Specialty guides for patient management during the coronavirus pandemic

Clinical guide for acute kidney injury in hospitalised patients with COVID-19 outside the intensive care unit during the coronavirus pandemic

14 April 2020, Version 1

As doctors we all have general responsibilities in relation to coronavirus and for these we should seek and act on national and local guidelines. We also have a specific responsibility to ensure that essential care continues with the minimum burden on the NHS. We must engage with those planning our local response. We may also need to work outside our specific areas of training and expertise and the General Medical Council has already indicated its support for this in the exceptional circumstances we may face: www.gmc-uk.org/news/news-archive/how-we-will-continue-to-regulate-in-light-of-novel-coronavirus

Who is this guide for?
This guidance is for use by all professionals looking after inpatients with COVID-19 outside intensive care settings.

Background

• Acute kidney injury (AKI) in critically ill patients is multifactorial.
• There is little reliable UK data on the incidence and outcomes of patients with COVID-19 and AKI outside the ICU.
• At this stage we do not have a full understanding of the aetiology of AKI in COVID-19 and the pathogenic role of systemic inflammation, hypovolaemia or other COVID-19 related pathology (such as thrombotic microangiopathy) in its genesis.
• Volume status is critical in reducing the incidence of AKI but the balance between respiratory and kidney function can be challenging.
Preventing avoidable AKI should be a key goal of the management of hospitalised patients, to reduce demand for renal replacement therapy (RRT).

AKI should be promptly recognised and managed appropriately, within the limits of our current understanding.

AKI confers an adverse risk of mortality and its presence reflects underlying morbidity and current illness severity.

The presence of AKI should inform assessments of prognosis and in some cases the appropriateness of escalation of care.

It is critical that we build on existing processes and knowledge and carry on doing the things we currently do well.

This guidance summarises our existing approach to AKI at high level with key points in COVID-19 disease-specific management included.

Initial presentation

- Fluid status and biochemistry should be checked for all patients presenting to hospital with proven or suspected COVID-19.

- Dehydration is common on admission:
  - intravenous fluids are required in many cases
  - choice of fluids is based on biochemistry
  - hypernatraemia is common at presentation and may also develop later.

- Urea/creatinine ratio can be useful in assessing risk of dehydration.
  - a urea/creatinine ratio above 100 suggests dehydration
  - urea is measured in mmol/L and creatinine in µmol/L.

- A urea/creatinine ratio above 100 can be seen with a significant gastrointestinal bleed.

Risk, monitoring and detection of AKI

1. AKI is detected by monitoring changes in serum creatinine or reductions in urine output (KDIGO, https://kdigo.org/guidelines/).

- Use KDIGO definitions (serum creatinine and urine output criteria) to recognise AKI.

- The NHS England AKI detection algorithm will identify patients with changes in serum creatinine suggestive of AKI (AKI warning test). They need clinical review to determine whether AKI is present or not. All laboratories in England produce an AKI warning score based on KDIGO.
KDIGO AKI Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine</th>
<th>Urine output</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>( \geq 1.5-1.9 \text{ times baseline (7 days)} ) OR ( 26.5 \mu\text{mol/L increase (48 hrs)} )</td>
<td>(&lt; 0.5 \text{ ml/kg/hr for } 6-12 \text{ hrs} )</td>
</tr>
<tr>
<td>2</td>
<td>( \geq 2.0-2.9 \text{ times baseline} )</td>
<td>(&lt; 0.5 \text{ ml/kg/hr for } \geq 12 \text{ hrs} )</td>
</tr>
<tr>
<td>3</td>
<td>( \geq 3.0 \text{ times baseline} ) OR ( \text{increase in creatinine to } \geq 354 \mu\text{mol/L} ) OR ( \text{Renal replacement therapy} )</td>
<td>(&lt; 0.3 \text{ ml/kg/hr for } \geq 24 \text{ hrs} ) OR ( \text{Anuria for } \geq 12 \text{ hrs} )</td>
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</tbody>
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2. Patients at increased risk for AKI* should have serum creatinine, sodium, potassium, urea and bicarbonate checked regularly, with results reviewed and acted on (at least once every 48 hours, but in most cases daily).

3. Patients at increased risk for AKI* should have fluid balance monitored.

Patient isolation and staff personal protective equipment (PPE) may make it more difficult to monitor fluid balance.

