

The patient with renal disease

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Abstract

The incidence of chronic renal failure is increasing throughout the world. The perioperative management of patients with chronic kidney disease (CKD) is complicated by both the underlying renal dysfunction, with associated disturbances of fluid and electrolyte homeostasis and altered drug clearance, and the presence of associated comorbid conditions. Preoperative assessment for these complex patients requires a multidisciplinary approach from anaesthetic, surgical and nephrology teams. Preservation of normal physiology along with prevention of further kidney injury are central to the management of patients with CKD. This article focuses on the perioperative care of patients, including pharmacological considerations of common medications used.

Keywords Chronic kidney disease; dialysis; renal failure

Introduction

Chronic kidney disease (CKD) is a progressive multisystem disease defined as either a glomerular filtration rate (GFR) of 60 ml/minute/1.73 m², markers of kidney damage, or both, for 3 months or more, irrespective of cause.

CKD is more prevalent in older individuals, women, racial minorities, and in people experiencing diabetes mellitus and hypertension. Although mortality has declined in patients with end-stage kidney disease (ESKD), the Global Burden of Disease (GBD) studies have shown that CKD has emerged as a leading cause of worldwide mortality.

It is, therefore, paramount that CKD is identified, monitored, and treated, and that preventative and therapeutic measures addressing CKD are systematically implemented worldwide.

Globally, the number of people receiving renal replacement therapy (RRT) exceeds 2.5 million and is projected to double to 5.4 million by 2030, although availability of RRT varies enormously between nations.¹

In the UK, there are approximately 3.25 million people living with CKD stages 3–5. A further 3.9 million people are estimated to have CKD stages 1–2. Together reaching a total of 7.2 million – more than 10% of the entire population.

The total annual economic burden of kidney disease in the UK is £7.0 billion, with £6.4 billion being direct costs to the

NHS – about 3.2% of NHS budgets. Despite increasing efforts for early detection and multimodal intervention, it is likely the demand for renal support and renal transplantation will increase significantly in future.²

CKD is defined by indicators of kidney damage imaging or proteinuria (commonly using albumin to creatinine ratio, ACR) and decreased renal function (below thresholds of GFR estimated from serum creatinine concentration). Current recommendations are to estimate GFR (eGFR) and transform it using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation³ (Table 1). The 2021 CKD-EPI equation is recommended for calculation of eGFR. This is more accurate than other equations such as the Modification of Diet in Renal Disease (MDRD) or Cockcroft and Gault equations for creatinine clearance. The inclusion of cystatin C in the CKD-EPI formula may provide a more accurate estimate of GFR without race.⁴

Functions of the kidney

- Excretion of waste and other foreign substance
- Regulation of blood ionic composition
- Acid–base balance
- Hormones: erythropoietin, renin, vitamin D₃
- Regulation of blood pressure
- Regulation of blood volume
- Maintenance of plasma osmolality
- Regulation of blood glucose level: gluconeogenesis

Aetiology

There are multiple causes of renal disease, briefly summarized in Table 2.

Pathophysiology

CKD causes multi-system dysfunction. This can be mediated by the primary disease process, the effects of uraemia, or both. An overview of possible effects is listed in Table 3.

Approach to the patient with renal disease

Preoperative

The aim of preoperative preparation of patients with CKD is to identify and optimize any pre-existing pathophysiology and risk factors to minimize the perioperative risk. This requires a multidisciplinary approach involving anaesthetists, surgeons and renal physicians. Table 4 lists some modifiable and non-modifiable factors.

History

Patients with CKD often have a complex medical history, take multiple drugs, and frequently have severe systemic complications from both the cause and effects of CKD. The aim is to identify and correct pathophysiology in order to minimize risk.

A full history should be taken including a review of other conditions and their management to date.

The cause and stage of a patient's CKD can be identified as well as any other co-morbidities.

What treatment is the patient receiving? Recent innovations in CKD therapy include sodium–glucose transport protein (SGLT)-2 inhibitors (even for non-diabetic patients) and finerenone, a

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Stages of chronic kidney disease (CKD)

CKD stage	Glomerular filtration rate (GFR) (ml/minute/m ²)	Description
1	≥90	Renal damage with normal GFR.
2	60–89	Renal damage with mild decrease in GFR
3A	45–59	Moderate decrease in GFR
3B	30–44	
4	15–29	Severe decrease in GFR
5	<15 (or dialysis)	Renal failure

Table 1

Causes of established renal failure

Aetiology	% total
Diabetes	30.4
Glomerulonephritis	13
Pyelonephritis	5.4
Hypertension	7.2
Polycystic kidney	6.9
Renal vascular disease	5.4
Other	16.8
Uncertain aetiology	14.8
Missing	10

Source: 2019 UK Renal Registry Report.

