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# Acute kidney injury—an overview of diagnostic methods and clinical management

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## Abstract

Acute kidney injury (AKI) is a common condition in multiple clinical settings. Patients with AKI are at an increased risk of death, over both the short and long term, and of accelerated renal impairment. As the condition has become more recognized and definitions more unified, there has been a rapid increase in studies examining AKI across many different clinical settings. This review focuses on the classification, diagnostic methods and clinical management that are available, or promising, for patients with AKI. Furthermore, preventive measures with fluids, acetylcysteine, statins and remote ischemic preconditioning, as well as when dialysis should be initiated in AKI patients are discussed. The classification of AKI includes both changes in serum creatinine concentrations and urine output. Currently, no kidney injury biomarkers are included in the classification of AKI, but proposals have been made to include them as independent diagnostic markers. Treatment of AKI is aimed at addressing the underlying causes of AKI, and at limiting damage and preventing progression. The key principles are: to treat the underlying disease, to optimize fluid balance and optimize hemodynamics, to treat electrolyte disturbances, to discontinue or dose-adjust nephrotoxic drugs and to dose-adjust drugs with renal elimination.

**Key words:** acute kidney injury, diagnosis, review, therapeutics

## Introduction

Acute kidney injury (AKI), formerly termed acute renal failure, is characterized by a sudden deterioration in renal function [1]. Numerous studies have found that AKI is associated with an increased mortality and adverse outcomes regardless of patient characteristics and the context in which injury occurs [2, 3].

Until a decade ago, there was a lack of uniform diagnostic criteria for AKI that led to a number of various definitions being

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**Table 1.** KDIGO's criteria for acute kidney injury [1]

| Stage | Increase in serum creatinine | Urine output |
|---|---|---|
| 1 | ≥0.3 mg/dL (26.5 μmol/L) within 48 h or 1.5–1.9 times baseline within 7 days | <0.5 mL/kg/h for 6–12 h |
| 2 | 2.0–2.9 times baseline within 7 days | <0.5 mL/kg/h for ≥12 h |
| 3 | ≥3.0 times baseline, or ≥4.0 mg/dL (354 μmol/L) increase within 7 days or initiation of RRT or in patients <18 years of age, decrease in estimated GFR to <35 mL/min/1.73 m$^2$ | <0.3 mL/kg/h for ≥24 h or Anuria ≥12 h |

used, making comparisons between studies difficult. In 2004, the risk, injury, failure, loss, end-stage renal disease (RIFLE) criteria for AKI was established [4]. In 2007, the AKI Network (AKIN) modified RIFLE criteria with the inclusion of an absolute change of serum creatinine (SCr) [5]. RIFLE and AKIN were later unified with the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) criteria [1]. The KDIGO criteria define and stage patients (three severity stages) according to changes in SCr levels and urine output (Table 1).

Urine output may be measured in real time, but commonly urine output has not been reported in studies on AKI, and thus the association between changes in urine output and outcomes in AKI are not well documented. Furthermore, it has been argued that the specificity of the urine output criteria for AKI is low, leading to many patients without AKI being misclassified to AKI [6]. However, oliguria without SCr elevation is not uncommon, and may also be associated with fluid overload where the elevation in SCr levels may be masked. Fluid overload in the context of AKI has been associated with poor outcomes [7]. Although, the KDIGO criteria for classification of AKI do not combine urine output with increases in SCr levels, there may be advantages in doing so. In a recent study, it was found that patients meeting both the SCr and urine output criteria had a dramatically worse prognosis than patients who only met either one of the two criteria [8].

The duration of injury is not included in the definition of AKI, but has been shown to be related to prognosis [9]. The term 'acute kidney disease' has been suggested for patients who have persistent AKI, defined as a duration >7 days, but <3 months. Thus, among patients who meet both SCr and urine output criteria for AKI, those in whom AKI is persistent have the worst prognosis.

