Perioperative Renal Protection

Dr.AL.Meenakshi sundaram

Dean
Government Theni Medical College
Theni, TamilNadu

Renal failure occurring around the time of surgery is a serious complication associated with considerable morbidity and mortality. Mostly and naturally it would be acute and hence prevention is better than cure in this setup. Appropriate perioperative strategies are required to protect renal function to optimize
patient outcome.

Renal dysfunction after surgery is often associated with multiple organ dysfunction syndrome and may increase mortality. The morbidity includes high risk of infection, prolonged intensive care unit and hospital stay, progression to chronic renal failure and dialysis-dependent end-stage renal disease (ESRD).

Various studies confirmed that patients undergoing cardiac and vascular surgery are at particular risk of developing per operative renal dysfunction

Definition of renal dysfunction

An international interdisciplinary collaborative group, the Acute Dialysis Quality Initiative (ADQI), has recently formulated a standard grading system for acute renal dysfunction. The term acute renal dysfunction encompasses the full range of abnormalities of renal function.

The acronym RIFLE defines three grades of increasing severity of acute renal dysfunction (R, risk; I, injury; F, failure) and two outcome variables (L, loss; E, end-stage) that are based on the change in serum creatinine or urine output

The RIFLE classification of acute renal dysfunction. GFR, glomerular filtration rate; UO, urine output; ARF, acute renal failure; ESRD, end-stage renal disease

Grade	Glomerular filtration rate Criteria	Urine output criteria
R, Risk	Serum creatinine increase: 1.5-fold; GFR decrease: >25%	UO <0.5 ml/ kg/h for 6 h
I, Injury	Serum creatinine increase: 2-fold; GFR decrease: >50%	UO <0.5 ml/ kg/ h for 12 h
F, Failure	Serum creatinine increase: 3-fold; GFR decrease: >75%; serum creatinine decrease: >350 µmol/litre (4 mg/dl) with acute increase >44 mmol/ litre (0.5 mg /dl)	UO <0.3 ml/ kg/ for 24 h or anuria for 12 h
L, Loss	Persistent ARF--complete loss of renal function for 4 weeks	
E, End -stage	ESRD--complete loss of renal function for 3 months	

Pathophysiology

The etiology of RF is classically divided into pre-renal, renal and post-renal causes. The majority of cases of ARF in surgical and critically ill patients are because of intrinsic renal causes; acute tubular necrosis is the most common.

Acute tubular necrosis

A combination of microvascular and tubular injury contribute to the development of ATN. Intra-renal vasoconstriction because of local vasoactive mediators, activation of tubuloglomerular feedback, structural endothelial damage,and leucocyte activation all lead to microvascular damage.

Mechanisms of tubular injury include epithelial apoptosis and necrosis, tubular obstruction, and transtubular leak of glomerular filtrate. Inflammatory responses induced by renal ischaemia–reperfusion injury also play a significant role in the development of ATN.

Nephrotoxic agents

Nephrotoxic agents commonly used in perioperative patients include non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, aldosterone-receptor antagonists, i.v. radio-contrast agents, aminoglycoside and betalactam antibiotics, amphotericin B, and cyclosporin.

Cardiac and vascular surgery

1. Renal hypo-perfusion outside the limits of auto-regulation , particularly during cardiopulmonary bypass (CPB), is a major determinant of ATN.
2. The systemic inflammatory response syndrome (SIRS) triggered by major surgery results in cell-mediated and cytotoxic injury.
3. ATN may also be exacerbated by renal embolic injury(aortic Atheroma, air, lipid, and tissue)
4. Prolonged surgery produces haemolysis: renal excretion of haem derivatives may result in renal tubular injury.
5. Toxic injury from the administration of nephrotoxic drugs
6. Non-elective cardiac surgery shortly after pre-operative cardiac catheterization increases the risk.(both the radiocontrast load and surgery itself).

Risk factors

The incidence is increasing because of the increasing age of the surgical population and the performance of more complex surgery.

