Anaesthesia and Renal Disease

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• Occurrence
• Problems associated with renal disease
• Pre-operative assessment
• Anaesthetic options
• Prevention of post-operative AKI
### Staging of chronic kidney disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>eGFR (ml/min/1.73m$^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>CKD with normal GFR but other renal damage (e.g. haematuria, proteinuria)</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>II</td>
<td>Mild CKD and other kidney damage</td>
<td>60-89</td>
</tr>
<tr>
<td>III</td>
<td>Moderate CKD</td>
<td>30-59</td>
</tr>
<tr>
<td>IV</td>
<td>Severe CKD</td>
<td>15-29</td>
</tr>
<tr>
<td>V</td>
<td>Established ESRF</td>
<td>&lt; 15 or on RRT</td>
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</tbody>
</table>
Causes of renal failure

- Diabetes: 25.6%
- Glomerulonephritis: 14.0%
- Hypertension: 7.4%
- Polystic kidney disease: 6.7%
- Pyelonephritis: 6.6%
- Renal vascular disease: 6.1%
- Other: 17.7%
- Uncertain: 15.9%
• Median life years remaining for incident patients requiring RRT
  • Aged 25 - 29  18.5 years
  • Aged 75+  2.4 years

• Overall 5 year survival on HD  30%

• More than 50% die from cardiovascular causes
Risk of death attributed to cardiovascular causes associated with individual risk factors for anaesthesia

Renal failure (serum creatinine > 150 μmol.l\(^{-1}\)) on admission

- Age adjusted odds ratio: 4.23 (95% CI 1.36 - 13.2), p < 0.013
- cf previous MI: 4.04 (1.6 - 10.19)  p < 0.003
- angina: 3.55 (1.48 - 8.82)  p < 0.004
- heart failure requiring medical treatment: 2.80 (1.23 - 13.2)  p < 0.014

Systemic effects of renal failure

CVS

- LVH
- Accelerated atherosclerosis
- Hypertension
- Conduction abnormalities

Respiratory

- Pulmonary oedema
Effects of renal failure

- Metabolic acidosis
- Altered haemostasis
  - platelet dysfunction
  - prothrombotic tendency and reduced fibrinolysis
- Autonomic neuropathy
  - delayed gastric emptying
  - parasympathetic dysfunction
Effects of renal failure

- Fluid and electrolytes
  - volume overload
  - hyperkalaemia - exacerbated by acidaemia, insulin deficiency and acute β - blockade
Causes of hyperkalaemia in chronic renal disease

Exogenous administration

Transcellular shifts

acidaemia

insulin deficiency

hypertonicity

acute beta receptor blockade

Drug effects

suxamethonium, ACEI, ARBs, spironolactone, amiloride, β-blockers, NSAIDS, digoxin, spironolactone
Treatment of Hyperkalaemia

- Calcium
- Glucose and insulin
  - 50ml 50% glucose
  - 10-15 units soluble insulin

Magnesium?

CHECK BLOOD GLUCOSE
Pharmacology

- Altered volume of distribution
- Effects of acidaemia
- Elevated $\alpha_1$ amino glycoprotein
Volatile agents

- Sevoflurane - elevated fluoride and compound A levels

  Concluded no risk of renal toxicity with < 4MAC hours exposure.

  Nishiyama T, Aibiki M, Hanaoka K - Inorganic fluoride kinetics and renal tubular function after sevoflurane anaesthesia in chronic renal failure patients receiving haemodialysis
  Anesth Analg 1996;83: 574-7
  Compared sevo anaesthesia in CKD patients and patients with Normal renal function, found no evidence of deterioration in Renal function or accumulation of inorganic fluoride

  Need to avoid very low flow anaesthesia?

