Review Article

Cardiac surgery-associated acute kidney injury: pathophysiology and diagnostic modalities and management

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Abstract

Acute kidney injury is a disease spectrum that can present with from mild renal dysfunction to complete renal failure that would require renal replacement therapy. Cardiac surgery-associated acute kidney injury is a complication that carries a grave disease burden. Risk factors are identified as being either modifiable or non-modifiable. This literature review aims to define the pathophysiology of cardiac surgery-associated acute kidney injury, the current definition and classification of acute kidney injury and the available diagnostic modalities, especially the use of biomarkers.

Keywords: cardiac surgery-associated acute kidney injury, cardiopulmonary bypass, acute renal failure, renal replacement therapy, kidney disease improved global outcomes

Submitted 30/9/19, accepted 21/11/19

Cardiovasc J Afr 2020; **31**: online publication www.cvja.co.za

DOI: 10.5830/CVJA-2019-069

Cardiac surgery presents with postoperative complications, particularly when cardiopulmonary bypass (CPB) is utilised.[1] Acute kidney injury (AKI) is still one of the most common complications with deleterious effects following cardiac surgery.[2] Over two million cardiac surgical procedures are performed around the world each year.[3] A recent systematic review and a meta-analysis found the total incidence of AKI in adult patients after cardiac surgery to be 22.3%.[4] AKI is a broad clinical syndrome,[5] presenting small changes in renal function markers and progressing to a need for renal replacement therapy (RRT).[6] The incidence of AKI in patients undergoing cardiac surgery in the African population is not documented.

The risk of postoperative death in patients undergoing cardiac surgery ranges from 5 to 30% when serum creatinine levels are ≥ 1.5 mg/dl, which makes serum creatine an independent risk factor for morbidity and mortality following cardiac surgery.[7]

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In a retrospective evaluation of adult patients in a cardiac intensive care unit (ICU) following coronary artery bypass graft (CABG) or valvular surgery by Machado *et al*.,[7] using the Kidney Disease Improving Global Outcomes (KDIGO) criteria in a group of patients who presented with elevated serum creatinine levels pre-operatively, patients with an elevated serum creatinine in the pre-operative period associated with high EuroSCORE values and an increased length of CPB and ICU stay, developed cardiac surgery-associated AKI (CSA-AKI).[7] In this cohort of 918 patients, 391 (43%) developed CSA-AKI. The diagnosis of AKI using the KDIGO criteria was shown to be a powerful predictor of 30-day mortality.[7]

Using the AKIN criteria to diagnose CSA-AKI, Vellinga *et al*.[8] found 14.7% of patients to have developed AKI. These patients were of advanced age, had low pre-operative estimated glomerular filtration rate (eGFR), chronic kidney disease and presented for emergency surgery. The patients who developed AKI were also found to have received loop diuretics and had received blood transfusion in the postoperative period.[8]

Bastin *et al*.[9] assessed 1 881 patients using the Risk Injury Failure End Stage, Kidney Disease (RIFLE), Acute Kidney Injury Network (AKIN) and KDIGO criteria in defining the epidemiology of AKI following cardiac surgery and compared the outcome of patients requiring RRT in the same population. The AKIN and KDIGO criteria were found to be comparable in predicting the incidence and outcome of AKI. An increase in age, low pre-operative eGFR, longer duration of CPB, increased length of ICU and hospital stay, and repeat surgery correlated with an increased risk of CSA-AKI.[9] A total of 122 (6.5%) patients required RRT: 117 patients within seven days and five patients seven days after surgery.[9] Their hospital mortality rate decreased from 82.9% previously to 53.8%, and this was attributed to more patients being started on RRT before their serum creatinine level was > 30 mmol/l.[9]

In a review article by Rosner and Okusa,[10] the incidence of AKI correlated with the type of surgery. Combined CABG and valvular surgery had an AKI incidence of 4.6% with 3.3% of the patients requiring RRT.[10] CABG alone had the lowest incidence of AKI of 2.5%, while valvular surgery had an incidence of 2.8%.[10]