Risk factors for perioperative acute renal failure. IABP, intra-aortic balloon pump; CPB, cardiopulmonary bypass

Pre-operative factors	Intra-operative factors	Post-operative factors
Chronic disease Advanced age Female Sex Chronic renal disease Diabetes mellitus Chronic cardiac failure Aortic and peripheral vascular disease Chronic liver disease Genetic Predisposition **Acute conditions** Hypovolaemia Sepsis Preoperative IABP Multiple organ dysfunction syndrome Drug nephrotoxicity	**Type of surgery** Cardiac Aortic Peripheral vascular Non-renal solid organ transplantation **Cardiac surgery** Prolonged CPB time Combined procedures Emergency surgery Previous cardiac surgery **Aortic surgery** Aortic clamp placement Intra-operative contrast	**Acute conditions** Acute cardiac Dysfunction Haemorrhage Hypovolaemia Sepsis Rhabdomyolysis Intra-abdominal hypertension MODS Drug nephrotoxicity

Prevention

The identification of high-risk patients and the implementation of prophylactic measures are the goals of perioperative renal protection. Strategies to reduce the occurrence of renal injury

in patients without evidence of acute renal dysfunction are referred to as primary prevention. The avoidance of additional renal injury in the setting of established acute renal dysfunction is termed secondary prevention. Both non-pharmacological and pharmacological interventions may be considered.

Non-pharmacological strategies

These include intravascular volume expansion, maintenance of renal blood flow and renal perfusion pressure, avoidance of nephrotoxic agents, strict glycaemic control, and appropriate management of post-operative complications.

Intravascular volume expansion

Perioperative hypovolaemia should be rapidly corrected by volume expansion with i.v. fluids, whether occurring before, during or after surgery. The role of crystalloids compared with colloids for intravascular volume expansion remains unclear. There is no categorical study to document difference between albumin and 0.9% sodium chloride in terms of the risk of ARF. The renal effects of different colloids have not yet been fully elucidated. Albumin and gelatin appear to be safe in patients with normal renal function. The safety of hydroxyethyl starch solutions in the setting of established renal impairment has not been clarified. Recent evidence suggests that hydroxyethyl starch is associated with a higher incidence of ARF than Ringer's lactate in critically ill patients with severe sepsis.

The benefit of isotonic fluid expansion for the prevention of radiocontrast-induced nephropathy has been clearly demonstrated. However, the ideal composition of such fluid and the optimal rate of infusion have not been determined and should be individualized. Surgical patients receiving contrast will benefit from the use of the lowest possible volume of non-ionic, iso-osmolar contrast in conjunction with isotonic fluids.

Maintenance of renal blood flow and renal perfusion pressure

Maintenance of adequate renal blood flow and perfusion pressure involves both cardiac output and systemic arterial pressure. The initial approach should be intravascular volume expansion to reverse hypovolaemia. Inotropic and vasopressor therapy may then be initiated for the management of low cardiac output and systemic arterial hypotension, respectively. Despite historic concerns, norepinephrine is an excellent first-line vasopressor agent. There is no firm evidence to suggest that the drug compromises renal, hepatic, or gastrointestinal blood flow

when used to treat arterial hypotension. Vasopressin and terlipressin may be useful agents in the treatment of post-operative catecholamine-resistant vasodilatory shock. The optimal therapeutic target for systemic arterial pressure for renal protection has not been established. A minimum mean arterial pressure of 65–75 mm Hg is often targeted in clinical practice; however, a higher target may be necessary in patients with pre-existing hypertension.

Avoidance of nephrotoxic drugs

Minimizing perioperative exposure to nephrotoxic drugs is crucial in the prevention of renal dysfunction. The use of once-daily aminoglycoside dosing and the use of lipid formulations of amphotericin B have been demonstrated to lower the risk of nephrotoxicity associated with these drugs. There are concerns regarding the risk of renal injury associated with the antifibrinolytic agent aprotinin. Recent controversial evidence suggests that the use of aprotinin during coronary artery bypass graft (CABG) surgery may be associated with an increased risk of ARF requiring dialysis.

Glycemic control

Strict glycemic control using intensive insulin therapy improved survival and reduced the incidence of ARF requiring RRT. Perioperative hyperglycemia during cardiac and vascular surgery is associated with increased renal morbidity and overall mortality. But adequate scientific data are not available to show rigorous intra-operative glycemic control reduces this.

Cardiac surgery

Limiting the duration of CPB and maintaining adequate flow and perfusion pressure are of primary importance for renal protection. Other strategies available: 1.avoidance of excessive haemodilution 2.avoidance of red cell transfusion 3.extracorporeal leucodepletion 4. haemofiltration during CPB. Off-pump surgery may theoretically offer renal protection. New developments in minimally invasive surgical techniques that avoid ascending aortic manipulation may result in a reduction in renal morbidity.

