Acute kidney injury in perioperative settings

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ABSTRACT
Acute kidney injury is a clinical syndrome which represents relevant and serious perioperative complication. It is associated with increased patient morbidity, mortality, prolonged hospital stays, and not to mention greater healthcare costs. Yet, the patients who suffered from temporary acute kidney injury in the perioperative period, and regardless of the final outcome, usually complain afterwards about emotional distress, coupled with poor quality of life associated with loss of energy and limited normal physical activity. Therefore, the role of the physician to predict a kidney vulnerable patient in the perioperative period is a task of great importance, albeit not an easy one. The key management is risk stratification of the patient in conjunction with hemodynamic and oxygen optimization, in addition to avoiding nephrotoxic agents during the entire perioperative period.

Key words: acute kidney injury, perioperative, risk stratification

Introduction
Acute kidney injury (AKI) in the perioperative period is a unique and common complication associated with a patient’s increased risk of morbidity, mortality, prolonged intensive care unit and hospital stays, as well as increased healthcare costs. (1-6) AKI usually occurs to 1% to 5% of all hospitalized patients within the incidence of perioperative AKI varying between 1% and 25% dependent of the type of surgery and definition of AKI. (1,7) However, there are many studies about incidence, risk factors and pathophysiological mechanisms of AKI emergence in patients submitted to cardiac and vascular surgery procedures, and those with preoperative pre-existing renal disease. But studies on incidence, risk factors and pathophysiological mechanisms of AKI emergence in a population with preoperative normal renal function submitted for non-cardiac and non-vascular general surgery procedures are still lacking. According to the studies, 1% of all patients with preoperative normal renal function submitted for a general surgical procedure have postoperative AKI. (8,9) Moreover, these studies show a three times higher risk in postoperative morbidity and a five times higher risk in postoperative mortality. (8) The perioperative period is characterized with certain hemodynamic derangements and insults that greatly impact the patient’s functional status. A careful and thorough evaluation of all organ systems and the patient’s functional status, together with an understanding of the type of surgery and its requirements, can therefore help us create controlled conditions and apply early and optimal preventive treatments and measures before deleterious renal insult occurs. (10,11)

Preoperative period
Risk stratification of the patient for perioperative AKI development is key...
during the preoperative period.. The etiology of AKI is multi-factorial. (12) The risk factors for AKI development are patient-related, anaesthesia-related and surgery-related. (12) Patient-related risk factors include advanced age, male sex, higher body mass index, a Revised Cardiac Risk Index score greater than 2, an American Society of Anesthesiologists physical score of 4 and 5, history of congestive heart disease, arterial hypertension, peripheral vascular disease, diabetes mellitus and a preoperative estimated glomerular filtration rate less than 60 ml/min/1.73m². (3,6,13-17) The Revised Cardiac Risk Index score (RCRI) was developed to predict major cardiac complications after non-cardiac surgery. (18,19) The RCRI score predicts perioperative cardiac risk by assigning one point for the following six independent factors: high risk surgery (intrathoracic, intra-abdominal or suprainguinal vascular), ischemic heart disease, congestive heart disease, history of cerebrovascular disease, diabetes mellitus requiring insulin therapy and preoperative serum creatinine greater than 175 μmol/l. (18) The American Society of Anesthesiologists physical score (ASA-PS) classification is a strong predictor for postoperative complication developments in patients in the perioperative period. (20) A study showed that higher ASA-PS was associated with the emergence of AKI. (20) Anaesthesia-related risk factors include anaesthetic technique (spinal and epidural anaesthesia induce more pronounced hypotension), anaesthetic drugs, the intraoperative patient’s position associated with rhabdomyolysis, blood products administration (especially a transfusion of erythrocytes older than 20 days), and intraoperative hemodynamic instability corrected with the use of inotropes and vasopressors. (21,22) Surgery-related risk factors include already mentioned high-risk surgery, prolonged surgery, type of surgery and the surgery’s special requirements, such as aortic cross clamping, induced hypotension, pneumoperitoneum in laparoscopic surgery, and other specific surgical techniques. (23-25) Another important preoperative strategy is to apply measures to enhance the patient’s cardiovascular and hemodynamic status by optimizing blood pressure and fluid balance with crystalloid solutions, transfusion of blood products and albumin according to the early goal directed therapy, review the patient’s drug list and the exclusion of nephrotoxic drugs, as well as consulting a nephrologist if doubts remain. (7)