O'Neal *et al*.[11] divided risk factors into pre-, intra- and postoperative risks. An increase in age, female gender and co-morbid diseases such as hypertension, diabetes mellitus, chronic kidney disease, hyperlipidaemia, peripheral vascular disease, anaemia and smoking were contributing factors in the pre-operative period.[11] CPB was an intra-operative risk factor

that played a part in the pathophysiology of CSA-AKI.[10] Red blood cells were damaged by the CPB circuit, which resulted in the release of free haemoglobin, damaging the renal tubules by depleting plasma haptoglobin levels and promoting the production of free oxygen radicals.[11]

In sub-Saharan Africa, a 2016 systematic review by Olowu *et al.*,[12] assessing the outcome of AKI in children and adult patients identified 3 881 records between January 1990 and November 2014 of patients with AKI. Forty-one records met their inclusion criteria, with 1 403 adults and 1 937 paediatric patients. The incidence of mortality was found to be 32% in adults and 34% in the paediatric population, but had increased intensely to 82 and 73%, respectively, when RRT was required but not received. They concluded that the scarcity of resources in health centres, especially RRT, stressed the need to practice preventative approaches in the management of AKI in this continent.[12]

Pathophysiology

The development of AKI following cardiac surgery is a complex clinical phenomenon.[13] It was previously described as being secondary only to ischaemia and reperfusion injury.[2] The pathophysiology of CSA-AKI has however recently been seen to be multifactorial, [2,11,14] and the causes have been classified as pre-renal, renal and post-renal.[14] Bellomo *et al.*[13] described the pathophysiology as involving several mechanisms of injury. Genetic factors have also been described as contributors to CSA-AKI.[2]

Renal ischaemia and reperfusion injury

Ischaemia and reperfusion injury have been described as the most common cause of CSA-AKI.[15] The mechanisms of injury are related to a decrease in oxygen delivery, poor nutrient transport and poor removal of waste products in the renal tubular cells.[15] Research has demonstrated that it is not merely the decrease in GFR that leads to AKI, but also the regional differences in renal blood flow.[16] These are due to the high metabolic demands of the outer renal medulla with lower partial oxygen pressures (PaO_2) of 10–20 mmHg relative to other parts of the kidney, making it susceptible to hypoxic episodes.[2,11]

In the peri-operative period, renal ischaemia can be due to low cardiac output (CO) following cardiogenic shock.[2] Activation of the sympathetic nervous system (SNS) and the renin–angiotensin–aldosterone system (RAAS) due to a reduction in CO will cause systemic vasoconstriction, thus decreasing renal blood flow and leading to a low GFR.[2] The major factors associated with AKI post cardiac surgery are a reduced functional reserve and peri-operative renal ischaemia.[17]

Inflammation and oxidative stress

Renal tissue hypoxia that results from renal hypo-perfusion due to a decrease in CO and GFR is responsible for the inflammatory process and oxidative stress that follows.[15] Endothelial cellular injury as a result of ischaemia initiates tissue inflammation.[15] Selectins facilitate the adhesion of leukocytes to the injured endothelium.[16] This promotes the cascade of an inflammatory response.[18] Pro-inflammatory cytokines such as tumour necrosis factor-alpha (TNF-α), interleukins 6 and 8 (IL-6, IL-8) and chemotactic cytokines have been implicated in contributing to the response of local tissue ischaemia that results in maladaptive inflammatory tissue response.[18] Neutrophil and monocyte/lymphocyte ischaemia-induced kidney damage has also been described. This inflammatory cascade eventually results in dysfunction of the renal endothelium nitric oxide system, which is important in the renal oxygen supply.[16]

