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REVIEW

Perioperative acute kidney injury following major abdominal surgery

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Abstract

Major abdominal surgery is associated with significant morbidity, not least the development of acute kidney injury. As a common perioperative complication, acute kidney injury is associated with increased length of stay, increased risk of perioperative infection and the potential development of chronic kidney disease. Moreover, the development of acute kidney injury is independently associated with an increased risk of death. Perioperative acute kidney injury is not a single entity, but describes a clinical syndrome with multiple causes including physical causes related to the surgical procedure, ischaemia-reperfusion injury and the use of potential nephrotoxins. Currently, acute kidney injury is defined by changes in serum creatinine level and urine output criteria, which although robust in heterogenous populations, may not perform as accurately in the perioperative period. This article discusses these issues including the potential role of novel biomarkers for early detection of perioperative acute kidney injury, as well as the use of predictive modelling. Treatment is mainly supportive but evidence suggests that more targeted therapy may lead to improved outcomes.

Key words: Abdominal surgery, Acute kidney injury, Biomarkers, Kidney replacement therapy, Perioperative

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Introduction

The development of acute kidney injury is a predictor of immediate and long-term adverse outcomes in hospitalised patients, and perioperative patients, particularly those undergoing cardiac or vascular procedures, are at high risk of developing acute kidney injury (O'Connor et al, 2016; Gameiro et al, 2018a). Acute kidney injury is defined by a rapid deterioration (hours to days) in kidney function and classified as stages 1–3 (determined by changes in serum creatinine level and/or urine output) using the Kidney Disease Improving Global Outcomes (KDIGO) classification (Figure 1a) (KDIGO, 2012a). Although the rise in serum creatinine level needed to meet the criteria for diagnosis of acute kidney injury may seem relatively small in an individual with normal kidney function, such a rise reflects a significant reduction in glomerular filtration rate and may lead to delayed identification of a patient with acute kidney injury (Bellomo et al, 2012). Furthermore, evidence suggests that minor increases in serum creatinine levels that fail to meet KDIGO criteria are still associated with an increased risk of mortality and longer hospital stay in the postoperative patient (Kork et al, 2015).

Problems with defining postoperative acute kidney injury

Defining postoperative acute kidney injury has proved difficult. Several classifications are used in the literature, ranging from percentage changes in creatinine level to the need for kidney replacement therapy. However, given the consensus around the KDIGO guidelines, it seems appropriate to maintain consistency and apply the KDIGO criteria to postoperative acute kidney injury. Therefore, postoperative acute kidney injury can be defined as that which occurs within 7 days of an operative intervention. Of note, in some cases, particularly emergent surgery in the presence of sepsis, acute kidney injury may be present before surgery starts. In some instances, renal dysfunction may persist for more than 7 days when it should be classified as acute kidney disease (Chawla et al, 2017).

Despite the general acceptance of the KDIGO classification for acute kidney injury it is worth noting that, when considering the perioperative period, potential confounders may

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Diagnostic criteria for acute kidney injury

- Serum creatinine increase ≥26.5 µmol/litre within 48 hours or
- Serum creatinine increase ≥1.5 times baseline which is known or presumed to have occurred within the last 7 days or
- Urine volume <0.5 ml/kg for 6 hours

a

Serum creatinine increase ≥26.5 µmol/litre within 48 hours or creatinine increase ≥1.5 times baseline	Stage 1	Urine output <0.5 ml/kg/hr for 6–12 hours
Serum creatinine increase to 2.0–2.9 times from baseline	Stage 2	Urine output <0.5 ml/kg/hr for ≥12 hours
Serum creatinine increase to ≥3.0 times from baseline or serum creatinine >354 µmol/litre or kidney replacement therapy	Stage 3	Urine output <0.3 ml/kg/hr for ≥24 hours or anuria for ≥12 hours

b

No KDIGO stage	Stage 1S	Biomarker positive
KDIGO stage 1	Stage1A	Biomaker negative
	Stage1B	Biomarker positive
KDIGO stage 2	Stage 2A	Biomarker negative
	Stage 2B	Biomarker positive
KDIGO stage 3	Stage 3A	Biomarker negative
	Stage 3B	Biomarker positive