Vascular surgery

Endovascular aneurysm repair (EVAR) is rapidly becoming the technique of choice for repair of abdominal aortic aneurysms, in preference to open surgical repair. Both techniques are

associated with worsening renal dysfunction in patients with pre-existing renal insufficiency. At present, it is not clear whether there is a significant difference between open repair and EVAR in terms of the occurrence of acute post-operative renal dysfunction in patients with CRF.

Post-operative complications

A number of post-operative complications are known to be associated with renal dysfunction. Prompt diagnosis and management of acute cardiac dysfunction, haemorrhage, sepsis, rhabdomyolysis, and intra-abdominal hypertension are essential to prevent the development of ARF. Rhabdomyolysis should be initially treated with aggressive intravascular volume expansion; diuretic therapy and urinary alkalinization may be considered. Abdominal compression syndrome caused by intra-abdominal hypertension is associated with diminished renal perfusion and may precipitate ischaemic ATN. Timely recognition of abdominal compression syndrome, by intra-vesical pressure measurement, followed by decompressive laparotomy may provide the optimal management of this condition.

Pharmacological strategies

The postulated pathophysiology of ATN suggests that perioperative interventions that optimize renal oxygen delivery may prevent ARF. However, pharmacological strategies that increase renal blood flow or decrease renal oxygen consumption have not proved successful.

Postulated pharmacological perioperative renal protection strategies

Drug	
Vasodilators	Dopamine agonists Adenosine antagonists Calcium-channel antagonists Angiotensin-converting enzyme inhibitors Sodium nitroprusside
Diuretics	Loop diuretics Osmotic diuretics
Natriuretic peptides	Atrial natriuretic peptide Urodilatin

	B-type natriuretic peptide
Antioxidants	N-acetylcysteine Corticosteroids
Other agents	Volatile anaesthetic agents Insulin-like growth factor-1 Erythropoietin Mesenchymal stem cells

Dopamine agonists

Dopamine acts on a number of different types of receptors. Renal blood flow is increased by dopaminergic receptor-mediated renal vasodilatation, beta-adrenoreceptor stimulation increases cardiac output, and alpha-adrenoreceptor increases renal perfusion pressure. A large multi-centre trial has demonstrated that low-dose dopamine does not prevent ARF.

Dopexamine is a synthetic dopamine analogue with beta adrenergic and dopaminergic effects but of questionable benefit.

Fenoldopam increases renal blood flow by its selective action on dopamine-1 receptors. At present, there is conflicting evidence regarding its usefulness as a potential renal protective agent.

Other renal vasodilator agents

Theophylline, calcium channel antagonists and angiotensin-converting enzyme inhibitors have not been shown to produce renal protection. A recent single centre trial demonstrated that sodium nitroprusside administration during the rewarming phase of CPB in patients undergoing CABG decreases the incidence of post-operative ARF.

Diuretics

In the setting of acute renal dysfunction, diuretics increase urine output by decreasing tubular re-absorption through several mechanisms. Increasing tubular flow maintains patency and prevents obstruction and back-leak. Loop diuretics inhibit tubular re-absorption in the loop of Henle´ whereas mannitol acts primarily
as an osmotic diuretic.

Natriuretic peptides

Natriuretic peptides induce a natriuretic and diuretic effect by increasing glomerular perfusion pressure and filtration. These peptides have shown conflicting results in the prevention of ARF.

N-acetylcysteine

Substantial evidence supports the prophylactic use of the antioxidant N-acetylcysteine (NAC), along with intravascular volume expansion, for the prevention of radio-contrast nephropathy.

Future strategies

Several experimental strategies are currently undergoing investigation including volatile anaesthetic agents, insulin-like growth factor-1, erythropoietin, and mesenchymal stem cells.