Nephrotoxins

Cardiac surgical patients are exposed to a variety of nephrotoxic agents in the peri-operative period. These may include drugs in the form of prescription medications such as antibiotics, antihypertensive agents, diuretics, non-steroidal anti-inflammatory agents (NSAIDS) and radiocontrast agents used during diagnostic medical procedures.[5,14]

Aminoglycosides and beta (β)-lactam antibiotics are the two groups of agents that have been implicated the most in causing acute interstitial nephritis, leading to drug-induced AKI.[2,5] These antibiotics can also cause direct injury to the kidneys.[2]

Hypertension has been shown to be one of the pre-operative risk factors of AKI in patients presenting for cardiac surgery.[11] Fuhrman and Kellum[2] have linked hypertension-related AKI to the use of angiotensin-2-receptor blocking agents (ARBs), which inhibit renal efferent arteriolar vasoconstriction in the pre-operative period.[2] Patients on ARBs and diuretic agents have an increased risk of hypovolaemia, which can worsen renal failure.[14]

Randomised control trials have shown the prophylactic use of loop diuretics, such as furosemide, to be ineffective and harmful when used in the peri-operative period in patients scheduled for cardiac surgery.[19-21] As part of their recommendations, Kellum,[2] Lameire[5] and the KDIGO AKI guideline work group[5] advised against the use of furosemide as a prophylactic agent in preventing AKI, and to avoid the use of diuretic agents in treating AKI.

NSAIDs have also been proven to worsen renal function in susceptible groups of patients.[14] Exposure to radiocontrast agents in the peri-operative period contribute to the risk of contrast-induced nephropathy and should ideally be avoided.[5,14]

Metabolic and neurohormonal activation

Cardiac surgery stimulates the SNS and the hypothalamic pituitary adrenal axis.[22] This activation results in the release of neurohormonal agents, including adrenaline and noradrenaline from the adrenal glands.[23] Zhang *et al.* reported that during cardiac surgery with CPB, plasma concentrations of adrenaline and noradrenaline reach peak levels.[24] The high plasma concentrations of these endogenous hormones give rise to erratic haemodynamic conditions that contribute to intra-operative renal injury.[22] This increase in sympathetic tone has led to the advocacy of the use of alpha-2-adrenergic agonists such as dexmedetomidine and clonidine to reduce the incidence of AKI.[22,25]

Genetics

A genome-wide association study (GWAS) for AKI after CABG surgery was performed in 2015 by Stafford-Smith and colleagues.[26] They discovered that other than the previously reported nine

loci of single nucleotide polymorphisms (SNP) related to renal function, there are two new loci that are specifically associated with an increased risk in AKI following cardiac surgery.[26] This discovery potentially increases the curiosity in researchers to further investigate the relationship between AKI and cardiac surgery at a genetic level.

Risk factors

The risk factors associated with AKI in this patient population can be grouped into patient-, surgery- and anaesthesia-related factors.[11] Risk factors associated with CSA-AKI can also be classified into non-modifiable and modifiable risks, enabling the identification of high-risk patients with modifiable risk factors that can be optimised for improved outcomes.[27] For the purposes of this review, the latter will be discussed.

Modifiable risk factors

The following modifiable risk factors will be discussed: the duration of CPB time, miniaturised extracorporeal circuit (mini-CPB), hypothermia, on-pump versus off-pump techniques, anaemia and blood transfusion, which contribute to the increased risk of AKI following cardiac surgery.[1,28]

Duration of CPB

CPB has been reported to induce systemic inflammatory response syndrome (SIRS), which is a mechanism related to the development of AKI in cardiac surgery patients.[1]