Figure 1. a. Current definition of acute kidney injury using the Kidney Disease Improving Global Outcomes (KDIGO) (2012a) classification as stages 1–3, as determined by changes in serum creatinine level and/or urine output. b. Suggested modification of the KDIGO classification through the addition of biomarkers in addition to serum creatinine level and urine output. Stage 1 acute kidney injury may be divided into three substages (1S, 1A and 1B) and stages 2 and 3 acute kidney injury subcategorised by presence of biomarkers (Ostermann et al, 2020). In stage 1S there is evidence of kidney injury but creatinine and urine output criteria are not reached. This has previously been referred to as sub-clinical acute kidney injury.

arise. When determining the acute kidney injury stage by KDIGO criteria, determination of the baseline is often difficult. In surgical patients, particularly elective surgical cases, a baseline serum creatinine level is often known, as is the timing of the renal 'insult', which helps with classification. However, there are also significant disadvantages of using the diagnostic criteria of serum creatinine level and urine output. The serum creatinine level may be affected by changes in volume status including total body water, which may mask acute kidney injury or result in a patient with no renal injury being mistakenly classified as having acute kidney injury. Furthermore, changes in the production of serum creatinine may occur, which result in fluctuations in the plasma concentration independent of changes in the glomerular filtration rate (Bjornsson, 1979; O'Connor et al, 2017). Urine output, although a functional marker of glomerular filtration rate, is subject to a variety of confounders that may lead to errors in acute kidney injury classification. For example, changes in volume status, relative hypotension and activation of the sympathetic nervous system can contribute to the presence of oliguria, which may not reflect renal injury. Therefore, isolated oliguria in the perioperative period must be viewed in the clinical context (Klein et al, 2018).

The role of novel biomarkers

Given these potential errors in classifying acute kidney injury stage by serum creatinine level and urine output, and that postoperative patients are at an enhanced risk of acute kidney injury, it follows that early detection using other methods may confer potential benefits. This may include prompt management to potentially limit acute kidney injury but also to confirm that the changes observed are a result of kidney injury rather than a physiological response to surgery such as postoperative oliguria.

Much effort has been focused on the role of potential biomarkers, which may help with early detection. To date, studies have concentrated mainly on cardiac surgery and, to a lesser extent, transplant and vascular surgery, groups where rates of acute kidney injury have been reported as high as 50% (Hobson et al, 2009; Hilmi et al, 2015). Adoption of the use of biomarkers of acute kidney injury has been advocated in enhanced recovery programmes

following cardiac procedures (Engelman et al, 2019). While the rate of postoperative acute kidney injury is lower in major abdominal surgery, it is still significant. The prognostic study by the STARSurg Collaborative found that acute kidney injury based solely on serum creatinine criteria occurred in 14% of such patients (STARSurg Collaborative, 2018). However, data assessing biomarker performance in major gastrointestinal or gynaecological surgery are sparse.

Evidence suggests that some critically ill patients who have positive damage biomarkers but do not fulfil acute kidney injury serum creatinine or urine output criteria have worse outcomes (Haase et al, 2011). This has led to a proposal that clinical information enriched by damage and functional biomarkers may lead to more sensitive definitions of acute kidney injury. Figure 1b shows a suggested modification of KDIGO stage 1 acute kidney injury to reflect three substages (1S, 1A, and 1B) and to subcategorise stages 2 and 3 by the presence or absence of biomarkers (Ostermann et al, 2020). Thus, stage 1S identifies an early stage when there is evidence of kidney injury that is not detected by creatinine and urine output criteria, which has previously referred to as sub-clinical acute kidney injury.