- Isoflurane and desflurane - not associated with renal toxicity
Volatile agents

- Possible reduction in renal injury by volatile anaesthetics, perhaps due to a reduction in inflammation

Lee HT, Ota-Setlik A, Fo Y, et al. - Protective effects of volatile anaesthetics against renal ischaemia - reperfusion injury in vivo

Anesthesiology 2004;101:1313-24
Induction agents

- Propofol - pharmacokinetics unaffected by CKD, although may need higher induction dose than normal controls (2.03 vs 1.39mg.kg$^{-1}$)

  Also time interval between cessation of propofol infusion and eye opening is significantly shorter in patients with renal failure than controls

- Thiopentone - increased plasma concentration due to reduced plasma protein binding so may need reduced dose
Neuromuscular blockers

- Cisatracurium: some advantage over atracurium in longer cases?
- Mivacurium: slower spontaneous recovery in renal failure
- Vecuronium: increased terminal half-life and prolonged duration of action
- Rocuronium: clearance reduced and duration of action significantly prolonged
- Neostigmine: clearance reduced, may get exaggerated parasympathetic effect especially if used with atropine
- Sugammadex: probably still effective since effect doesn’t rely on renal excretion of cyclodextran-relaxant complex
Analgesics

- Paracetamol - generally safe, although prolonged use associated with analgesic nephropathy
- NSAIDS - exacerbate hypertension, precipitate oedema, hyponatraemia and hyperkalaemia, increase risk of GI bleeds, increase risk of cardiovascular complications
- Morphine - morphine 6 glucuronide - t½ increased from 2 to 27 hours
- Fentanyl 7% excreted unchanged in urine
- Codeine and dihydrocodeine significantly prolonged half lifes
Analgesics

- **Alfentanil** - t½ and clearance unchanged but reduced protein binding increases free fraction, so reduce dose but not dosing interval

- **Remifentanil** - not dependent on renal function for elimination

- **Oxycodone** - hepatic metabolism to noroxycodone and oxymorphone which has analgesic activity and accumulates in renal failure - t½ increased from 2.3 to 39 hours

- **Tramadol** - 30% excreted unchanged by kidney, and active metabolite o-methyltramadol excreted by kidneys. Uraemia associated with lower seizure threshold
Regional anaesthesia

• Concerns about bleeding tendency and effects of hypotension on renal blood flow

• BUT - achieving a T4 - T10 sympathetic block may be beneficial in renal disease or patients at high risk of AKI


Guay J  The benefits of adding epidural analgesia to general anaesthesia: a meta-analysis

J Anesth 2006; 20:335-40
Regional anaesthesia

- AND no effect on RBF in healthy volunteers if maintain normotension and isovolaemia

What is the problem?

Biharic et al, Annals of surgery 2009

- 10500 patients, retrospective cohort study - AKI after major surgery worsens long term survival in patients with normal baseline renal function. May result directly from kidney failure or complications in other organ systems. Patients who completely recover after post-op AKI still have increases hazard ratio for death of 1.20 (95% confidence interval 1.10-1.31, p<0.001)

Awad & Okusa, Am J Physiol Renal Physiol 2007

- Increasing recognition that distant organ injury occurs after AKI and it is often failure of that organ which leads to death
Abelha et al, Nefrologia 2009

Retrospective study - AKI after non-cardiac surgery is an independent predictor for hospital mortality (odds ratio 3.12, 95% confidence interval 1.41 - 6.9, p<0.005)

Observational studies suggest that post-operative AKI increases duration of critical care and hospital stay

Associated organ dysfunction, electrolyte and acid-base disorders, and increased risk of fluid overload may in turn contribute to post-operative immobility, Infection and poor wound healing
## RIFLE staging of acute kidney injury

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<tr>
<th>Stage</th>
<th>GFR criteria</th>
<th>urine output criteria</th>
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<tbody>
<tr>
<td>Risk</td>
<td>Increased serum creatinine ×1.5 or GFR decrease &gt;25%</td>
<td>UO &lt;0.5ml/kg/hr for 6 hours</td>
</tr>
<tr>
<td>Injury</td>
<td>Increased serum creatinine ×2 or GFR decrease &gt;50%</td>
<td>UO &lt;0.5ml/kg/hr for 12 hours</td>
</tr>
<tr>
<td>Failure</td>
<td>Increased serum creatinine ×3 or GFR decrease &gt;75% or serum creatinine &gt; 353</td>
<td>UO &lt;0.5ml/kg/hr for 24 hours or anuria for 12 hours</td>
</tr>
<tr>
<td>Loss</td>
<td>Persistent AKI - complete loss of kidney function (ie dialysis dependent for &gt;4 weeks)</td>
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<tr>
<td>End stage kidney disease - dialysis dependent for &gt;3 months</td>
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### AKIN staging of acute kidney injury