In a 2012 meta-analysis by Kumar *et al*.,[29] nine studies were included, resulting in a cohort of 12 466 patients, where a total of 756 patients developed AKI following cardiac surgery, correlating to longer durations of CPB.[29] Similarly, Mao *et al*.[1] had indicated a strong association between cardiac surgery-related AKI with longer CPB times. Mini-CPB has been found to offer benefits of improved renal function following cardiac surgery.[1] It led to a lesser inflammatory response with reduced haemodilution when compared to the standard CPB systems.[1] Benedetto *et al*.[30] investigated the occurrence of AKI when using the mini-CPB to that of the conventional CPB in patients for planned CABG surgery and showed that in patients where the mini-CPB was used, there were fewer reported cases of cardiac surgery-associated AKI compared to the conventional CPB.[30]

Hypothermia

During cardiac surgery, patients are often cooled down to systemic temperatures below 32°C allowing longer periods of decreased blood flow.[1] In a meta-analysis of 19 randomised, controlled trials with 2 218 patients, therapeutic hypothermia was not seen to prevent the development of AKI or the requirements for RRT.[31]

It has been postulated that the process of rewarming the patient post cardiac surgery could be one of the reasons related to increased ischaemia and reperfusion injury to the kidneys.[32] This hypothesis was tested in a study by Boodhwani *et al*.[32] on the effects of mild hypothermia and rewarming on renal function following CABG surgery. In this randomised control trial, patients undergoing elective CABG surgery were assigned to two groups. In the first group, patients were cooled down to a temperature of 32°C during CPB and then randomly assigned to be rewarmed to 34°C or 37°C. Results showed elevated serum creatinine levels in patients who were rewarmed to 37°C. They concluded that rewarming to 37°C should be avoided as it contributed to postoperative renal injury.[32]

On-pump versus off-pump technique

CPB is implicated in inducing a SIRS response that causes AKI related to cardiac surgery.[1, 33] Off-pump coronary artery bypass (OPCAB) induces less SIRS response when compared to on-pump CABG surgery.[34] Better renal perfusion and decreased systemic embolisation have been found.[1] There is still however conflicting evidence in the current literature when comparing these two techniques, with some authors showing that OPCAB is superior to the on-pump technique, while other authors have shown no variation.[35-37]

Anaemia

In AKI, peri-operative anaemia contributes to a decrease in oxygen delivery to the renal tubules, therefore promoting oxidative stress, especially in the already compromised renal medulla.[38] The oxidative stress is as a result of the reduction in red blood cells, which also have an antioxidant function.[39] Anaemia is further worsened by cardiac surgery as cardiac output is further decreased, influencing renal perfusion pressures.[38] CPB-related complications resulting in poor platelet function combined with anaemia, which requires blood transfusion, was seen as a factor that contributed to the additional risk of AKI.[38]

Blood transfusion

The transfusion of packed red blood cells is not without complications. Koch *et al*.[40] showed that the duration of red blood cell storage can contribute to complications following cardiac surgery. They concluded that the transfusion of red blood cells older than two weeks was associated with an increased risk of postoperative cardiac surgery complications.

Structural and functional changes to red blood cells were shown to include the depletion of adenosine triphosphate (ATP) and 2,3 diphosphoglyrecate (2.3 DPG) in the red blood cell.[41] Alterations in the structural proteins of red blood cells made them less deformable and contributed to pro-inflammatory cellular states.[41] This abnormal state of the red blood cells causes injury to target organs such as the kidneys and impairs the necessary oxygen delivery.[38] Poor oxygen delivery to the kidneys causes an insult to the renal tissue, a phenomenon termed 'kidney attack',[42] resulting in ischaemic injury.[16]

Hypovolaemia

Hypovolaemia has been recognised as a significant risk factor in the development of AKI following cardiac surgery.[5] A patient's volume status plays an important role in the peri-operative period as it is related to CO.[1] A low CO causes activation of the SNS which ultimately stimulates the RAAS, thus resulting in renal vasoconstriction.[1] The choice between crystalloids and colloids for intravascular volume expansion is still a topic of debate.[5]

Diagnosis of AKI

The kidneys receive 20% of the heart's CO.[43] A reduction in renal blood flow, whether generalised or localised, can cause a decrease in GFR, thus resulting in AKI.[15] GFR is used

commonly in the medical field as a surrogate measurement of global kidney functioning.