However, to date it is unknown as to whether isolated changes in urinary biomarkers, for example, are important in terms of postoperative outcomes. Multiple different biomarkers have been described and evaluated for their ability to predict, diagnose and classify the severity of acute kidney injury (Table 1). The urinary biomarker, dickkopf-3, a cytokine and marker of tubular stress, strongly predicts the development of postoperative acute kidney

Table 1. Reported biomarkers for acute kidney injury

	Biomarker	Source	Potential use in acute kidney injury
Urinary biomarkers	Alanine aminopeptidase Alkaline phosphatase γ-glutamyl transpeptidase	Proximal tubule cells	Diagnosis and severity
	Calprotectin	Neutrophils, monocytes	Intrinsic acute kidney injury
	Dickkopf-3	Tubular stress marker	Prediction of acute kidney injury
	Glutathione-s-transferases	Proximal and distal tubular cells	Diagnosis
	Tissue inhibitor metalloproteinase-2 and insulin-like growth factor binding protein-7	Cell cycle arrest markers	Prediction, diagnosis and severity
	Interleukin-18	Proinflammatory cytokine released from tubular cells	Prediction and diagnosis
	Kidney injury molecule 1	Proximal tubule cells	Prediction, diagnosis and severity
	N-acetyl-glucosaminidase	Tubular	Diagnosis
	Netrin-1	Tubular	Diagnosis
Urinary and plasma biomarkers	Chitinase 3-like protein 1	Endothelial cells, macrophages, neutrophils	Diagnosis and severity
	Cystatin C	Cysteine protease inhibitor produced by nucleated red cells Filtration marker	Diagnosis and severity
	Liver-type fatty acid binding protein	Proximal tubule	Diagnosis
	Neutrophil gelatinase-associated lipocalin	Tubular cells and neutrophils	Diagnosis and severity
	Osteopontin	Tubular cells	Diagnosis and severity
	Proencephalin A	Filtration marker	Prediction, diagnosis and severity

Adapted from Ostermann et al (2020)

injury (Schunk et al, 2019). Tissue metalloproteinase-2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP7) are also markers of 'renal stress' that are excreted in the urine; when their levels are raised, this has been strongly correlated with the severity of acute kidney injury (Ostermann et al, 2020).

Epidemiology of postoperative acute kidney injury

Acute kidney injury is common in hospitalised patients, particularly in those who are critically ill. The AKI-EPI study demonstrated that over 57% of all intensive care unit admissions had acute kidney injury using KDIGO criteria, of which 50% were admitted following elective or emergency surgical procedures (Hoste et al, 2015). Similarly, data from the USA revealed that postoperative acute kidney injury accounts for approximately 40% of all cases of acute kidney injury, with abdominal surgery carrying a lower risk compared to cardiac surgery (Grams et al, 2016). The incidence of perioperative acute kidney injury following abdominal surgery varies depending on the procedure, with patients undergoing emergency laparotomy at the highest risk (Kork et al, 2015).

Pathogenesis and risk factors

Acute kidney injury is a syndrome defined, currently, by changes in serum creatinine level and urine output, which offers no information as to the underlying cause of the acute kidney injury. Even in cases where the renal 'insult' is known, such as following surgery, the pathogenesis is complex and often multifactorial rather than reflecting a single underlying pathophysiology. Furthermore, histological diagnosis through renal biopsy is rarely obtained, although it is often assumed that the cause is related to tubular injury and subsequent necrosis. Renal oxygen demand represents 7% of total body oxygen requirement, the majority of which is required by tubular cells for solute reabsorption. Therefore, any hypoxic insult through reduced perfusion, for example, can lead to leucocyte activation and local inflammatory mediator release, leading initially to microcirculatory change that may ultimately result in tubular necrosis (Ince, 2014).

The pathogenesis of postoperative acute kidney injury may be viewed together with potential risk factors for perioperative acute kidney injury, as shown in **Figure 2**. In broad terms, risk factors for acute kidney injury can be considered as patient-related, operative and anaesthetic risk factors, many of which are well described.

Patient-related factors

Patient characteristics associated with the development of acute kidney injury postoperatively include male sex, older age, a history of diabetes and/or hypertension, congestive cardiac failure, albuminuria, higher number of medications and high American Society of Anaesthesiology Physical Status score (Kheterpal et al, 2009). Obesity is associated with compensatory changes, usually resulting in hyperfiltration and obesity-related glomerulopathy. These can both contribute to chronic kidney disease and are also thought to contribute to acute kidney injury. Bariatric patients have a 6–8% risk of acute kidney injury following abdominal surgery (Suneja and Kumar, 2014).

