Prescribing in CKD

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Measuring/Estimating Renal Function

**Table 3 - Formulas for estimating glomerular filtration rate**

\[
\text{Cockroft-Gault}^5 : \frac{(140 - \text{age}) \times [\text{BW}]}{72}
\]

\[
\text{Modified MDRD}^6 : 186.3 \times \frac{\text{SCr}^{-1.154} \times \text{age}^{-0.203} \times 0.742}{\text{if female}} \times 1.210 \text{ (if African American)}
\]

*Age, years; BW, kg; SCr, mg/dL.*

*An online calculator based on the modified MDRD equation can be found at [this link](#).*

Factors Affecting Prescribing

- Medications or their metabolites may cause nephrotoxicity
- Increased sensitivity
- Efficacy reduced
- Decreased excretion of parent drug and possible metabolites which have the potential to accumulate, causing toxicity.

Nephrotoxicity and AKI

- Avoided where possible
- Different mechanisms: compromise circulation, cause volume depletion or alter renal haemodynamics, direct glomerular insult

- ACEI ARB Renin Inhibitor Alopurinol Aminoglycosides Ciclosporin Cotrimoxazole Diuretics Lithium NSAIDs Penicillins PPIs Rifampicin Tacrolimus Vancomycin

**Current CKD Classification Based on Severity and Therapy**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (ml/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or ↑ GFR</td>
<td>≥ 90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mild ↓ GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR for transplant</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure D for dialysis</td>
<td>&lt; 15 (or dialysis)</td>
</tr>
</tbody>
</table>
Case 1
89yo male

- Background:
  - Hypertension
  - Hypercholesterolaemia
  - Atrial fibrillation
  - TIA x 2
  - Exsmoker
  - CKD III, baseline creat 135

- Medications:
  - Atorvastatin 20mg
  - Lercanidipine 10mg
  - Warfarin as per INR
  - PRN Paracetamol

- Functional decline in recent months with poor mobility.
- Changed from warfarin to abigatran 110mg bd at patient request
- Presents to ED following a 5 day diarrhoeal illness, with GCS 12/15
- NCCT: massive intracranial haemorrhage with midline shift
- Labs: AoCKI, sCreat 270
- Supportive care

NOACs

<table>
<thead>
<tr>
<th>Rivaroxiban (xarelto)</th>
<th>Dabigatran (pradaxa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor Xa inhibitor</td>
<td>Direct thrombin inhibitor</td>
</tr>
<tr>
<td>Use with caution in elderly</td>
<td>Use with caution in elderly</td>
</tr>
<tr>
<td>Use with caution CrCl 15-49</td>
<td>Use with caution CrCl 30-50</td>
</tr>
<tr>
<td>Dose reduce</td>
<td>Dose reduce</td>
</tr>
<tr>
<td>Ensure renal function stable</td>
<td>Ensure renal function stable</td>
</tr>
<tr>
<td>Contraindicated with CrCl &lt;15</td>
<td>Contraindicated with CrCl &lt;30</td>
</tr>
</tbody>
</table>

Case 2:
78 yo male

- Background:
  - CCF
  - Osteoarthritis
  - Hypercholesterolaemia
  - T2DM
  - CKD III, baseline sCreat 150

- Medications:
  - Metformin 1g bd
  - Gliclazide 90mg od
  - Aspirin 75mg od
  - Valsartan 160mg
  - PRN Ibuprofen 400mg bd

- Presents to ED weak and lethargic following 4 day history of diarrhoea and vomiting
- On arrival, BP 80/55mmHg, GCS 13/15
- Labs: Urea 48, Creat 505, K 6.2, PH 7.17, Lac 7

- AKI
- Hypoperfusion
- Volume depletion
- Loss of autoregulation (ACEi/NSAIDs)
- Lactic acidosis secondary to metformin accumulation
NSAIDs
- Decrease renal prostaglandin production
- AKI
- CKD
- Hypertension
- Oedema
- Hyperkalaemia/Type IV RTA
- Acute interstitial nephritis
- Analgesic nephropathy

Metformin
- Renally excreted
- Lactic acidosis rare complication
- Risk factors
  - Renal impairment
  - Tissue hypoperfusion
- Dosing recommendations based on CrCl

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Dosing Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-90</td>
<td>Max 2g daily</td>
</tr>
<tr>
<td>30-60</td>
<td>Max 1g daily</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Avoid</td>
</tr>
</tbody>
</table>

ACEi/ARB
- Induce efferent arteriolar vasodilatation through blockade of angiotensin II
- When renal perfusion is impaired -> decline in GFR
- Situations:
  - Hypotension
  - Decrease true or effective circulating blood volume
  - Critical RAS
- Measure eGFR prior to initiating ACEi and within 2 weeks after any dose increment
- Do not stop unless eGFR declines >25%
- Do not stop unless K >5.5 mmol/L –
  - consider low-dose K-wasting diuretic
  - dietician

Analgesics
- WHO Analgesic Ladder

1. Non-opioid +/- adjuvant
   - Paracetamol
   - NSAIDs
   - Adjuvant agents - gabapentin/pregabalin
   - Lidocaine Patch 5%
2. Weak opioid +/- non-opioid +/- adjuvant
   - Tramadol
   - Codeine
3. Strong opioid +/- non-opioid +/- adjuvant

Case 3
63yo female
- Background:
  - ESKD 2 IgAN
  - CRT 2012
  - Baseline sCreat 90
  - Asthma
- Medications:
  - Prograf 2mg bd
  - MMF 500mg bd
  - Prednisolone 5mg
  - PRN ventolin

Case 3
63yo female
- Unwell x 2 weeks. Recently prescribed augmentin for LRTI by GP. Nil improvement in symptoms.
- Attends ED - Pyrexial 38.9degrees. BP 105/60mmHg, HR 110bpm. Reduced air entry on auscultation. CXR right midzone consolidation.
- Commenced on clarithromycin and discharged home 3 days later after significant clinical improvement.
- Presents again 2 days later - tremors and nausea.
- Labs: Creat 225, K 6.3, HCO3 19, Tac 13
Immunosuppressants

- Triple therapy
  - Calcineurin Inhibitors
  - Antimetabolites
  - Steroids
- Brand specific and NOT interchangeable

CNI – prevent activation/proliferation of T calls
- Narrow therapeutic window
- Interactions
- Toxicity

CYP 450 3A4 Inducers
- DECREASE Tac/CyA levels -> increasing risk of rejection
  - Phenytoin/rifampicin/isoniazid

CYP 450 3A4 Inhibitors
- INCREASE Tac/CyA levels -> toxicity
  - Fluconazole/amiodarone/clarithromycin

Bowel Cleansing

- Safe:
  - lactulose
  - senna
  - movicol
  - microlax enemas.
- PO4 enemas should be avoided -> APN
  - Tubular and interstitial CaPO4 deposits
  - Induce AKI or CKD
  - Timing of insult varies
  - Risk factors

Vaccination

- All CKD patients should be offered annual vaccination with influenza vaccine
- All patients with:
  - eGFR <30ml/min/m2
  - and those at high risk of pneumococcal infection should receive pneumococcal vaccine unless CI.
- Revaccination -5 years.
- Live vaccines - appreciation of patients immune status important

Thank you