Despite the uniform AKI criteria that have been developed, AKI remains a clinical diagnosis and has to be put into the clinical context where it occurs. The AKI criteria should not be used by the clinician as an absolute 'truth', but rather as a frame for decisions, for example, on when to initiate measures aimed at preventing further damage to the kidney.

## Kidney injury biomarkers

By the time KDIGO SCr criteria for AKI are met, the decline in glomerular filtration rate (GFR) and likely structural damage that preceded that decline have been present for several hours. It has been hypothesized that delayed detection of AKI is one of the reasons why intervention trials aimed at treating AKI have failed. Therefore, a lot of effort has been put into finding biomarkers that could detect kidney injury earlier, before functional biomarkers (SCr and serum cystatin C) have changed, and which would be related to the clinical course of AKI, predict the need of dialysis, or other complications. These biomarkers provide information on tubular injury, which commonly precedes functional decline. In Table 2, the most well-studied biomarkers are summarized. Of these, liver-type fatty acid-binding protein (L-FABP) is approved for use in Japan, neutrophil gelatinase-associated lipocalin (NGAL) may be used in some localities in Europe and the combination of tissue inhibitor of metalloproteinase-2 (TIMP-2) and insulin-like growth factor-binding protein 7 (IGFBP-7) is approved for use in the USA.

Early studies that found biomarkers to be useful in detecting established AKI [10–13, 16] were followed by large prospective studies [14, 17–23]. NGAL and interleukin 18 (IL-18), both in plasma and urine, were tested as early markers of injury following cardiac surgery [17, 18, 22, 23]. However, the ability of any of these markers to predict AKI was modest.

Recently, the combination of two biomarkers for tubular cell cycle arrest, TIMP-2 and IGFBP-7, has shown promising diagnostic performance to predict a doubling of SCr within 12 h in patients with sepsis [AUC (area under curve) ≈ 0.8] [24, 25]. Both these biomarkers share the property of inducing G1 cell cycle arrest that is thought to prevent proliferation of damaged cells and thereby protecting the kidney. The strength of TIMP-2*IGFBP-7 may lie in the high negative predictive values found for excluding AKI stages 2 and 3 [14]. The test can be performed at the bedside (NephroCheck®) [26].

## Risk factors for AKI

The onset of AKI is multifactorial, and several patient-specific factors can contribute to the risk of AKI. Patients with chronic kidney disease (CKD), impaired left ventricular systolic function, advanced age commonly defined as >75 years of age, diabetes and dehydration are at particularly high risk of AKI [1, 15]. In addition, specific surgery-related factors including time spent on heart–lung machine, the use of an intra-aortic balloon pump, need for blood transfusions and hemodilution are associated with AKI [27]. Patients with CKD are not only more likely to require dialysis in conjunction with AKI, but also to develop end-stage renal disease with need for renal replacement therapy (RRT) after an episode of AKI [28]. In order to prevent AKI, it is important to identify patients at high risk before surgery or exposure to potentially nephrotoxic agents.

Several risk stratification models for AKI have been developed [29]. Commonly, these prediction models have included patient characteristics such as age, sex and renal function, and comorbidities such as diabetes and chronic obstructive pulmonary disease. A limitation of most of these studies has been that the predicted outcome has been dialysis-requiring AKI, which is a rare event [30].

Recently, two studies have investigated if a bolus dose of furosemide, the so called 'furosemide stress test', may predict progression of AKI stages 1–3 [31]. Furosemide is given as a single dose of 1.0 mg/kg in furosemide-naïve patients, or a dose of 1.5 mg/kg in patients with ongoing furosemide treatment. The AUC for predicting progression to stage 3 AKI was 0.87 when an output of 200 mL urine for the first 2 h was used as cutoff, which is a much higher AUC than any kidney injury biomarker has achieved. In a recent study, eight prediction models for AKI after cardiac surgery were investigated, and found to have poor or modest abilities to predict a postoperative SCr elevation of >50%, with AUCs between 0.65 and 0.75 [32].

