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# Perioperative acute kidney injury

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## Abstract

Perioperative acute kidney injury (AKI) is not uncommon and is associated with considerable morbidity and mortality. Recently, several definition systems for AKI were proposed, incorporating both small changes of serum creatinine and urinary output reduction as diagnostic criteria. Novel biomarkers are under investigation as fast and accurate predictors of AKI. Several special considerations regarding the risk of AKI are of note in the surgical patient. Co-morbidities are important risk factors for AKI. The surgery in itself, especially emergency and major surgery in the critically ill, is associated with a high incidence of AKI. Certain types of surgeries, such as cardiac and transplantation surgeries, require special attention because they carry higher risk of AKI. Nephrotoxic drugs, contrast dye, and diuretics are commonly used in the perioperative period and are responsible for a significant amount of in-hospital AKI. Before surgery, the anaesthetist is required to identify patients at risk of AKI, optimize anaemia, and treat hypovolaemia. During surgery, normovolaemia is of utmost importance. Additionally, the surgical and anaesthesia team is advised to use measures to reduce blood loss and avoid unnecessary blood transfusion. Hypotension should be avoided because even short periods of mean arterial pressure <55–60 mm Hg carry a risk of postoperative AKI. Higher blood pressures are probably required for hypertensive patients. Urine output can be reduced significantly during surgery and is unrelated to perioperative renal function. Thus, fluids should not be given in excess for the sole purpose of avoiding or treating oliguria. Use of hydroxyethyl starch needs to be reconsidered. Recent evidence indicates a beneficial effect of administering low-chloride solutions.

**Key words:** acute kidney injury; perioperative complications; perioperative management; surgery



**Editor's key points**

- Perioperative acute kidney injury is associated with major morbidity and mortality.
- Use of serum creatinine in diagnosis is imperfect, and several novel biomarkers are under development to improve detection.
- Contributing factors include patient comorbidities, specific surgeries, nephrotoxins, fluid and blood management, and haemodynamic stability.

The term acute kidney injury (AKI) is used to describe a rapid deterioration (hours to days) of renal function. This rapid deterioration leads to accumulation of plasma waste products, such as urea and creatinine. Acute kidney injury is not an uncommon disorder and is associated with considerable morbidity and mortality. The definition of AKI has changed and evolved over the years, making the comparison of incidence and prevalence among studies difficult. It is estimated that 2–18% of all hospital inpatients acquire AKI.[1–3] The incidence of AKI is reported to be between 22 and 57% in critical care patients.[4 5] Unlike the traditional belief that patients recovering from AKI usually return to their baseline renal function, recent reviews of the literature show AKI to be a significant risk factor for chronic kidney disease.[6 7] Acute kidney injury is also known to induce distant organ damage, which in turn contributes further to morbidity and mortality.[8]

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Perioperative AKI is a leading cause of morbidity and mortality. It is associated with increased risk of sepsis, anaemia, coagulopathy, and mechanical ventilation.[9] In a prospective study of 1200 patients having non-cardiac non-vascular surgery, AKI was associated with increased morbidity and mortality.[10] A study investigating patients after general surgery reported an eight-fold increase in mortality in patients with perioperative AKI,[11] whereas a more recent large-scale study of patients undergoing intra-abdominal surgery found that non-AKI patients had a 30 day mortality of 1.9%, compared with 31% in patients with AKI.[12] Notably, mortality is higher in patients with perioperative AKI even after complete renal recovery.[9]

Perioperative AKI is a feared phenomenon with deleterious effects. Methods to ameliorate the burden of perioperative AKI are constantly sought. In this review, we discuss definitions of AKI, the pathophysiology of AKI relevant to the perioperative period, and specific considerations of AKI that are of special relevance in the surgical patient. With this knowledge, we consider methods to identify patients at risk of AKI and review the current recommended perioperative management aimed to prevent perioperative AKI.

## Definition of acute kidney injury

The first attempts to define AKI date back to the 17th century. Nevertheless, the term acute renal failure appeared for the first time in 1951.[13] Since then, many definitions have been used by investigators and clinicians, resulting in a lack of clarity and preventing comparable research. A review on the different classification systems found more than 35 definitions of acute renal failure.[14] The various definitions attempted to describe diverse aspects of AKI. Glomerular filtration rate (GFR) roughly expresses the overall function of the different parts of the kidney; a rapid decline in GFR defines AKI.[15] Given that a 24 h urine creatinine clearance test is not straightforward to apply in everyday practice, serum creatinine (sCr) change from baseline is considered a reasonable substitute and is roughly correlated with the change in GFR (although sCr becomes abnormal only after GFR declines significantly).[2] Most definitions use urine output and sCr as markers of renal function because they are unique to the kidney and easily measured.