### Intraoperative period

The etiology of AKI is prerenal, renal and postrenal. In the perioperative period AKI is usually a consequence of prerenal and renal intrinsic cause. (7) The underlying mechanism of intraoperative AKI development is multi-factorial. However, the first and most important strategy is to maintain hemodynamic stability during surgery. The aim is to maintain both renal perfusion pressure and systemic arterial pressure that are appropriate for the individual patient and for the surgical requirements at the same time. (11) Aggressive fluid therapy is sometimes not enough to overcome the hypotension, and vasopressors must then be applied. According to recommendations, mean arterial pressure should be greater than 65 mmHg and systolic blood pressure greater than 100 mmHg. (11) Because the outer kidney medulla has high metabolic and oxygen demands, it is necessary to maintain hemodynamic stability with renal blood flow. (26) This makes the patient extremely vulnerable to hypoperfusion and hypoxia, especially patients with reduced renal reserves. (27-29) Another strategy is to prevent activation of the inflammation process associated with the surgery. However, every major surgery activates systemic inflammatory response syndrome in the organism which contributes to AKI development by cell-mediated and cytotoxic injury. (7,30) Also, hemolysis due to prolonged surgery with the excretion of the hex products contributes to renal tubular injury. (7) Moreover, avoiding the administration of nephrotoxic drugs during the surgical procedure can also minimize renal injury during this vulnerable period. In addition, ischemia-reperfusion injury in some surgeries presents a noxious factor for the kidneys, as well as intraoperative tissues manipulation that contributes to embolic insult to the kidneys. (26)

### Postoperative period

During the postoperative period, pharmacological and non-pharmacological preventive measures must be applied in the risky patients. The aim of the treatment is optimising blood supply and oxygen delivery to the kidneys, minimizing demands and avoiding use of nephrotoxic drugs. (12)

### Optimizing blood supply and oxygen delivery

This measure is usually accomplished by maintaining the euvolemic patient and preserving renal autoregulation, which can be obtained by intravascular fluid administration, optimization and preservation of the patient’s cardiac function, and maintaining hemodynamic stability. Recommendations state that crystalloid solutions and albumins can be used for intravascular volume replacement without fear of kidney damage. (7) The goal is to maintain mean arterial pressure greater than 65 mmHg, and even higher for elderly and diabetic patients. (31) If the patient has an acceptable intravascular volume load and the mean arterial pressure value is not satisfactory, then first-line vasopressor noradrenalin can be implemented. This treatment is recommended for treating hypotension as it does not compromise renal, hepatic or gastrointestinal blood flow. (7) Vasopresin and terlipressin can also be used to treat postoperative catecholamine resistant vasodilatory shock. (7) Since blood loss is a reality of surgery, studies recommend that haemoglobin levels should be maintained up to 100 g/l and hematocrit be greater than 21% to prevent perioperative renal ischemia and AKI. (12) Once all the factors are considered, it is evident that early goal directed therapy is the path that should
be persuaded as it involves using fluids, blood products and inotrope drugs to achieve target kidney protective physiological values of hemodynamic parameters, such as cardiac output, cardiac index and tissue oxygen delivery. (32,33)

**Decreasing demands**

The aim of this measure is to minimize the kidney’s, especially the outer medulla’s, metabolic rate and demands. One way to attain this is to sedate the patient. Another approach is the application of the loop diuretic furosemide. This reduces kidney oxygen demands by blocking the Na/K-ATP pump, which is a large energy consumer. (12) By doing so, more energy is conserved for the ischemic kidney. (12) Equally, mannitol can be used to decrease oxygen demands by increasing renal blood flow and scavenging free toxic radicals. (34) Additional and larger clinical trials are all that is required to support its benefit in the perioperative period.

**Avoiding nephrotoxic drugs**

Every clinician should be aware of the nephrotoxic effect of certain drugs in the perioperative period. Nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided in patients with hypovolemia and sepsis regardless of the renal function. (35) These drugs impair renal autoregulation by inhibiting prostaglandin mediated dilatation of the afferent glomerular arteriole resulting in decreased renal blood flow in the state of systemic vasoconstriction. They also can cause acute interstitial nephritis. Angiotensin converting enzyme inhibitor (ACEi) and angiotensin II receptor blockers (ARBs) should be excluded on the day of surgery since they have no renal protective benefits in the perioperative period and can cause refractory hypotension. (36) These drugs prevent the local action of bradykinins, which cause a constriction of the efferent glomerular arteriole and in this way maintains glomerular perfusion pressure in the renal autoregulation process. Certain antibiotics, such as aminoglycosides, which in high concentrations are responsible for renal tubular toxicity and require drug levels monitoring, or those that cause acute interstitial nephritis, such as penicillins, cephalosporins and fluoroquinolones, should also be avoided. (26) Likewise, minimizing the requirements of diagnostic and therapeutic procedures with an intravenous contrast agent application is also advisable.

**Conclusion**

Perioperative AKI is a serious complication and should be promptly recognized. It has implications on both short-term and long-term morbidity and mortality. (37) Every patient should therefore be preoperatively submitted to the General Surgery AKI Risk Index scoring system. (1) Having an ideal renal biomarker with high specificity and sensitivity would be helpful. Although this marker still does not exist, some new potential biomarkers are in the experimental stage and require validation in larger studies prior to application in the clinical practice. Hence, we should always bear in mind that patients with AKI have three possible outcomes: return to baseline renal function, development of chronic kidney disease in the previously normal kidney, or progression of the pre-existing chronic kidney disease. Every delay in the AKI recognition and treatment, as well not applying risk stratification and preventive measures, can therefore change the outcome and quality of life of patients who develop AKI after major surgery.

**REFERENCES**