**Table 2.** Biomarkers of acute kidney injury

| Type of biomarker | Biomarker | Description | Kinetics |
|---|---|---|---|
| Tubular injury | Kidney injury molecule 1 [10] | Tested in urine. Upregulated after injury to proximal tubuli. Activates immune cells leading to clearance and remodeling of injured cells. | Detected 12–24 h after injury, and will peak at 48–72 h post-injury |
| | IL-18 [11] | Tested in urine and serum. Upregulated after ischemic injury to proximal tubuli. Has pro-inflammatory characteristics. | Detected within the first 6 h after injury, and will peak at 12–18 h post-injury |
| | NGAL [12] | Tested in urine and serum. Is released both from distal and proximal tubuli from damaged cells and actives protective enzymes, and prevents production of radicals. NGAL is also released from liver and neutrophils in sepsis. | Detected within 3 h of injury, and will peak at 6 h post-injury |
| | L-FABP [13] | Tested in urine. Protein that is expressed in proximal tubuli after ischemic injury. | Detected within 1 h after injury, and will peak within 6 h post-injury |
| | TIMP-2 and IGFBP-7 [14] | Tested in urine. Both these biomarkers induce G1 cell cycle arrest that prevents proliferation of endothelial cells. | Detected within 12 h of injury |
| Glomerular filtration | Cystatin C [15] | Tested in serum. Protein, which is produced at a constant rate and filtered freely, reabsorbed and metabolized in the proximal tubuli. | Detected 12–24 h after injury, and will peak within 48 h post-injury |

## Diagnostics

AKI is rarely symptomatic, and signs and symptoms are related to the underlying cause rather than AKI itself. Examinations and treatments are dependent on the clinical setting and underlying causes. The medical history should be reviewed, including exposure to nephrotoxic agents. Urinary outflow obstruction should be excluded. If the underlying cause of AKI is not obvious, renal ultrasound should be performed in order to exclude hydronephrosis, and to assess kidney size, where a kidney length <8 cm may be indicative of CKD instead of AKI, but does not exclude acute-on-CKD [33].

Blood and urine samples should be collected in order to analyze blood cell counts, electrolytes, SCr, serum albumin, standard bicarbonate and dipstick urine analysis. Analysis of urinary sediment may also be a guide to determine the etiology of AKI [34]. Urine output should always be monitored in patients with AKI because oliguria and anuria is common, and is an earlier marker of progressive AKI than SCr [1].

### Common causes of AKI

The definition of AKI does not include its etiology and it is diagnosed as a single entity, regardless of pathogenesis (Figure 1). However, it is important to determine the cause of AKI to improve patient outcomes. Historically, the etiology of AKI was divided into three categories: prerenal, renal and postrenal. The combination of prerenal and renal causes of AKI is common, for example, in sepsis or cardiac surgery. There is an underdiagnosis of AKI, and missed AKI is associated with a worse prognosis [36]. In many cases, AKI is identified at late stages or remains unknown, and the underlying causes are not examined.

Contrast-induced AKI (CI-AKI) after coronary angiography is relatively common with an incidence of 2.6–13% [37]. Drugs associated with AKI are, among others, nonsteroidal anti-inflammatory drugs (NSAID), several antimicrobials and several chemotherapeutic agents [38]. The association between angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers and AKI in patients who undergo surgery is controversial. Some studies have found an increased risk [39], others no increased risk [40], and yet further studies a decreased risk of AKI among treated patients [41]. Drug-induced AKI can, in most cases, be alleviated by replacing the nephrotoxic drug with a similar less-nephrotoxic drug, or changing administration practices.

Noncardiac surgery is thought to be associated with a lower risk of AKI than cardiac surgery [42]. However, AKI in noncardiac surgery patients is largely understudied. In one study where AKI was defined as a >50% increase in SCr levels after noncardiac surgery, 7% developed AKI [43]. In patients undergoing cardiac surgery the incidence of AKI is between 1% and 50% depending on the type of procedure and the classification of AKI [2]. AKI is common in patients with sepsis, and patients with septic shock and AKI have an almost doubled in-hospital mortality [44].