The diagnosis of CSA-AKI has evolved with time. Ronco[44] described what she calls the 'evolution of AKI diagnostic syntax', as shown in Fig. 1. She illustrated how between the years 1950 and 2016, the diagnosis of AKI had evolved from being a clinical finding to the development of molecular biomarker tests.[44] Studies have been performed that compare the differences in the diagnosis of AKI using serum creatinine levels to urine output volumes.

Criteria for diagnosis of AKI

In 2004, the Acute Dialysis Quality Initiative (ADQI) group described the RIFLE kidney disease criteria to classify the diagnosis of AKI.[45] An increase in a RIFLE score stage was shown to lead to an increase in the risk of death.[5] The RIFLE criteria utilised serum creatinine levels or GFR, and the patient's urine output to stratify them into risk, injury, failure and loss, or end-stage kidney disease grades according to the duration and loss of their renal function.[14] The RIFLE criteria are known to follow up the changes in renal function as observed over a period of seven days.[45]

The AKIN was subsequently developed as a modification of the RIFLE criteria by decreasing the threshold of serum creatinine levels in the first 48 hours of the diagnosis of AKI.[9] The AKIN further classified patients that require RRT into AKIN stage 3 and removed eGFR criteria as part of their work-up. Regardless of their differences, the RIFLE and AKIN classification criteria have proven to be useful in identifying patients with AKI.[9]

Table 1. The staging of AKI according to Kellum *et al.*[5]

Stage	*Serum creatinine*	*Urine output*
1	1.5–1.9 times baseline within 1 week or ≥ 0.3 mg/dl increase within 48 hours	< 0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	< 0.5 ml/kg/h for ≥ 12 hours
3	3.0 times baseline or increase in serum creatinine to ≥ 4.0 mg/dl or the initiation of RRT or in patients < 18 years, a decrease in eGFR to < 35 ml/min/1.73 m²	< 0.3 ml/kg/h for ≥ 24 hours or anuria for ≥ 12 hours

In 2013, the international AKI guideline work group brought together international experts from several medical specialities to produce a uniform definition and classification of AKI, as well as prevention strategies, pharmacological treatment and RRT guidelines.[5,46] This programme standardised the definition of AKI by bringing together the RIFLE and AKIN criteria and producing the KDIGO criteria for AKI.[46]

AKI by KDIGO is defined as an increase in serum creatinine of ≥ 0.3 mg/dl (or 26.5 µmol/l) for a period of ≤ 48 hours, or a rise in serum creatinine of ≥ 1.5-fold from the baseline, which is presumed to have occurred in the preceding seven days.[9] The diagnosis, evaluation and management of AKI, a KDIGO summary, divides AKI into three stages as illustrated in Table 1.[5] Table 2 demonstrates the differences in AKI diagnosis between the RIFLE score, and AKIN and KDIGO criteria.[7]

In the KDIGO criteria, patients with AKI can be diagnosed by solely using serum creatinine levels. This criterion has been shown to be a good predictor of 30-day mortality rate in patients undergoing cardiac surgery, who had displayed serum creatinine levels above the normal threshold pre-operatively.[7]

