

(REVIEW ARTICLE)



Pathology associated with kidney failure and anesthesia

Maria I. Dalamagka *

Department of Anesthesia, General Hospital of Larisa, Greece.

Magna Scientia Advanced Research and Reviews, 2024, 12(01), 106–109

Publication history: Received on 10 August 2024; revised on 26 September 2024; accepted on 28 September 2024

Article DOI: <https://doi.org/10.30574/msarr.2024.12.1.0149>

Abstract

Chronic kidney disease (CKD) is defined as either a glomerular filtration rate (GFR) of $<60 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$ for 3 months or more, irrespective of cause, or kidney damage leading to a decrease in GFR, present for 3 months or more. The damage may manifest as abnormalities in the composition of blood or urine, on radiological imaging, or in histology. CKD is classified into five stages depending on GFR, ranging from Stage 1 - normal GFR to Stage 5 - established renal failure. Patients with kidney disease undergoing surgery and anesthesia are at high risk for increased adverse events that include, cardiovascular complications and mortality, and further deterioration of renal function and development of acute kidney injury (AKI) due to perioperative injuries that are caused by hemodynamic instability, hypovolemia, or drug toxicity. Special consideration should be placed on preventing further deterioration of renal function as well as protection of existing renal function in patients with moderate to severe impairment from the effects of anesthetics and pain medications. Analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs) can contribute to a reduction of the residual renal function in CKD and should be avoided. Renal IR injury is a risk factor for acute renal failure and delayed graft function. Pathogenic factors for renal IR include, but are not limited to, the following: oxidative stress, inflammation, cellular necrosis, and apoptosis. Further clinical studies are required to address the optimal medication regimen that can be used for postoperative pain management in the more severe stages of CKD, including hemodialysis.

Keywords: Chronic kidney disease; GFR; Acute kidney injury; Renal function.

1. Introduction

More than 1.8 million people in the UK have a diagnosis of chronic kidney disease- CKD with around a further million thought to be undiagnosed. The estimated disease prevalence in the UK of CKD stages 3–5 is thought to be between 4.3% and 8.5% and this appears to be increasing. The global prevalence of CKD is 9.1%. In 2017, CKD was recognised as the 12th leading cause of death, responsible for 1.2 million deaths each year worldwide. Deaths attributable to CKD are set to increase further, with predictive modelling suggesting that by 2040 2.2 million people will die annually because of CKD. Chronic kidney disease is defined by the Renal Association as an abnormality of kidney structure or function that lasts more than 3 months. It only becomes evident when fewer than 40% of nephrons are functioning. Tests which enable diagnosis include electrolyte abnormalities due to tubular disorders, proteinuria (albumin to creatinine ratio (ACR) $> 3 \text{ mg/mmol}$), haematuria of renal origin, histological or radiological abnormalities in structure and abnormal function with resultant raised creatinine and/or cystatin C (eGFR $<60 \text{ ml/min/1.73 m}^2$) on more than two occasions 90 days apart. Glomerular filtration rate (GFR) is the internationally accepted measure to express renal function. However, GFR is not routinely measured because it is a complex procedure that involves measurement of plasma or urinary clearance of an exogenous marker such as inulin. More commonly, eGFR is used: this uses serum creatinine, cystatin, or both, age, and sex to mathematically derive the eGFR. According to the NIDDK, more than 30 million American adults may have CKD. Safe anesthetic management requires an understanding of CKD pathophysiology to prevent aggravation of pre-existing disease. Patients who are dialysis-dependent are at particularly high risk of requiring emergency medical and surgical interventions due to frequent presence of comorbidities such as acute

* Corresponding author: Maria I. Dalamagka

cardiovascular events, heart failure, vascular-access-related infections, endocarditis, bowel ischemia/bleeding, limb ischemia/necrosis, bone fractures, and cancer. Chronic kidney disease is associated with an increased risk of ischaemic heart disease. Most patients do not progress to end-stage renal failure but die as a result of fatal cardiovascular complications. Left ventricular hypertrophy can occur because of chronic volume overload, pressure overload, or both. Patients undergoing renal replacement therapy (RRT) may exhibit calciphylaxis, which describes accumulation of calcium in small blood vessels. Patients with end-stage renal failure were considered hypocoagulable. Acquired uraemic platelet dysfunction and thromboasthenia decrease platelet adhesion and increase vessel wall fragility, which contribute to bleeding diatheses [1-9].