### Prerenal AKI

Prerenal AKI occurs because plasma flow and intraglomerular pressure are inadequate to maintain filtration capacity. The most common cause is hypovolemia, followed by a decreased cardiac output or impaired autoregulation, which may be induced by NSAIDs. Prerenal AKI is usually reversible in terms of normalizing baseline SCr, but may still involve an injury. The autoregulation of the pre- and postglomerular arterioles are required both for adequate renal blood flow and to maintain hydrostatic pressure in the glomeruli.

### Postrenal AKI

Postrenal AKI is caused by an obstruction of urinary flow. A number of causes exist as benign prostatic hyperplasia, urethral stricture, pelvic or abdominal cancers, neurological causes as multiple sclerosis, ureter obstruction from kidney stones or ureter injury following surgery or trauma [35, 44]. The initial action is to exclude urinary outflow obstruction, and thereafter,

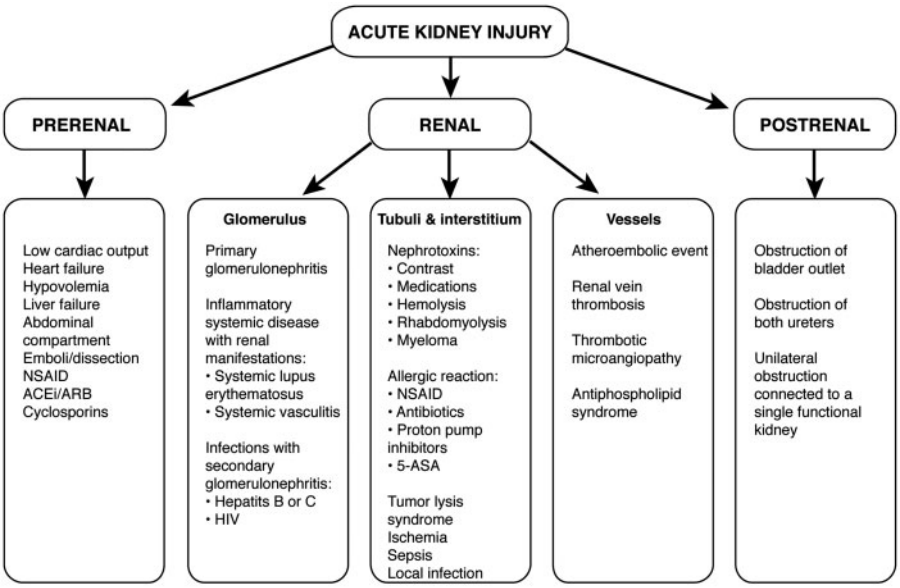


**Fig. 1.** Causes of AKI [35]. ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers; 5-ASA, 5-aminosalicylic acid.

ultrasound should be performed to rule out hydronephrosis [26]. In cases where flank pain is present, the preferred imaging should be computed tomography without contrast in order to rule out kidney stones.

### Renal AKI

Renal AKI may be linked to nephrotoxic drugs, other nephrotoxins, infection, sepsis, renal ischemia, malignant hypertension or inflammation (e.g. glomerulonephritis, vasculitis, allergic reaction). In the absence of a clear cause of AKI, inadequate response to treatment, or findings of both hematuria and proteinuria in patients with AKI, inflammatory diseases of the renal parenchyma such as glomerulonephritis and vasculitis should be suspected [26].

### Combination of prerenal and renal AKI

In many cases, prerenal and renal AKI exist concurrently. AKI may occur in sepsis, despite the absence of hypotension. The causes are multifactorial including sympathetic activation, and hormonal and inflammatory mediation [45]. Concomitant prerenal and renal AKI is also observed in disorders such as rhabdomyolysis, and hypercalcemia, in which severe hypovolemia combined with the toxic effects of myoglobin and calcium causes AKI [46]. Rhabdomyolysis is commonly associated with hypovolemia, thus leading to prerenal AKI, and direct nephrotoxic effects of myoglobin and heme proteins, and may also lead to intraluminal cast formation and tubular obstruction. After cardiac surgery the causes of AKI are often a combination of ischemia, inflammation, hypotension, embolism, and free hemoglobin from blood transfusions.