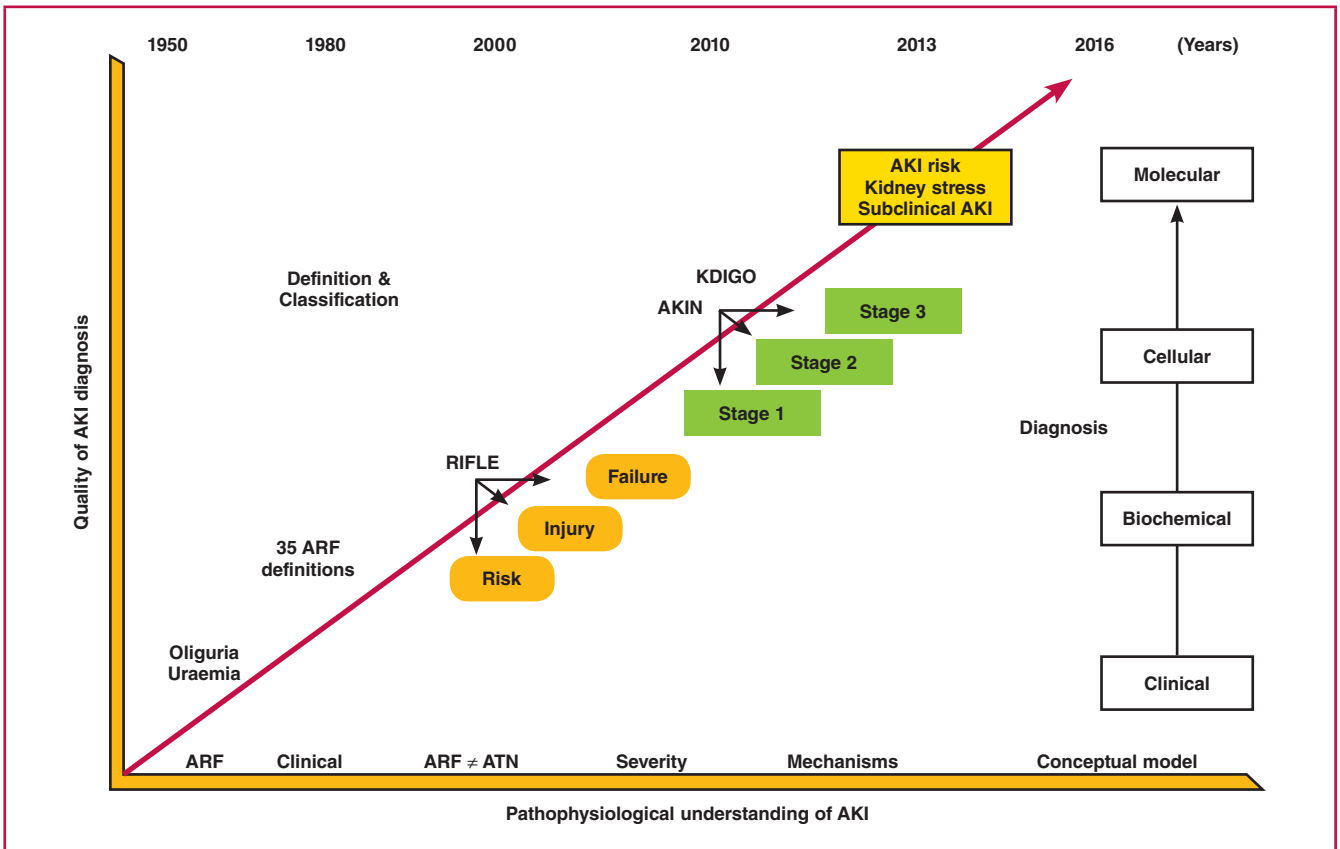

Fig. 1. The evolution syntax of AKI diagnosis by Ronco.[44]

Table 2. The classification and staging of the RIFLE, AKIN and KDIGO criteria as modified by Machado *et al*.[7]