The first publication of consensus criteria for AKI was published in 2004. The system was named RIFLE (risk, injury, failure, loss of kidney function, end-stage renal failure) and used sCr or urine output to define AKI.[16]

In 2004, the term AKI was proposed as a replacement for the former acute renal failure. The change of terms highlighted the fact that loss of function and failure are preceded by a structural and physiological injury to the kidney. Later, in 2007, a modified definition of the RIFLE criteria was published by the Acute Kidney Injury Network (AKIN).[17] Although the AKIN criteria evolved from the RIFLE criteria, a major advance was the understanding that even small changes in sCr concentrations are associated with increased morbidity and mortality.[18 19] The AKIN criteria allowed definition of AKI even without knowledge of baseline sCr.

Several studies conducted on postoperative AKI attempted to compare the predictive value of the two methods.[20 21] Both schemes predict outcome of AKI with different sensitivity and specificity. The comparison also highlighted the need to select baseline sCr carefully when the diagnosis of AKI is based solely on the net sCr change. If the selected baseline sCr is the first postoperative sCr or the sCr after fluid resuscitation, over-diagnosis of AKI can occur.[21]

In 2012, a clinical practice guideline of AKI was proposed by the Kidney Disease: Improving Global Outcomes (KDIGO) Foundation. The guideline includes a comprehensive review of AKI definition, risk assessment, diagnosis, prevention, treatment, and renal replacement therapy. The group accepted the existing RIFLE and AKIN criteria for the definition of AKI and proposed simple, practical criteria of AKI.[22] The KDIGO criteria include both a relative and an absolute change of sCr and accept a short (48 h) and an extended (7 days) time frame for diagnosis of AKI. The urine output criteria remained practically unchanged. The KDIGO recommendations relevant to perioperative AKI are discussed in the perioperative management section.

A comparison of the three different classifications is presented in Table 1.

Despite the continued effort to standardize the definition of AKI using sCr, these methods have several flaws. The increase in sCr is late in the course of AKI such that by the time the diagnosis is made using standard laboratory methods the disease is well established. In addition, sCr can be influenced by volume overload, nutrition, steroids, and muscle trauma.[2]

Recently, major advances suggest that biomarkers might help to detect AKI early, identify the aetiology, predict outcome, and tailor specific therapies. Biomarkers are molecules that report on renal function or damage that relate specifically to different biological functions of the kidney.[23] For example, *N*-acetyl-β-d-glucosamininidase in the urine is a direct marker of lysosomal injury in the proximal tubule, whereas cystatin C in the urine is a marker of reduced uptake by damaged proximal tubules.[23] Some other promising biomarkers are kidney injury molecule-1, microalbumin, neutrophyl gelatinase-associated lipocalin, interleukin 18, and liver fatty acid binding protein.[23 24] A promising study conducted in intensive care units (ICUs) showed that the combined use of the two novel biomarkers insulin-like growth factor binding protein 7 and tissue inhibitor of metalloproteinases-2 was a sensitive and fast way to detect AKI.[25] A similar study showed that insulin-like growth factor binding protein 7 and tissue inhibitor of metalloproteinases-2 can also be used for the detection of post-cardiac surgery AKI.[26]

Several issues remain to be solved before these biomarkers can be used in clinical practice. For example, should urinary biomarkers be normalized to urinary creatinine concentrations?[27] What is their specificity and sensitivity? Can we accurately define the sensitivity and specificity when making comparisons with a rather imperfect gold standard, such as sCr? Should a single biomarker or a combination of several be used?[24]

A major issue concerning AKI criteria is their relevance to the perioperative period. Many surgical patients arrive in hospital without preoperative sCr concentrations. As was mentioned above, this can lead to over-diagnosis of AKI. On the contrary, when patients do arrive with a preoperative sCr concentration, the opposite can occur because in the immediate postoperative period sCr concentrations can be lower than baseline as a result of haemodilution after massive fluid administration and fluid shifts. Comparing these postoperative and preoperative values can lead to under-diagnosis of AKI and consequently delay treatment.

A major concern is whether or not intraoperative urine output is reliable as a criterion for AKI. As discussed below, recent studies suggest that urine output can be reduced significantly during surgery and is unrelated to perioperative renal function.[28 29]

## Mechanisms of perioperative acute kidney injury

Causes of AKI were traditionally divided into prerenal, intrinsic, and postrenal, which provides a convenient classification, but