Table 2

mineralocorticosteroid receptor antagonist for CKD in diabetic patients. Ongoing trials will likely increase the range and number of drugs used to modify the progress of CKD.⁵

For patients with CKD stage 5, does the patient receive RRT? If this is the case, the following information is crucial:

- What modality of RRT (haemodialysis or peritoneal dialysis) do they receive and via what access (e.g. arteriovenous fistula, long-term haemodialysis catheter or a Tenckhoff peritoneal dialysis catheter)?
- When was RRT last provided, and when is it next due?
- What is the patient's 'dry weight'? This is the patient's normal weight following RRT and may be used to estimate their current fluid status.
- Is the patient formerly restricted in the volume of fluid they drink per day?
- What volume (if any) of urine does the patient produce per day?

Unless surgery is urgent, it is usually possible to provide RRT prior to theatre. For emergency procedures, the period for optimization may be short and may require critical care involvement. Transfer of the patient to a tertiary centre for renal care in the perioperative period may be required.

Investigations

Specific clinical investigations, in addition to those performed routinely in the preoperative period, should be guided by history and examination findings, urgency of surgery (immediate,

urgent, expedited, elective) and grade of surgery (minor, moderate, major or major), but may include:

- Complete blood count to evaluate for anaemia, thrombocytopenia.
- Coagulation studies if significant platelet dysfunction or recent heparinization.
- eGFR: allows modification of drug to compensate for reduced clearance.
- Renal panel: sodium, potassium, chloride, urea, creatinine, calcium, and bicarbonate levels.
- Arterial blood gas measurements for pH & acid-base balance
- Chest radiograph to evaluate fluid status, cardiomegaly or metastatic calcification.
- Electrocardiogram: may demonstrate the presence of established myocardial infarction, uraemic pericarditis or cardiac chamber hypertrophy.

Other tests

Resting or stress echocardiogram depending upon symptoms/signs of heart failure and ECG findings. Coronary angiography may be indicated but must be justified over the risk of contrast nephropathy. The use of preoperative cardiopulmonary exercise testing should be discussed with anaesthetic staff.

Drugs

The list of concurrent drugs must be comprehensively reviewed prior to theatre. Of particular note will be:

- antihypertensives, including β -blockers and angiotensin-converting enzyme (ACE) inhibitors
- hypoglycaemic agents: oral and injectables
- anticoagulants and antiplatelet agents
- chemotherapeutic agents and disease-modifying drugs, e.g. steroids, tacrolimus.

Intraoperative management

Haemodynamic management and fluid therapy: targeted approaches to perioperative haemodynamic management have been shown to improve patient and renal outcomes after high-risk surgery. Such goal-directed therapy strategies involve titrating fluid boluses and/or inotropic drugs to endpoints such as cardiac output (as provided by oesophageal Doppler, pulse contour waveform analysis, or dilutional techniques) or markers of end organ perfusion (such as arterial lactate). The composition of resuscitation fluids remains an area of controversy. There is

Clinical manifestations/complications of chronic kidney disease

Cardiovascular system

- Salt and water retention, hypertension, left ventricular hypertrophy
- Cardiomyopathy, congestive cardiac failure, and subclinical pulmonary oedema
- Accelerated atherosclerosis
- Altered lipoprotein metabolism
- Complications of arteriovenous fistula or shunts, e.g. heart failure, limb ischaemia, steal syndrome, pulmonary atheroembolism
- Uraemic pericarditis, pericardial effusion
- Cardiovascular autonomic neuropathy
- Calciphylaxis and vascular calcification
- Anaemia

Haemostasis and coagulation

- Uraemic thrombocytopenia, prothrombotic tendency/hypercoagulation and reduced fibrinolysis
- Vascular access thrombosis

Metabolic acidosis

- Bone resorption
- Negative nitrogen balance, muscle wasting, growth retardation

Musculoskeletal system

- Renal osteodystrophy
- Rhabdomyolysis after major surgery

Endocrine system

- Secondary and tertiary hyperparathyroidism, vitamin D deficiency, diabetes mellitus

Gastrointestinal system

- Delayed gastric emptying
- Anorexia, vomiting, reduced protein intake, malnutrition, reduced calcium absorption

Immune system

- Immunosuppression due to uraemia or drugs
- Infection and impaired wound healing