Operative factors

Operative factors include emergent surgery that may already be complicated by acute kidney injury. Intraperitoneal procedures carry the greatest risk, particularly where there is a rise in intra-abdominal pressure. Raised intra-abdominal pressure leads to a rise in renal vascular resistance, causing reduced perfusion and subsequent ischaemic injury (Demarchi et al, 2014). Laparoscopic procedures that induce a pneumoperitoneum and transient rises in intra-abdominal pressure have been investigated extensively with conflicting results. Some reports suggest that using laparoscopic techniques did not increase the risk of acute kidney injury. Others reported that controlled pressures of 15 mmHg did not affect the incidence of acute kidney injury but that CO_2 inflation time alone was linked to increased rates of acute kidney injury and should be minimised in patients with known renal disease (Teixeira et al, 2014).

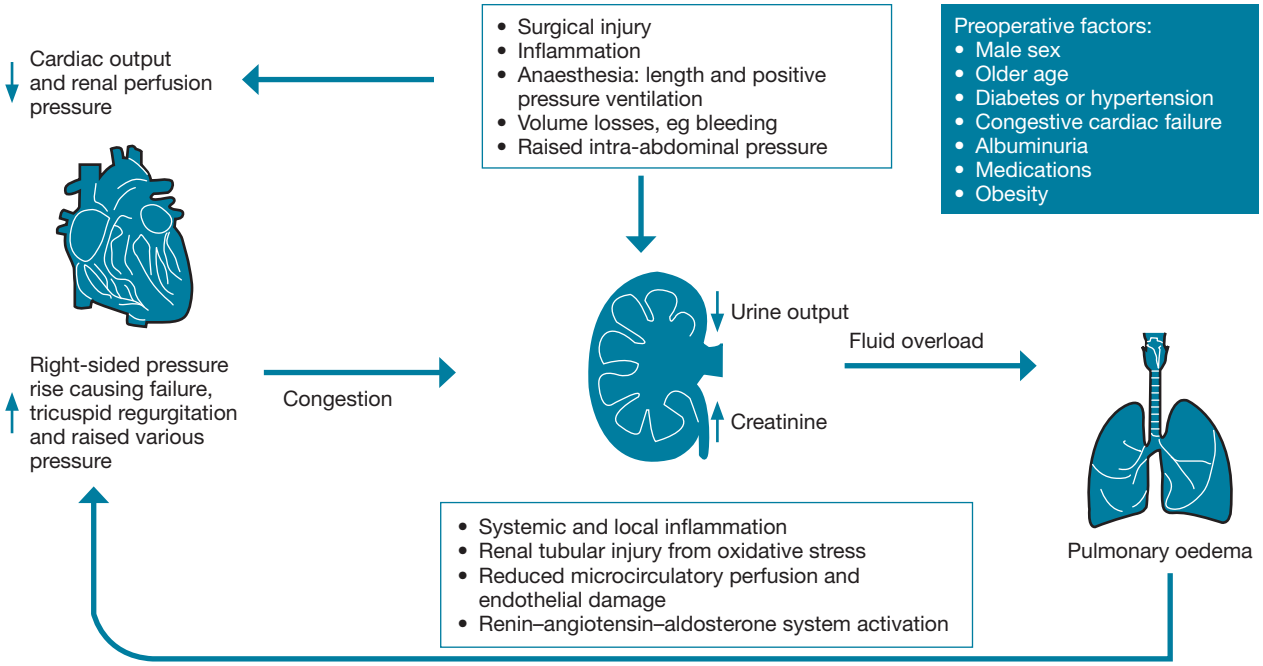

Figure 2. Potential pathogenesis of postoperative acute kidney injury encompassing operative, anaesthetic and patient characteristics.

Additionally, the surgical insult itself can lead to systemic and local inflammation, causing renal tubular injury from oxidative stress, reduced microcirculatory perfusion and endothelial damage (Meersch et al, 2017).

Anaesthetic factors

Anaesthetic factors that potentially increase the risk of acute kidney injury include duration of anaesthesia as well as intraoperative hypotension with vasopressor or inotrope use (Teixeira et al, 2014). Indeed, several observational studies have demonstrated associations between intraoperative hypotension and acute kidney injury, with a mean arterial pressure <55 mmHg for longer than 20 minutes shown to impact on acute kidney injury risk (Sun et al, 2015). Hypotension may be related to arterial and venous dilation in response to general and regional anaesthetic techniques, but compounded by positive pressure ventilation reducing preload with a consequent reduction in cardiac output. Fluid used for volume replacement may also impact on the risk of acute kidney injury, as does the use of potentially nephrotoxic medications.