1.1. Anesthetic management of patients in CKD

Depending on the patient's status and the surgical procedure, the preoperative evaluation may require close communication between the primary care physician, nephrologist, surgeon, and anesthesiologist to determine if a patient is optimized for surgery. The following assessments are recommended for patients with CKD: comorbid conditions, severity of CKD assessed by level of kidney function, complications related to level of kidney function, risk for loss of kidney function, and risk for cardiovascular disease. The risk for cardiovascular complications should be promptly evaluated. The patient should undergo a routine electrocardiogram. All present preoperative abnormalities, such as anemia, hyperkalemia, and metabolic acidosis, should be preoperatively corrected. A hemoglobin value of 10 g/dl is strongly recommended. Calcium chloride, insulin and dextrose, sodium bicarbonate, and resins can be used to correct hyperkalemia. If the patient is under dialysis treatment, the final dialysis prior to surgery should be scheduled 12-24 hours before surgery. The anesthetic management of patients suffering from CKD is complex. Due to delayed gastric emptying and neuropathy, there is risk of gastric acid aspiration. Gastric aspiration prophylaxis can be managed using sodium citrate, metoclopramide, anti-H₂ drugs, and rapid induction. Short-acting anesthetic drugs are recommended (propofol, remifentanyl, cisatracurium, vecuronium). Sevoflurane can deteriorate renal function by fluoride ion and compound A production, so isoflurane remains the preferred anesthetic inhalator agent. When selecting a neuromuscular blocking agent (NMBA) for use in patients with CKD, the anesthesiologist should consider the impact of renal impairment on the elimination of the drug, the potential for drug accumulation with incremental doses, and the production of active metabolites. To prevent postoperative residual curarization (PORC), long-acting NMBAs should be avoided. Opioids may be used, as they have no direct toxic effects on the kidney. They do, however, have an antidiuretic effect, and they may cause urinary retention. Patients with Stage 5 CKD who have undergone renal transplantation require immunosuppression. These drugs are usually given by the oral route. If enteral administration is inappropriate, then IV administration with dose adjustment will be required. Desflurane and isoflurane are metabolised to a minimal extent and there are no concerns regarding their use in CKD. Atracurium is the neuromuscular blocking agent (NMBA) of choice in patients with CKD. Its metabolism is unique. Atracurium undergoes ester hydrolysis and Hofmann degradation, both of which are independent of renal function. Cisatracurium can also be used in patients with CKD. It is predominantly eliminated by Hofmann degradation. Sugammadex has been used successfully in clinical research to reverse blockade from aminosteroid NMBAs in patients with severe renal impairment. Opioids have no direct nephrotoxic effects. They do have an antidiuretic effect, which may manifest clinically as urinary retention. Remifentanyl is not dependent on renal function for its elimination. An appropriate dose reduction of morphine and Fentanyl should be considered. Regional anaesthesia is a useful way of avoiding systemic drug accumulation and can be used as the primary anaesthetic technique, depending on the type of surgery. Central neuraxial blockade is not absolutely contraindicated, but consequent hypotension must be attended to in order to prevent worsening of renal perfusion. The ability of the kidneys to excrete water and sodium is impaired, causing difficulty in handling large fluid loads. As glomerular filtration decreases, sodium and water are retained and because of the increased hydrostatic pressure, fluid moves into the extravascular space leading to the clinical manifestations of fluid overload such as generalised and pulmonary oedema. Loss of nephron function results in renal retention of potassium. As GFR declines, the remaining nephrons adapt by increasing renal excretion and this works as a compensatory mechanism when the GFR is >15 ml/min. The tendency towards hyperkalaemia is ameliorated by instituting a low potassium diet and avoiding drugs known to cause hyperkalaemia [10-22].