Fluid and electrolyte homeostasis

- Hyperkalaemia
- Volume overload
- Dehydration

Central nervous system

- Myoclonus, mental slowing, convulsions, coma
- Autonomic and peripheral neuropathy

Dialysis-related

- Sudden cardiac death, hypotension, arrhythmias
- Residual heparinization
- Dialysis disequilibrium syndrome, cerebral oedema
- Dialysis amyloidosis

Table 3

Risk factors for perioperative acute kidney injury

Patient	Operative	Pharmacological
Age	Emergency surgery	Non-steroidal anti-inflammatory agents
Male sex	Cardiac surgery	Angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers
Chronic kidney disease	Liver transplant surgery	Antibiotics (aminoglycosides, glycopeptides, etc.)
Chronic cardiac failure	Vascular surgery	Immunosuppressive drugs (calcineurin inhibitors)
Hypertension	Intraperitoneal surgery duration of surgery	Hydroxyethyl starch solutions
Chronic liver disease	Major haemorrhage	Radiocontrast agents
Diabetes mellitus	Sepsis	
Limited cardiovascular reserve	Blood transfusion	
	Intraoperative hypovolaemia and hypotension	

Table 4

currently no clear consensus regarding any superiority between albumin and crystalloids. For crystalloids, use of balanced salt solutions is preferred to 0.9% saline, which has been associated with development of hyperchloraemic acidosis, decreased renal blood flow (RBF), and increased risk of acute kidney injury (AKI).⁶

Maintaining adequate mean arterial pressure is essential for preserving renal function, both to ensure adequate renal perfusion pressure and to maintain the transglomerular pressure gradient for ultrafiltration. The use of norepinephrine has been shown to improve RBF, GFR, and urine output in experimental models of septic-AKI and clinical settings. Ensuring a mean arterial pressure (MAP) of >60–65 mmHg (>75 mmHg in patients with chronic hypertension) is recommended to prevent AKI, and a more individualized approach to intraoperative arterial pressure management should also be taken in this process.^{6,7}

Many potentially modifiable risk factors for AKI, in both cardiac and non-cardiac surgery, include haemodilution, haemoglobin level, intraoperative transfusion, hypotension, inadequate oxygen delivery, the use of diuretics, vasopressors, inotropes and cardiopulmonary bypass.^{6,7} Goal-directed intraoperative management to reduce the risk of postoperative AKI through optimizing renal perfusion.

Preoperative medications have also been extensively evaluated as both risk and protective factors for a variety of post-operative complications. For example, statins may have a protective effect against perioperative AKI.⁸

Avoidance of nephrotoxic drugs

These include non-steroidal anti-inflammatory drugs and certain antibiotics. Renal tubular toxicity may occur at high aminoglycoside concentrations, e.g. gentamicin. Acute interstitial nephritis can occur with other antibiotics, e.g. penicillin, cephalosporins and fluoroquinolones. For detailed information, it is advisable to use a relevant pharmacological formulary.

Treatment of urinary tract obstruction

A urinary catheter is essential to accurately monitor urine output and to rule out urinary tract obstruction. Other considerations include careful identification of the ureters in pelvic surgery. If post-renal obstruction is suspected an ultrasound of the renal tract and urgent urological opinion/intervention is essential.

Monitoring

Care must be taken to preserve existing arterio-venous fistulas. Blood pressure cuffs must be on the opposite arm or leg. Despite the potential for cardiovascular instability in these patients, arterial cannulation should also be avoided unless absolutely necessary to preserve arteries for future surgery.

Contrast-induced nephropathy (CIN)

CIN is widely defined as an increase in serum creatinine of more than 44 µmol/litre or 25% above baseline at 72 hours following the contrast load. Factors increasing the risk of CIN include pre-existing hypovolaemia and the use of high doses of iodinated, hyper-osmolar contrast media. These may cause pathological vasoconstriction in vulnerable kidneys. In susceptible patients, pre-hydration with IV crystalloid may be of benefit

and where possible, the use of the lowest possible volume of non-ionic, iso-osmolar radiocontrast. Multiple drugs have been used in an attempt to reduce CIN, with overall unimpressive results.⁹

Vascular access

Maintenance of vascular access patency is of vital importance in patients with stage 5 CKD on haemodialysis. The type of vascular access device may be temporary or more permanent depending on clinical need. Use of indwelling dialysis lines for anaesthesia should be cautioned against except in an emergency. Options for permanent access include native arteriovenous fistulae, arteriovenous grafts (AVG), and long-term catheters. Temporary vascular access includes: acute short-term non-cuffed catheters which may or may not be tunneled; long-term tunneled cuffed catheters; and subcutaneous port catheter systems. Complications related to vascular access include infection, stenosis, thrombosis and aneurysm.