Risk prediction models

Risk prediction models use combinations of independent predictors and assign a relative weighting to predict a clinical outcome. Model performance should be assessed on a validation cohort but is often based on the development (derivation) sample only which, even after corrections such as bootstrapping, tend to show optimistic results (Hodgson et al, 2019). Risk prediction models for surgical patients are potentially attractive in that in most cases the patient baseline data are known. Importantly for acute kidney injury models this includes baseline renal function, the time of insult is known, and the patients are monitored closely postoperatively. A systematic review on risk prediction models for major non-cardiac surgery found that only one involved general surgical patients; none of the models described were externally validated or had any impact analyses (Wilson et al, 2016).

The most comprehensive model examined data from 75 952 patients in the American College of Surgeons – National Surgical Quality Improvement Programme. However, acute kidney injury was defined as a rise in serum creatinine level by 177 µmol/litre or more. The model used 11 parameters: age 56 years or older, male sex, emergency surgery, intraperitoneal surgery, diabetes mellitus necessitating oral therapy, diabetes mellitus necessitating insulin therapy, active congestive heart failure, ascites, hypertension, mild preoperative renal insufficiency, and moderate preoperative renal insufficiency (Kheterpal et al, 2009).

The STARsurg Collaborative published data from 173 UK hospitals including 4544 patients undergoing both elective and emergency abdominal surgery, of which 14.2% of patients sustained an acute kidney injury (STARsurg Collaborative, 2018). Variables identified as being associated with the development of acute kidney injury included age, male sex, American Society of Anesthesiologists grade, preoperative estimated glomerular filtration rate and use of preoperative angiotensin-blocking drugs. Subsequently, the Simple Postoperative AKI Risk classification (SPARK) model aimed to broadly identify patients at risk of critical acute kidney injury (defined as KDIGO>2), post-acute kidney injury death or dialysis at 90 days, low stage acute kidney injury and no acute kidney injury. The patients had no pre-existing renal disease and acute kidney injury was assessed against the KDIGO definition. The model was derived from a discovery cohort of over 51 000 patients and the variables used were age, estimated glomerular filtration rate, proteinuria, sex, surgical duration, emergency surgery, diabetes, angiotensin-blocking drugs, dipstick albuminuria, hypoalbuminemia, hyponatraemia and anaemia. Each risk factor was further subdivided into severity and assigned a score, and four risk categories were defined (Park et al, 2019). The model was externally validated with a further 29 715 cases with reasonable performance.

The past decade has seen interest in embedding prediction models into the complex electronic technology which is increasingly central to healthcare practice. Potentially powerful techniques such as machine learning are increasingly being described, which could be used to enable accurate prediction models within electronic health records. They could identify patients at highest risk of adverse outcomes, direct further diagnostic tests that may incur extra cost or time to perform and underpin interventional strategies for prevention or treatment. Indeed, attempts have been made to harness machine learning techniques within the electronic patient record to improve the accuracy of models. One such model used 285 demographic, socioeconomic, administrative, clinical, pharmacological and laboratory variables that were compiled into several statistical models, all of which provided accurate prediction of acute kidney injury and were externally validated (Thottakkara et al, 2016). Although machine learning models are currently in their infancy, they could provide a more accurate method of identifying high-risk patients.

Management of perioperative acute kidney injury

Preoperative management

In order to manage perioperative acute kidney injury, measures should be initiated preoperatively where at all possible. A patient that requires major abdominal surgery should be risk stratified for the chance of developing acute kidney injury. These data can then be used to facilitate discussions between the surgical, anaesthetic and intensive care teams, which may then dictate the type of surgery attempted and postoperative destination. Efforts should be made to limit exposure to potential nephrotoxic agents including contrast media; other drugs such as angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers may be suspended over the perioperative period, although the evidence supporting this approach is sparse. Non-steroidal anti-inflammatory drugs should be stopped or avoided in patients deemed at high risk, as should metformin and aminoglycosides where possible. To date, no preoperative interventions have been shown to reduce the incidence of postoperative acute kidney injury.