2. Results and Discussion

Renal ischemia/reperfusion (IR) injury is a leading cause of preoperative acute kidney injury (AKI), which frequently complicates major vascular, cardiac, transplant, and liver surgeries. AKI has been shown to occur after some major surgeries. Novel interventions that protect against IR injury are needed to improve early graft function after kidney transplantation. Available general and local anesthetics, including third generation inhaled anesthetics, propofol, and amide-class local anesthetics, are effective and safe with a low incidence of side effects. Propofol, a widely used anesthetic, has shown potential as a novel organ-protective agent through its efficient membrane-targeted and cytoprotective effects. This is not surprising since lipid emulsions are major components of propofol, which

accumulating data show provide organ protective effects against IR injury in many organs, such as the heart, kidney, liver, and intestines. Sevoflurane and enflurane, did not cause deterioration of postoperative renal function in patients with preexisting renal issues. The metabolism of enflurane to inorganic fluoride during and after surgery did not cause a clinically significant level of renal disease or dysfunction. There is significant clinical evidence for volatile anesthetic-mediated organ protection. Sevoflurane preconditioning significantly lessened the postoperative rise of transaminase levels in patients undergoing liver resection. A short period of sevoflurane preconditioning in patients undergoing coronary artery bypass graft surgery was shown to significantly decrease both the release of a myocardial contractile dysfunction marker and the levels of plasma cystatin C concentrations. Ketamine ameliorate the upregulation of inflammatory pathways and reduction of metabolism caused by hypoxia. Thiopental pretreatment reduced renal IR injury induced by free radicals. Opioids may be used, as they have no direct toxic effects on the kidney. They do, however, have an antidiuretic effect. Patients with Stage 5 CKD who have undergone renal transplantation require immunosuppression. Nonsteroidal anti-inflammatory drugs (NSAIDs) can contribute to a reduction of the residual renal function in CKD and should be avoided.

Chronic kidney disease may result in a wide array of neurological manifestations including myoclonus, asterixis, chorea, uraemic encephalopathy and seizures. Autonomic neuropathy is common in patients with CKD because of decreased baroreceptor sensitivity, sympathetic overactivity and parasympathetic dysfunction. In haemodialysis, dialysate is pumped in a counter-current direction to blood flow and solutes equilibrate after diffusion across a semipermeable membrane. This too has associated complications, which include those related to vascular access, hypotension, arrhythmias and dysequilibration syndrome. Disease-specific treatment should be continued throughout the perioperative period where it is safe and practicable to do so. Certain medications such as ACE inhibitors remain controversial in the preoperative setting with no consensus regarding whether preoperative ACE inhibitor therapy is beneficial or harmful. Therefore, preoperative antihypertensive management should be considered on an individual basis and remains at the discretion of the anaesthetist. Should a patient require dialysis before surgery, liaise with the patient's specialist team.

3. Conclusion

The majority of research studies have focused on the non-anesthetic effects of propofol, such as its antioxidant, immunomodulatory, analgesic, and neuroprotective effects. It was found that propofol and ketamine were the 2 anesthetic agents that produced the least renal oxidative stress. AKI incidence, morbidity, and ICU stay were all found to be significantly lower for patients who received dexmedetomidine. Bupivacaine's ability to decreased cell damage suggests that it may have some protective effects against renal IR injury. Further clinical studies are required to address the optimal medication regimen that can be used for postoperative pain management in the more severe stages of CKD, including hemodialysis.