Role of day case surgery

Despite the obvious associated comorbidity, end stage renal failure (ESRF) is not in itself a contraindication to ambulatory surgery. Especially combined with regional techniques, it is quite possible to discharge patients on the same day.

Timing of surgery

The treatment regime for patients already on RRT must be known. For haemodialysis, this is usually three times a week, whereas peritoneal dialysis is usually performed nightly. This will affect not only fluid and electrolyte balance but also drugs relying on renal clearance. It is not essential that patients are dialysed on the day of surgery, but there must be a clear plan for any adjusted timing of treatment.

Postoperative management

Renal dysfunction after surgery is associated with multiple organ dysfunction and contributes to excess mortality. Prompt diagnosis and management of acute cardiac dysfunction, haemorrhage, sepsis, rhabdomyolysis, and intra-abdominal hypertension are essential to prevent the development of AKI. Admission to critical care facilities may be suitable for patients with significant comorbidity and after major surgical procedures. Other organ systems should be supported as appropriate, and homeostasis maintained (e.g. diabetic control, electrolyte disturbances).

Pharmacological considerations: in patients with CKD, the effect of altered clearance, production and accumulation of active metabolites, and the risk of aggravating pre-existing kidney disease with drug administration must be considered. Dose adjustment is not usually necessary until the GFR is 50 ml/minute/1.73 m². CKD may influence both the pharmacokinetics and the pharmacodynamics of a drug (Table 5).

Perioperative drugs: many anaesthetic drugs reduce renal blood flow, GFR, and urine output and are excreted by the kidneys, either unchanged or as metabolites. Dosing may require adjustment for patients with significant renal impairment. For example, reduced seizure thresholds and altered protein binding properties for local anesthetics may reduce the maximum safe dose by 25%.

Pharmacokinetic changes due to chronic kidney disease (CKD)

Pharmacokinetic parameter	CKD changes	Impact on drug dosing
Absorption	Decreased intestinal metabolism and raised gastric emptying time and pH	Minimal: no dosing impact
Distribution	Decreased serum albumin, increase total body water	Moderate for some drugs, (phenytoin, theophylline, digoxin, aminoglycosides)
Metabolism	Decreased function of cytochrome P-450 enzymes ¹⁰ and drug transporter proteins. Decreased Phase I and II metabolism	Moderate for some drugs, (morphine, warfarin)
Excretion	Decreased glomerular filtration rate, impaired tubular secretion and reabsorption; increased proteinuria Decreased non-renal excretion: biliary, pulmonary and salivary	Major for some drugs with extensive renal elimination (cimetidine, sitagliptin, lisinopril) Biliary (erythromycin)

Minimal: no dosing impact anticipated, Moderate: some drugs require monitoring and dose adjustment, Major: accurate dose adjustment and drug monitoring is required.

Table 5

Analgesia: analgesic drugs, particularly opioids and related classes, may have significantly prolonged duration of action (e.g. codeine, dihydrocodeine, tramadol, morphine) or enhanced side effects (e.g. pethidine-, tramadol-related convulsions).

In general, management involves smaller doses, delivered less frequently, and with particular attention to sedative or depressant effects. It is also important that the doses may need to be further modified when the patient is undergoing dialysis or haemofiltration.

Summary

Patients presenting for surgery with renal insufficiency or failure present a significant challenge. It is imperative to understand the causes of, and prevent, further renal injury during the perioperative period. Universal acceptance of preoperative GFR calculations and new markers of CKD, such as cystatin C, will help to identify and risk stratify patients for a particular surgical procedure. Judicious fluid management, maintenance of normovolaemia, and avoidance of hypotension are priorities for the successful prevention of further renal injury. Existing drug management should be optimized, Nephrotoxic drugs should be identified and, if possible, discontinued before a patient with CKD undergoes elective surgery. The pharmacokinetic and pharmacodynamics changes must be taken into consideration with many drugs having reduced renal and non-renal clearance in CKD. ♦

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Practice points

- Acute kidney injury (AKI) is a common attributable cause of morbidity and mortality in the perioperative period
- Identification of risk factors and pre-emptive avoidance is preferable to reactive treatment of AKI
- Specific regard to appropriate drug administration, and to avoiding hypovolaemia and hypotension are key factors
- Complex patients (e.g. dialysis and pre-dialysis) should be managed in conjunction with the wider multidisciplinary team