Perioperative management

One of the important modifiable factors for preventing acute kidney injury is the avoidance of intraoperative hypotension. Hypotension may be caused by intravascular fluid depletion, systemic vasodilation as a result of direct action of the anaesthetic agents or a systemic inflammatory response. It is common practice to give liberal intravenous fluid in an attempt to maintain mean arterial pressure and prevent acute kidney injury. Correcting hypovolaemia is essential, although a study in general surgical patients suggested that a more liberal approach to volume balance rather than a restrictive protocol is associated with a reduced incidence of postoperative acute kidney injury (Myles et al, 2018). Volume status can be optimised via goal-directed haemodynamic fluid therapy, which assesses the

effect of a fluid bolus, inotrope or vasopressor on a measurable endpoint such as cardiac output derived from monitoring techniques. Intraoperative blood pressure should be targeted towards a mean pressure of 65 mmHg and, where needed, volume resuscitation should be with balanced solutions rather than 0.9% saline unless there is a specific indication for the use of a different fluid regimen.

Postoperative management

In keeping with perioperative management, attention should be focused on preventing hypotension and therefore preserving organ perfusion. Postoperative hyperglycaemia should be avoided as should non-steroidal anti-inflammatory agents. Where opiate sparing may be an issue in postoperative analgesia, then anti-inflammatory agents may be considered on an individualised basis. Where angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers have been withheld then consideration should be given to recommencing these agents where there is no evidence of acute kidney injury nor need for ongoing haemodynamic support. Again, this decision should be made on an individualised level.

Where postoperative acute kidney injury is recognised, the underlying cause should be sought given the multifactorial causes of acute kidney injury. In particular, renal tract obstruction should be excluded and efforts made to mitigate further renal injury and the complications of acute kidney injury. To that end, the management of perioperative acute kidney injury is the same as the general management of any patient with acute kidney injury and should follow the KDIGO guidelines (KDIGO, 2012b). These guidelines include diagnostic work-up to determine the cause of acute kidney injury, haemodynamic optimisation and avoidance of nephrotoxins, with the degree of intervention related to the stage of acute kidney injury. Specifically, the KDIGO bundle can be applied, comprising supportive measures including maintenance of blood pressure, avoidance of nephrotoxins and directed fluid therapy. This approach reduces postoperative acute kidney injury in patients deemed high risk, as determined by biomarker positivity, but not in patients with established acute kidney injury (Meersch et al, 2017). In patients with emergent metabolic complications of acute kidney injury, kidney replacement therapy should be considered, although there is limited evidence in terms of the timing of extracorporeal support in patients with postoperative acute kidney injury. The STAART-AKI trial (STAART-AKI Investigators et al, 2020), comparing accelerated indications (12 hours from a rise in serum creatinine level or oliguria being identified) or standard indications (eg hyperkalaemia) for initiation of kidney replacement therapy, found that there was no mortality benefit in the accelerated group and that it may increase the risk of long-term dialysis dependence (STAART-AKI Investigators et al, 2020).

Outcomes from postoperative acute kidney injury

Perioperative acute kidney injury is associated with increased length of stay and subsequently hospital costs. Furthermore, there is an increase in adverse cardiovascular events, in-hospital complications and 30-day readmission rate. There is also an increase in postoperative complications, including infection, need for tracheostomy and prolonged mechanical ventilation. The incidence of end-stage kidney disease is higher, particularly in patients with chronic kidney disease who develop postoperative acute kidney injury, and acute kidney injury is a risk factor for mortality in all patients (Gameiro et al, 2018b).

Conclusions

Acute kidney injury is a frequently occurring perioperative complication. Early identification and optimisation aim to reduce patient morbidity and mortality, and routine implementation of risk prediction models may improve patient outcomes if appropriate measures are instigated. The use of novel biomarkers may help identify those at highest risk of developing acute kidney injury. In terms of future treatment, as yet novel therapies are awaited but improvements may be observed where the measures discussed are implemented.