References

- [1] Livio M, Gotti E, Marchesi D. Uraemic bleeding: role of anaemia and beneficial effect of red cell transfusions. *Lancet*. 1982; 2:1013-1015.
- [2] Ocak G, Lijfering W.M, Verduijn M. Risk of venous thrombosis in patients with chronic kidney disease: identification of high-risk groups *J Thromb Haemost*. 2013; 11:627-633.
- [3] Títóff V, Moury H.N, Títóff I.B. Seizures, antiepileptic drugs, and CKD *Am J Kid Dis*. 2019; 73:90-101.
- [4] Craig R.G, Hunter J.M. Recent developments in the perioperative management of adult patients with chronic kidney disease *Br J Anaesth*. 2008; 101:296-310.
- [5] National Institute for Health and Care Excellence. Chronic kidney disease in adults: assessment and management, clinical guideline CG182 NICE, London, 2015.
- [6] Wright M, Southcott E, MacLaughlin H. Clinical practice guideline on undernutrition in chronic kidney disease. *BMC Nephrol*. 2019; 1620:370.
- [7] Gemmell L, Docking R.D, Black E. Renal replacement therapy in critical care *BJA Educ*. 2017; 17:88-93.
- [8] Bradley T, Teare T, Milner Q. Anaesthetic management of patients requiring vascular access surgery for renal dialysis *BJA Educ*. 2017; 17:269-274.
- [9] Lea-Henry T.N, Carland J.E, Stocker S.L. Clinical pharmacokinetics in kidney disease *CJASN*. 2018; 13:1085-1095.

- [10] Fukazawa Kyota, Lee H. Thomas. Volatile anesthetics and AKI: risks, mechanisms, and a potential therapeutic window *JASN*. 2014; 25:884-892.
- [11] R. G. Craig, J. M. Hunter. Recent developments in the perioperative management of adult patients with chronic kidney disease, *BJA: British Journal of Anaesthesia*, Volume 101, Issue 3, September 2008, Pages 296–310, <https://doi.org/10.1093/bja/aen203>.
- [12] Centers for Disease Control and Prevention. National Chronic Kidney Disease Fact Sheet, 2017. National Chronic Kidney Disease Fact Sheet, 2017.
- [13] Krishnan M. Preoperative care of patients with kidney disease. *Am Fam Physician*. 2002 Oct 15;66(8):1471-6, 1379. PubMed PMID: 12408421.
- [14] Domi R, Huti G, Sula H, Baftiu N, Kaci M, et al. From Pre-Existing Renal Failure to Perioperative Renal Protection: The Anesthesiologist's Dilemmas, *Anesth Pain Med*. 2016; 6(3):e61545. doi: 10.5812/aapm.32386.
- [15] Sellbrant I, Brattwall M, Jildenstål P, Warren-Stomberg M, Forsberg S, Jakobsson JG. Anaesthetics and analgesics; neurocognitive effects, organ protection and cancer reoccurrence an update. *Int J Surg* 2016; 34: 41–46.
- [16] Andrews DT, Royse C, Royse AG. The mitochondrial permeability transition pore and its role in anaesthesia-triggered cellular protection during ischaemia-reperfusion injury. *Anaesth Intensive Care* 2012; 40: 46–70.
- [17] L, Ruffenach G, Kararigas G, et al. Intralipid protects the heart in late pregnancy against ischemia/reperfusion injury via Caveolin2/STAT3/GSK-3 β pathway. *J Mol Cell Cardiol* 2017; 102: 108–116.
- [18] Li J, Motayagheni N, Barakati N, Eghbali M. Intralipid protects the heart in late pregnancy against ischemia/reperfusion injury by reducing cardiomyocyte apoptosis via Mir122 induction. *Circ Res* 2017; 119:A442.
- [19] Motayagheni N, Eghbali M. Complete reversal of xylazine-induced bradycardia with intralipid in female mice. *Circ Res* 2016; 119:A253.
- [20] Motayagheni N, Phan S, Eshraghi C, Eghbali M. Inhibition of leptin receptor abolishes intralipid-induced cardioprotection against ischemia-reperfusion injury. *Cardiology* 2016; 134: 241.
- [21] Motayagheni N, Eghbali M. Reversal of xylazine-induced bradycardia with intralipid. *Cardiology* 2016; 134: 431.
- [22] Motayagheni N. From bupivacaine to intralipid: Leading edge. *J Anesth Clin Res* 2016; 4: 00164.