these previously collected data. All procedures received the approval of the Institutional Review Board of the Johns Hopkins Medical Institutions (jhmeirb@jhmi.edu) and all patients provided written informed consent. In part 1 of the study we conducted a pilot study in which we monitored minute-to-minute urine flow precisely using photo-optical methods that digitally report urine flow in ml/min (URINFO 2000, Baxter, Deerfield, IL, USA).[13] Because this device was withdrawn from clinical availability, this aspect of our study was terminated after enrolment of 50 patients. The second part of this study involved the retrospective analysis of prospectively collected data from patients enrolled in our autoregulation studies.

Perioperative care

Patients received routine institutional care, including continuous radial artery pressure monitoring and an indwelling urinary catheter. Midazolam, fentanyl, isoflurane, and vecuronium were used for anaesthesia and muscle relaxation. Non-pulsatile flow with a target between 2.0 and $2.4\,L\,min^{-1}\,m^{-2}$ was used for CPB. Mannitol was added to the CPB priming solution at the discretion of the surgeons. Alpha-stat pH management was performed and oxygenation and normocarbia were ensured by continuous inline arterial blood gas monitoring that was calibrated hourly. Phenylephrine was administered to treat low BP based on institutional standards.

Transcranial Doppler-based autoregulation monitoring

Bilateral middle cerebral artery blood flow velocity was measured continuously by transcranial Doppler (TCD) monitoring (DWL, Compumedics, El Paso, TX, USA) with two 2.5-MHz transducers fitted on a headband. Arterial pressure from a radial artery catheter and TCD signals were sampled with an analogue-to-digital converter using ICM+ software (University of Cambridge, Cambridge, UK) at 58 Hz and filtered as previously described.[12] A continuous, moving Pearson's correlation coefficient between MAP and TCD blood flow velocity signals was then calculated to generate the variable mean velocity index (Mx).[8–12] When MAP is outside the limits of CBF autoregulation, Mx approaches 1, whereas it is close to 0 or negative when MAP is within the limits of autoregulation.

Patient outcomes

We defined AKI based on the definition of the Kidney Disease: Improving Global Outcomes (KDIGO) classification system: stage 1, 1.5–1.9 times baseline or $>0.3\,mg\,dL^{-1}$ increase in serum creatinine; stage 2, an increase in plasma creatinine 2.0–2.9 times baseline; and stage 3, an increase in plasma creatinine 3 times baseline or an increase in serum creatinine to $>4.0\,mg\,dL^{-1}$ or initiation of renal replacement therapy.[3] The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration creatinine equation.[14] Patients meeting any of the KDIGO criteria were considered to have AKI. Other complications were defined based on the Society of Thoracic Surgery National Cardiac Surgery Database definitions (www.sts.org)