Key points

- Postoperative acute kidney injury is common following major abdominal surgery.
- The development of postoperative acute kidney injury is associated with increased morbidity and mortality, and associated healthcare costs.
- Management to prevent postoperative acute kidney injury should begin in the preoperative period where urgency allows and continue through the perioperative and postoperative period.
- The implementation of risk prediction models as well as novel biomarkers may allow earlier identification of those individuals at highest risk.

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Conflicts of interest

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References

Bellomo R, Kellum JA, Ronco C. Acute kidney injury. Lancet. 2012;380(9843):756–766. https://doi.org/10.1016/S0140-6736(11)61454-2

Bjornsson TD. Use of serum creatinine concentrations to determine renal function. Clin Pharmacokinet. 1979;4(3):200–222. https://doi.org/10.2165/00003088-197904030-00003

Chawla LS, Bellomo R, Bihorac A. Acute kidney disease and renal recovery: consensus report of the acute disease quality initiative (ADQI) 16 workgroup. Nat Rev Nephrol. 2017;13(4):241–257. https://doi.org/10.1038/nrneph.2017.2

Demarchi AC, de Almeida CT, Ponce D et al. Intra-abdominal pressure as a predictor of acute kidney injury in postoperative abdominal surgery. Ren Fail. 2014;36(4):557–561. https://doi.org/10.3109/0886022X.2013.876353

Engelman DT, Ben Ali W, Williams JB et al. Guidelines for perioperative care in cardiac surgery: enhanced recovery after surgery society recommendations. JAMA Surg. 2019;154(8):755–766. https://doi.org/10.1001/jamasurg.2019.1153

Gameiro J, Fonseca JA, Dias JM et al. Neutrophil, lymphocyte and platelet ratio as a predictor of postoperative acute kidney injury in major abdominal surgery. BMC Nephrol. 2018a;19(1):320. https://doi.org/10.1186/s12882-018-1073-4

Gameiro J, Fonseca JA, Neves M, Jorge S, Lopes JA. Acute kidney injury in major abdominal surgery: incidence, risk factors, pathogenesis and outcomes. Ann Intensive Care. 2018b;8(1):22. https://doi.org/10.1186/s13613-018-0369-7

Grams ME, Sang Y, Coresh J et al. Acute kidney injury after major surgery: a retrospective analysis of veterans health administration data. Am J Kidney Dis. 2016;67(6):872–880. https://doi.org/10.1053/j.ajkd.2015.07.022

Haase M, Devarajan P, Haase-Fielitz A et al. The outcome of neutrophil gelatinase-associated lipocalin-positive subclinical acute kidney injury: a multicenter pooled analysis of prospective studies. J Am Coll Cardiol. 2011;57(17):1752–1761. https://doi.org/10.1016/j.jacc.2010.11.051

Hilmi IA, Damian D, Al-Khafaji A et al. Acute kidney injury following orthotopic liver transplantation: Incidence, risk factors, and effects on patient and graft outcomes. Br J Anaesth. 2015;114(6):919–926. https://doi.org/10.1093/bja/aeu556

Hobson CE, Yavas S, Segal MS et al. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. Circulation. 2009;119(18):2444–2453. https://doi.org/–1161/CIRCULATIONAHA.108.800011

Hodgson LE, Selby N, Huang TM, Forni LG. The role of risk prediction models in prevention and management of AKI. Semin Nephrol. 2019;39(5):421–430. https://doi.org/10.1016/j.semnephrol.2019.06.002

Hoste EA, Bagshaw SM, Bellomo R et al. Epidemiology of acute kidney injury in critically ill patients: The multinational aki-epi study. Intensive Care Med. 2015;41(8):1411–1423. https://doi.org/10.1007/s00134-015-3934-7

Ince C. The central role of renal microcirculatory dysfunction in the pathogenesis of acute kidney injury. Nephron Clin Pract. 2014;127(1-4):124–128. https://doi.org/10.1159/000363203

Kidney Disease Improving Global Outcomes. Section 2: AKI definition. Kidney Int Suppl. 2012a;2(1):19–36. https://doi.org/10.1038/kisup.2011.32

Kidney Disease Improving Global Outcomes. Section 3: prevention and treatment of AKI. Kidney Int Suppl. 2012b;2(1):37–68. https://doi.org/10.1038/kisup.2011.33