Class	*RIFLE SCr or GFR*	*Stage*	*AKIN SCr*	*Stage*	*KDIG0 SCr*
Risk	Increases Scr X 1.5 or GFR decrease > 25% (within 7 days)	1	Increase in SCr ≥ 0.3 mg/dl or ≥ 150–200% (1.5–2-fold) from baseline (within 48 hours)	1	Increase in SCr by ≥ 0.3 mg/dl within 48 hours or increase in SCr 1.5–1.9 times baseline, which is known or presumed to have occurred within the previous 7 days
Injury	Increase Scr X 2.0 or GFR decrease > 50%	2	Increase in SCr to more than 200 to 300% (> 2–3-fold) from baseline	2	Increase in SCr to 2.0–2.9 times baseline
Failure	Increase Scr X 3.0 or GFR decrease > 75% or SCr ≥ 4.0 mg/dl or acute increase ≥ 0.5 mg/dl	3	Increase in SCr to more than 300% (> 3-fold) from baseline or SCr ≥ 4.0 mg/dl with an acute increase of at least 0.5 mg/dl or the initiation of renal replacement therapy	3	Increase in SCr to 3.0 times baseline or increase in SCr to ≥ 4.0 mg/dl or initiation of renal replacement therapy
Loss	Persistent acute renal failure = complete loss of kidney function > 4 weeks				
End-stage kidney disease	End stage of kidney disease (> 3 months)				

The use of serum creatinine levels in diagnosing AKI is not without its limitations. Inconsistencies still arise in the application of the diagnostic criteria and not only for the KDIGO criteria but also for the RIFLE score and AKIN criteria.[5] Creatinine measurements require many hours and days to identify any evidence of renal injury, and at the same time, mild renal injury can be missed as the kidneys might still maintain normal GFR.[11] It is therefore evident that AKI is a continuum from initial injury to the kidneys, to the development of the disease and then eventual kidney failure.[44]

In the hope of increasing awareness about the mortality and morbidity burden of AKI among clinicians, Kellum *et al*.[42] introduced a new concept known as 'kidney attack'. They proposed five steps that are important in improving outcomes in patients with AKI.[42] The first two steps offer a window period to intervene and possibly prevent further injury. They are known as the risk-assessment and early-detection steps. The other steps are early management, organ support and the recovery phase.[42]

When the initial attack occurs to the kidneys, molecular changes follow, which result in cellular damage. This leads to a variety of cellular markers known as biomarkers to be expressed and released by cells.[47] Clinical evidence has proven that biomarkers are present two days prior to the development of AKI,[48] therefore allowing for the subclinical diagnosis of renal injury.[44] This demonstrates that cellular and molecular biomarkers have the potential to be superior during the early diagnosis of AKI.[44]

Biomarkers in the diagnosis of AKI

The ADQI working group recommended the use of renal injury biomarkers in the diagnosis of AKI to supplement the RIFLE and AKIN scores.[49]

Neutrophil gelatinase-associated lipocalin (NGAL)

NGAL is a biomarker that can be measured in both the urine and plasma.[47] It is an acute-phase reactant protein released by inflammatory cells as well as leukocytes and epithelial cells of the loop of Henle and the collecting ducts of the renal tubules.[47] Urinary NGAL was shown to be superior to plasma NGAL in the early diagnosis of CSA-AKI.[1] Mishra *et al*.[50] found that urinary NGAL increased up to 25-fold within the first two hours following cardiac surgery, making it a highly sensitive and specific predictor of CSA-AKI.

It has however been shown that urinary NGAL levels can also be elevated in other inflammatory conditions, making it less specific.[47] In a study by Wagener *et al*.,[51] high levels of urinary NGAL correlated to the duration of CPB and aortic cross clamp.

Interleukin-18 (IL-18)

IL-18 is an inflammatory marker released by dendritic cells, monocytes and macrophages.[47] Urinary IL-18 was shown to peak six hours post cardiac surgery.[3] Urinary IL-18, together with NGAL and kidney injury molecule (KIM-1), are less sensitive and less specific in patients with co-morbid disease.[47]

Cystatin C

Cystatin C is a low-molecular weight protein released by all the nucleated cells of the body, and its levels can be measured in both the urine and plasma.[47] It is an inhibitor of cysteine proteases,[52] and an early diagnostic biomarker of AKI.[47] Cystatin C is freely filtered at the glomerulus, which renders it an appropriate marker for GFR.[52,53] This biomarker has been researched in the paediatric population admitted for cardiac surgery.[52,53] It was demonstrated by Hassinger *et al*.[53] to be a good early predicter of AKI after CPB in children.[53]