## Treatment and management of AKI

### General principles

The treatment of AKI is aimed at limiting damage and preventing further loss of GFR. There are several key principles to follow, where the most important are to treat the underlying cause, and to achieve normovolemia and hemodynamic stability. In addition, electrolyte disturbances should be treated, nephrotoxic drugs discontinued or dose-adjusted, and drugs with renal elimination should be dose-adjusted [47]. Potassium-sparing diuretics and ACE inhibitors should be discontinued in order to avoid progression of AKI and hyperkalemia. Acid–base disturbances, mainly in the form of metabolic acidosis, are frequent in moderate to severe AKI (stages 2 and 3), where treatment of the underlying causes is the primary objective. A cornerstone of the management of all patients with AKI is to monitor urine output, and to initially monitor SCr several times a day.

### Hemodynamic optimization

#### *Fluid therapy*

For all cases in which hypovolemia is the suspected cause of AKI, the first priority is to restore fluid balance with the aim to increase cardiac output, in order to stabilize hemodynamics, and renal blood flow, without inducing fluid overload. Evaluation of hydration status is difficult, and several methods have recently become available in clinical practice such as measuring bioimpedance and ultrasound assessment of vena cava and left ventricle dimensions [48]. The rate of rehydration should be individually assessed [49].

#### *Choice of fluid*

Several studies have shown that crystalloid solutions with high chloride content may be harmful and lead to a deterioration of renal function [50, 51]. It is thought that high chloride concentration at the macula densa increases tubuloglomerular feedback causing preglomerular vasoconstriction and decreased renal perfusion [51]. A recent meta-analysis found an association between resuscitation with fluids containing high chloride content and increased risk of AKI, metabolic acidosis and time on mechanical ventilation [52]. However, a recently published randomized trial in the intensive-care setting found no difference in the risk of AKI or dialysis in patients treated with saline compared with a balanced crystalloid solution [53]. In studies where the synthetic colloid hydroxyethyl starch has been used in sepsis and critically ill patients, an increased risk of AKI has

been found, leading to cessation of its use [54]. Albumin is considered to be harmless to the kidney, but its advantage over crystalloid solutions has not been demonstrated [49]. In conclusion, current knowledge suggests that patients with AKI, in need of fluid therapy, should be treated with a balanced crystalloid solution.

*Fluid overload*

It has long has been believed that infusion of large volumes of fluids can treat or prevent AKI by maintaining renal perfusion and urine output. This was further fueled by a study published 15 years ago where so called 'early goal-directed therapy', including infusion of generous amounts of fluids, was found to increase survival in patients with severe sepsis [55]. However, in the last decade this has been challenged in a number of studies that have demonstrated harm from excess fluids [48, 56, 57]. Recently, in a randomized controlled trial (RCT), it was found that 'permissive oliguria' after major abdominal surgery was not associated with higher NGAL levels or lower measured GFR compared with usual care [58]. Fluid overload may lead to an increased intra-abdominal pressure, and edema in the kidney that is surrounded by a nonexpandable fibrous capsule, thereby reducing perfusion pressure in the kidney [59, 60]. Current sepsis guidelines [61] recommend that the target central venous pressure should be 8 mmHg, a level that may lead to decreased renal perfusion and AKI [62]. In order to prevent fluid overload, a new strategy of fluid resuscitation has been proposed by the Acute Dialysis Quality Initiative that consists of four phases: the rescue, optimization, stabilization and de-escalation phases [63]. In the rescue phase, boluses of fluid are administered in life-threatening hemodynamic instability; in the optimization phase, when the patient is hemodynamically stable, careful administration of fluids is done with the aim to maintain hemodynamic stability; in the stabilization phase, when the patient is in a stable condition, a zero or negative fluid balance is aimed for; and finally, in the de-escalation phase, excess fluid is removed.