Kheterpal S, Tremper KK, Heung M et al. Development and validation of an acute kidney injury risk index for patients undergoing general surgery: results from a national data set. Anesthesiology. 2009;110(3):505–515. https://doi.org/10.1097/ALN.0b013e3181979440

Klein SJ, Lehner GF, Forni LG, Joannidis M. Oliguria in critically ill patients: a narrative review. J Nephrol. 2018;31(6):855–862. https://doi.org/10.1007/s40620-018-0539-6

Kork F, Balzer F, Spies CD et al. Minor postoperative increases of creatinine are associated with higher mortality and longer hospital length of stay in surgical patients. Anesthesiology. 2015;123(6):1301–1311. https://doi.org/10.1097/ALN.0000000000000891

Meersch M, Schmidt C, Zarbock A. Perioperative acute kidney injury: An under-recognized problem. Anesth Analg. 2017;125(4):1223–1232. https://doi.org/10.1213/ANE.0000000000002369

Myles PS, Bellomo R, Corcoran T et al. Restrictive versus liberal fluid therapy for major abdominal surgery. N Engl J Med. 2018;378(24):2263–2274. https://doi.org/10.1056/NEJMoa1801601

O'Connor ME, Kirwan CJ, Pearse RM, Prowle JR. Incidence and associations of acute kidney injury after major abdominal surgery. Intensive Care Med. 2016;42(4):521–530. https://doi.org/10.1007/s00134-015-4157-7

O'Connor ME, Hewson RW, Kirwan CJ et al. Acute kidney injury and mortality 1 year after major non-cardiac surgery. Br J Surg. 2017;104(7):868–876. https://doi.org/10.1002/bjs.10498

Ostermann M, Zarbock A, Goldstein S et al. Recommendations on acute kidney injury biomarkers from the acute disease quality initiative consensus conference: a consensus statement. JAMA Netw Open. 2020;3(10):e2019209. https://doi.org/10.1001/jamanetworkopen.2020.19209

Park S, Cho H, Park S et al. Simple postoperative AKI risk (spark) classification before noncardiac surgery: a prediction index development study with external validation. JASN. 2019;30(1):170–181. https://doi.org/10.1681/ASN.2018070757

Schunk SJ, Zarbock A, Meersch M et al. Association between urinary dickkopf-3, acute kidney injury, and subsequent loss of kidney function in patients undergoing cardiac surgery: an observational cohort study. Lancet. 2019;394(10197):488–496. https://doi.org/10.1016/S0140-6736(19)30769-X

STAART-AKI Investigators; Canadian Critical Care Trials Group; Australian and New Zealand Intensive Care Society Clinical Trials Group et al. Timing of initiation of renal-replacement therapy in acute kidney injury. N Engl J Med. 2020;383:240–251. https://doi.org/10.1056/NEJMoa2000741

STARSurg Collaborative. Prognostic model to predict postoperative acute kidney injury in patients undergoing major gastrointestinal surgery based on a national prospective observational cohort study. BJS Open. 2018;2(6):400–410. https://doi.org/10.1002/bjs5.86

Sun LY, Wijeysundera DN, Tait GA, Beattie WS. Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. Anesthesiology. 2015;123(3):515–523. https://doi.org/10.1097/ALN.0000000000000765

Suneja M, Kumar AB. Obesity and perioperative acute kidney injury: a focused review. J Crit Care. 2014;29(4):694.e691–696. https://doi.org/10.1016/j.jcrc.2014.02.021

Teixeira C, Rosa R, Rodrigues N et al. Acute kidney injury after major abdominal surgery: a retrospective cohort analysis. Crit Care Res Pract. 2014;2014:1–8. https://doi.org/10.1155/2014/132175

Thottakkara P, Ozrazgat-Baslanti T, Hupf BB et al. Application of machine learning techniques to high-dimensional clinical data to forecast postoperative complications. PLoS One. 2016;11(5):e0155705. https://doi.org/10.1371/journal.pone.0155705

Wilson T, Quan S, Cheema K et al. Risk prediction models for acute kidney injury following major noncardiac surgery: systematic review. Nephrol Dial Transplant. 2016;31(2):231–240. https://doi.org/10.1093/ndt/gfv415