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<th>Stage</th>
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<tr>
<td>1</td>
<td>Increase in serum creatinine of ≥26.4 μmol/l or increase to ≥150-200% from baseline</td>
<td>&lt;0.5 ml/kg/hr for &gt;6 hours</td>
</tr>
<tr>
<td>2</td>
<td>Increase in serum creatinine to &gt;200 to 300% from baseline</td>
<td>&lt;0.5 ml/kg/hr for &gt;12 hours</td>
</tr>
<tr>
<td>3</td>
<td>Increase in serum creatinine to &gt;300% from baseline (or serum creatinine ≥354μmol/l with an increase of ≥44μmol/l or receiving renal replacement therapy)</td>
<td>&lt;0.3 ml/kg/hr for 24 hours or anuria for 12 hours</td>
</tr>
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Progression of kidney disease

Three possible outcomes

1. Return to baseline function

2. Development of chronic kidney disease in previously normal kidneys

3. Accelerated progression of disease in patients with pre-existing kidney disease with fivefold increased risk for end stage disease
Who is at risk?

- Kheterpal et al, Anesthesiology 2009 - data from 152,244 operations in USA 2005:
  - ≥ 56 years
  - male
  - active congestive cardiac failure
  - presence of ascites
  - hypertension
  - emergency surgery
  - intraperitoneal surgery
  - pre-op creatinine > 106μmol/l
  - diabetes (tablet or insulin controlled)
Intra-operative management and haemodynamic optimisation

Optimisation of intravascular volume and cardiac output - Brienza et al, Crit Care Med 2009

- Meta-analysis of 20 RCTs (mostly using PAFCs) - high risk patients (emergency surgery, high revised cardiac risk index, ASA, age>60).

- Optimisation of CO or oxygen delivery reduced risk of perioperative AKI either started pre-op (odds ratio 0.70, 95% confidence interval 0.53-0.94, p=0.02), intra-op or early post-op (odds ratio 0.47, 95% confidence interval 0.27-0.81, p=0.006)

- Unable to comment on mortality
Peri-operative fluid therapy

Colloids v crystalloids

SAFE (Saline v Albumin Fluid Evaluation) - randomised in ICU - albumin safe but no better

VISEP severe sepsis 10% pentastarch v HES 200/0.5 v Ringer’s lactate - no difference in mortality but higher rare of AKI (34.9 v 22.8%) and more days on RRT for HES group
Peri-operative fluid therapy

Which crystalloid?

- Isotonic saline - hyperchloraemic acidosis - may be associated with hyperkalaemia and coagulation disturbances


- Waters et al Anesth Analg 2005; 100:1518-24 - isotonic saline v Ringer’s lactate for abdominal aortic reconstruction - no difference in renal function but saline group required greater amounts of blood component therapy
Peri-operative fluid therapy


- Small study renal transplant patients randomised to receive isotonic saline or Ringer’s lactate with serum creatinine as primary outcome at day 3. Trial halted early due to high incidence of hyperkalaemia (>6mEq/l) in saline group.
Intra-operative management and haemodynamic optimisation

- Maintain blood pressure appropriate for patient’s normal level
- Furosemide - no evidence of benefit (or harm)
- “Renal” dopamine - no value
- Mannitol aids diuresis but generally no value in non-cardiac surgery setting (but some value in reducing compartment pressures in rhabdomyolysis)
Intra-operative management – Pharmacological strategies

- **Theophylline** - reverses adenosine mediated renal artery vasoconstriction. No evidence of benefit.

- **Fenoldopam** - selective dopamine agonist. Conflicting evidence.

- **ANP** - Possible benefit in cardiac surgery. Reduced need for dialysis post-op in patients with early renal dysfunction.

- **N-acetylcysteine** - prevention of contrast induced nephropathy. No evidence of benefit in peri-operative or ICU setting.