*Vasoactive drugs*

Vasoactive drugs lead to systemic vasoconstriction and an increased blood pressure that increases renal perfusion [64]. A moderate dose of norepinephrine is thought to reduce the risk of AKI in patients with vasodilated shock [64, 65]. However, this has been challenged in a recently published study [66]. In animal studies, norepinephrine administration has been found to increase renal blood flow and GFR [64]. Moreover, an increase in mean arterial blood pressure from 60 to 75 mmHg using norepinephrine resulted in an increase in GFR and renal oxygen delivery in patients with vasodilated shock after cardiac surgery [67]. A higher mean arterial pressure has also been shown to reduce the need for dialysis in sepsis patients [66].

Dopamine is a renal vasodilator acting on both the pre- and postglomerular arterioles and thereby increasing renal blood flow. The administration of a low dose of dopamine has been thought to increase renal perfusion. However, studies have not shown a beneficial effect in treating or preventing AKI and adverse effects such as arrhythmic events have been identified [1, 26]. Therefore, the recommendation currently is to not use dopamine in patients with AKI [26, 47, 68].

Vasopressin is another drug that increases blood pressure, and is commonly used as a second-line drug in conjunction with norepinephrine in order to stabilize hemodynamics. In one study where norepinephrine was compared with norepinephrine in combination with vasopressin, the authors found a trend toward a lower risk of AKI in the combination group [69].

The inotropic and vasodilating drug levosimendan increases cardiac output, and may be used when a restricted fluid therapy is warranted in patients with compromized cardiac function [70]. Levosimendan is a calcium sensitizer, and unlike several vasopressor drugs, it improves right ventricular function, which reduces central venous pressure leading to reduced venous stasis in the kidney. Furthermore, levosimendan dilates preglomerular arterioles, improving renal circulation [71]. The renal effects of levosimendan are under investigation [72].

## Drug treatment for AKI

Several drugs have been tested for AKI, but none has been established as standard treatment in clinical practice. Many studies have been underpowered and results have been inconsistent. The most-studied treatments for AKI are discussed below.

*Diuretics*

Furosemide has several renoprotective characteristics like blocking of oxygen-consuming sodium channels in the tubules, increased diuresis leading to a reduced oxygen demand in the kidney and washout of kidney-toxic molecules [73]. However, clinical studies have failed to demonstrate that furosemide improves the prognosis in AKI, except in patients with fluid overload [74]. The use of furosemide as prevention of AKI in conjunction with cardiac surgery or contrast exposure has been linked to a higher risk of AKI [75].

*Acetylcysteine*

The protective effect of acetylcysteine is considered to be mainly related to its antioxidant properties, but also inducing vasodilation in the renal medulla by stabilizing nitric oxide and by inhibiting ACE [76]. Acetylcysteine has not been shown to prevent AKI associated with cardiac surgery or in patients with sepsis [77, 78]. In the setting of CI-AKI, results have been contradictory, but several meta-analyses suggest that acetylcysteine provides some protection against CI-AKI, especially in patients at high risk [76, 79, 80]. Due to the heterogeneity of study results, it is difficult to establish a clear consensus, but the KDIGO work group has proposed that oral acetylcysteine along with intravenous isotonic crystalloid solutions should be used in patients at high risk of CI-AKI [68].

*Sodium bicarbonate*

Sodium bicarbonate has been used for the treatment and prevention of AKI associated with heme-pigment nephropathies (myoglobin, hemoglobin and bilirubin), and in tumor lysis syndrome. Sodium bicarbonate is thought to increase the solubility of these products preventing the formation of obstructive methemoglobin cylinders and crystals in the tubules [81]. In addition, sodium bicarbonate is thought to reduce oxidative stress and free radicals [81]. This led to the hope that sodium bicarbonate may prevent AKI. A pilot study that included 100 cardiac surgery patients randomized either to sodium bicarbonate or crystalloids found a reduced risk of AKI in the intervention arm [82]. However, in the full-scale RCT no preventive effect of sodium bicarbonate was found, but instead in an intention-to-treat analysis there was a significant association between sodium bicarbonate and an increased risk of AKI [83]. Similarly, another trial reported no preventive effects of sodium bicarbonate [84]. In

prevention of CI-AKI, sodium bicarbonate solutions have not shown to be superior compared with sodium chloride solutions [26]. Thus, sodium bicarbonate is not recommended for the prevention or treatment of AKI currently [81, 85].