Conclusion:

In spite of so many trials and contradictive results per operative renal protection is still an enigma. But some practical strategie can be tried for perioperative renal protection

Preoperative
Optimize volume status, cardiac output, and systemic arterial pressure Withhold nephrotoxic drugs Maintain glycaemic control in diabetic patients Correct metabolic and electrolyte disturbances Delay surgery until recovery of acute renal dysfunction if possible Arrange pre-operative dialysis for dialysis-dependent patients Administer isotonic i.v. fluids and N-acetylcysteine for prevention of radiocontrast-induced nephropathy
Intraoperative

Optimize volume status, cardiac output, and systemic arterial pressure

Avoid nephrotoxic drugs

Consider maintaining tight glycaemic control in all patients

Cardiac surgery

Maintain adequate flow and mean systemic arterial pressure during CPB

Limit the duration of CPB

Avoid excessive haemodilution

Avoid red cell transfusion

Consider extra-corporeal leucodepletion

Consider haemofiltration during CPB

Consider off-pump coronary artery bypass surgery

Vascular surgery

Consider abdominal aortic endovascular aneurysm repair

Post-operative

Avoid nephrotoxic drugs

Maintain strict glycaemic control in all patients

Promptly treat acute cardiac dysfunction

Control haemorrhage

Manage sepsis aggressively

Recognize and treat rhabdomyolysis

Recognize and treat intra-abdominal hypertension

Provide appropriate organ support for multiple organ dysfunction syndrome

Institute renal replacement therapy for RIFLE grade F acute renal dysfunction

References:

1. Chertow GM, Levy EM, Hemmermeister KE, et al. Independent association between acute renal failure and mortality following cardiac surgery. Am J Med 1998; 104: 343–8

2. Hertzer NR, Mascha EJ, Karafa MT, et al. Open infrarenal abdominal aortic repair: the Cleveland Clinic experience from 1989 to 1998. J Vasc Surg 2002; 35: 145–54
3. Bellomo R, Ronco C, Kellum JA, et al. Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8: R204–R212
4. Kellum JA. Acute kidney injury. Crit Care Med 2008; 36: S141–5
5. Bonventre JV, Weinberg JM. Recent advances in the pathophysiology of ischemic acute renal failure. J Am Soc Nephrol 2003; 14: 2199–210
6. Thakar CV, Arrigain S, Worley S, et al. A clinical score to predict acute renal failure after cardiac surgery. J Am Soc Nephrol 2005; 16: 162–8
7. Aronson S, Fonte ML, Miao Y, et al. Risk index for perioperative renal dysfunction/failure: critical dependence on pulse pressure hypertension. circulation 2007; 115: 733–42
8. Wijeysundera DN, Beattie WS, Djaiani G, et al. Off-pump coronaryartery surgery for reducing mortality and morbidity: meta-analysis of randomized and observational studies. J Am Coll Cardiol 2005; 46: 872–82
9. Bown MJ, Norwood MG, Sayers RD. The management of abdominal aortic aneurysms in patients with concurrent renal impairment. Eur J Vasc Endovasc Surg 2005; 30: 1–11
10. Zacharias M, Gilmore IC, Herbison GP, et al. Interventions for protecting renal function in the perioperative period. Cochrane Database Syst Rev 2005; 3: CD003590
11. Friedrich JO, Adhikari N, Herridge MS, et al. Meta-analysis: low-dose dopamine increases urine output but does not prevent renal dysfunction or death. Ann Intern Med 2005; 142: 510–24
12. Renton MC, Snowden CP. Dopexamine and its role in the protection of hepatosplanchnic and renal perfusion in high-risk surgical and critically ill patients. Br J Anaesth 2005; 94: 459–67
13. Landoni G, Biondi-Zoccai GG, Tumlin JA, et al. Beneficial impact of fenoldopam in critically ill patients with or at risk for acute renal failure: a meta-analysis of randomized clinical trials. Am J Kidney Dis 2007; 49: 56–68
14. Bagshaw SM, Delaney A, Haase M, et al. Loop diuretics in the management of acute renal failure: a systematic review and meta-analysis. Crit Care Resusc 2007; 9: 60–8
15. Haase M, Haase-Fielitz A, Bagshaw SM, et al. Phase II, randomized, controlled trial of high-dose N-acetylcysteine in high-risk cardiac surgery patients. Crit Care Med 2007; 35: 1324–31
16. Hynninen MS, Niemi TT, Poyhia R, et al. N-acetylcysteine for the revention of kidney injury in abdominal aortic surgery: a randomized, double-blind, placebo-controlled trial. Anesth Analg 2006; 102: 1638–45
17. Stephen T Webb, J Stephen D Allen:Continuing Education in Anesthesia,Critical Care and Pain, BJA Vol 8, Number 5, 2008