Plasma cystatin C was shown to be more specific and sensitive in the early diagnosis of AKI compared to serum creatinine in infants undergoing cardiac surgery under bypass.[52] Cystatin C has however also been shown to be less specific and sensitive in patients with co-morbid diseases and sepsis.[54]

Insulin-like growth factor binding protein 7 (IGFBP-7) and tissue inhibitor of metalloproteinases-2 (TIMP-2)

Urinary IGFBP-7 and TIMP-2 are cell cycle-arrest proteins.[47] In a study assessing the risk of AKI in 50 patients who had cardiac surgery on CPB, both IGFBP-7 and TIMP-2 showed specificity and sensitivity in predicting AKI as early as four hours following surgery.[55] In a systematic review and meta-analysis by Liu *et al*.,[34] it was shown that these two biomarkers are reliable in the early detection of AKI in adult patients.[34] IGFBP-7 and TIMP-2 have emerged as novel biomarkers of AKI compared to the others, as cell cycle arrest is considered the pathophysiological mechanism in the development of AKI.[47]

In 2014 the Food and Drug Administration (FDA) approved the marketing of the nephrocheck test, a laboratory instrument that detects the presence of IGFBP-7 and TIMP-2 proteins in the urine of patients at risk of developing AKI following cardiac surgery.[56] This apparatus is the first of its kind (Fig. 2). The amount of measured proteins provides an indication of

Fig. 2. Nephrocheck (TIMP-2*IGFBP7) test, an FDA-approved laboratory test that measures urinary levels of cell cycle-arrest proteins to identify patients at risk of developing AKI following cardiac surgery.[56]

renal tubular stress prior to tubular damage.[57] The results of the test provide a score that is based on the individual's risk of developing AKI within 12 hours of cardiac surgery.[56] In a prospective cohort study by Oezkur *et al*.,[57] the nephrocheck test was proven to be a strong predictor of postoperative CSA-AKI.[57]

Management of AKI

A reduction in the incidence and long-term renal outcomes of patients with CSA-AKI requires management that not only focuses on treating established disease, but to identify peri-operative risks as well.[58,59] This follows a complex route, given the multifactoral pathogenesis of the disease process. The hallmark in managing CSA-AKI is modifying risk factors.[13] Peri-operative fluid management influences renal perfusion. A positive fluid balance has been shown to increase incidence of mortality,[5] while haemodynamic stability optimises renal perfusion, thus preventing AKI.[59] Several trials have proven that the use of diuretics has unfavourable outcomes and loop diuretics are reserved for cases of fluid overload, especially in mechanically ventilated patients.[5,59,60] Vasodilators such as dopamine and fenoldopam are not effective in the prevention of AKI.[59]

The use of nephrotoxic agents such as aminoglycosides, contrast media, NSAIDs and ARBs should be avoided where possible.[5,59]

As part of their recommendations, the KDOGO group suggests maintaining an adequate nutritional status and normoglycaemia in the peri-operative management of CSA-AKI. A total energy intake of 20 to 30 kcal/kg per day at any KDIGO stage, as well as a glucose level of not more than 8.3 mmol/l (149 mg/dl) is recommended.[5] The timing of RRT has been a topic of debate; however a recent meta-analysis showed that early initiation of RRT has its benefits. It demonstrated a reduction in 28-day in-hospital mortality rates of up to 58% when RRT was initiated within 24 hours following the diagnosis of CSA-AKI.[61]

Conclusion

CSA-AKI is a complex disease spectrum. The identification, prevention and modification of patient and surgical risk factors can assist in reducing cases and thus the disease burden. The diagnosis remains an area of challenge and the use of novel biomarkers seems to be more promising in identifying at-risk patients earlier than conventional methods, such as the use of serum creatinine levels and urine output measurements.

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