*Statins*

Statins, which are used to prevent cardiovascular events, are thought to reduce free oxygen radicals in the renal tubules and to modulate inflammatory responses, which has led to the assumption that statins may prevent AKI. In a paper published in 2012 it was found that a high dose (80 mg) of atorvastatin before administration of contrast agent was associated with a lower risk of CI-AKI [86]. Later, an RCT on perioperative atorvastatin therapy found no preventive effect of AKI after cardiac surgery [87]. Moreover, recently an RCT on perioperative rosuvastatin treatment found an increased risk of AKI in the rosuvastatin group [88]. Similarly, another RCT on patients with sepsis-associated acute respiratory distress syndrome concluded that rosuvastatin was associated with the secondary outcome of persistent AKI [89]. Regarding CI-AKI, a recent meta-analysis of studies on statin-naïve patients undergoing coronary angiography showed that statin treatment before contrast exposure may have a protective effect [90]. Due to these conflicting results, statin therapy for AKI prevention is not currently recommended.

### Remote ischemic preconditioning

Remote ischemic preconditioning (RIPC) is a procedure of short episodes of ischemia induced at a remote site, which is thought to induce ischemic-protective mechanisms to other organs such as the kidney [91]. The underlying mechanisms are not fully understood, but a recent study suggested that inducement of cell cycle arrest in renal tubuli may be a potential mechanism [91]. In cardiac surgery populations, results of RIPC have been contradictory. In an early RCT in 120 patients, it was found that RIPC was associated with a lower risk of AKI [92]. In a later RCT in 240 patients undergoing cardiac surgery with a high risk of AKI, a similar finding was reported [93]. However, other studies have found no preventive effects of RIPC for AKI in patients undergoing cardiac surgery [94, 95]. Two smaller studies demonstrated a reduction in CI-AKI after the use of RIPC [96, 97]. Since data are inconclusive and contradictory, there is currently no firm recommendation to use RIPC to prevent AKI.

### Dialysis

The current recommendation on when to start RRT involves life-threatening changes in fluids, electrolytes, the acid–base balance or uremic complications [1]. However, controversy exists over the benefit of initiating dialysis at an early stage, when life-threatening complications have not yet developed, versus later stage [98]. The accumulated data from clinical trials with varying quality and observational studies have not concluded an optimal timing for start of RRT. A recent RCT [The Artificial Kidney Initiation in Kidney Injury (AKIKI) trial] found that early versus delayed RRT in the intensive care unit offered no benefit in terms of outcome [99]. While the most recent randomized trial [the Early vs Late Initiation of Renal Replacement Therapy in Critically Ill Patients With Acute Kidney Injury (ELAIN) trial] showed that early initiation of continuous RRT reduced mortality, hospital length of stay and duration of RRT compared with those with late initiation [100]. Interestingly, the late initiation group in the ELAIN trial resembled the early initiation group in the AKIKI trial, and may explain the contradictory results.

## Summary

AKI is common and associated with poor outcomes. Despite a number of intervention studies, no effective treatment or prevention of AKI has been found. Therefore, efforts should be made to limit damage in patients with AKI by use of crystalloid solutions instead of fluids with a high chloride content, avoiding fluid overload, and discontinuing or dose-adjusting nephrotoxic drugs. In addition, if the cause of AKI is not obvious, postrenal outflow obstruction and medication-induced AKI have to be excluded in order to prevent further damage to the kidney.

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## Conflict of interest statement

This article is not under consideration elsewhere and none of the content has been previously published. All authors have read and approved the manuscript and there is no disclosure of any potential conflict of interest. M.J.H. has received consulting honoraria from Actelion and Pfizer.

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