- Fluid balance may be monitored by measuring urine output over defined time periods and/or daily body weight, in combination with accurate charting of oral and intravenous fluid intake.
- The preferred method of monitoring fluid balance should be determined locally. In the pandemic situation, decontamination of equipment may influence the choice of method.
- Urinary catheterisation is not routinely required in people with AKI but may be required if (1) AKI is progressing to stage 3 or (2) lower urinary obstruction is suspected.
* Patients with COVID-19 are at increased risk of AKI. The following are specific additional AKI risks in this patient cohort:

1. Those undergoing treatments that increase risk of AKI:
   - diuretic therapy that may have caused hypovolaemia
   - non-invasive ventilation.

2. Those with significant pre-existing risk factors for AKI in the setting of any acute illness:
   - chronic kidney disease (CKD) stage 3B or higher (eGFR <45mL/min/1.73m²)
   - diabetes mellitus
   - cardiac failure
   - history of AKI
   - drugs that increase the risks of AKI in the setting of hypovolaemia [non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists (ARBs), SGLT2 inhibitors).

**Investigation of AKI**

Investigations should take into account the most common causes of AKI in the setting of COVID-19: volume disturbance, low blood pressure hypoxia and sepsis. In addition, it will be more difficult to obtain some routine investigations (eg renal ultrasound).

1. All patients with AKI should have urinalysis; normally patients with AKI due to pure hypovolaemia would be not be expected to demonstrate significant haematuria or proteinuria (no more than 1+ blood or 1+ proteinuria).

2. Renal imaging may be harder to arrange; this may affect the imaging modality and the threshold for requesting tests. Imaging should be requested when clinical features that increase the probability of obstructive uropathy are present.** Imaging modality should depend on local arrangement, but non-contrast CT KUB is an acceptable equivalent if ultrasound is not possible.

** Features increasing probability of obstructive uropathy:** lower urinary tract symptoms:

- previous renal calculi
- age
- male gender
- long-term urethral catheter
- prostatic disease
- pelvic malignancy
- progressive AKI, non-responsive to first-line management strategies and without obvious cause.
Management of AKI
Fluid management in the setting of AKI and COVID-19:

- Assessment of volume status must take account of respiratory status as well as renal function. Perform a daily volume assessment.

- Where respiratory function permits, and when clinical assessment is consistent with volume depletion, administer a fluid challenge to determine if AKI is volume responsive [use crystalloids as per NICE clinical guideline CG174 (https://www.nice.org.uk/Guidance/CG174), either 0.9% saline or balanced crystalloids unless hypernatraemia]. **Note that patients with elevated body temperature and increased respiratory rate will have greater insensible fluid losses. In the UK climate, 0.5–1 litre/day is lost from the lungs and skin but several litres of sweat can be lost during fever or with exertion.**

- Review medications and stop or suspend those that may be contributing to AKI. **Note that diuretics are generally not nephrotoxic (unless in high dose) but can cause AKI due to hypovolaemia.**

- Do not administer IV fluids without a fluid assessment.

- If other causes of AKI are likely, then investigation and management should follow NICE clinical guideline NG148 (https://www.nice.org.uk/guidance/NG148).

- Potassium binders (patiromer and sodium zirconium) can be used as part of the emergency management of acute life-threatening hyperkalaemia alongside standard care [NICE technology appraisals (TA599 https://www.nice.org.uk/guidance/TA599) and (TA623 https://www.nice.org.uk/guidance/TA623)]. In a setting where resources for providing RRT may be stretched, these agents may have a role in delaying or preventing the need for RRT.

- A separate guideline has been issued for **RRT for AKI**.
**Medications in AKI** — full guidance on medicines optimisation is given at Think Kidneys and a useful reference source is The Renal Drug Database (https://renaldrugdatabase.com/).

**Consider withholding medicines that may worsen renal function in those with AKI:**
- contrast media
- NSAIDs
- ACE Inhibitors
- angiotensin receptor blockers
- diuretics in those who are volume depleted.

**Common medicines that may require dose adjustment or cessation in those with worsening renal function:**
- opiates
- gabapentin and pregabalin
- metformin
- antibiotics (eg penicillins, vancomycin, teicoplanin)
- anticoagulants
- digoxin
- gentamicin
- SGLT2/DPP-4

**Referral**
Referral pathways to escalate care of a patient with COVID-19 from a general ward setting may be to:
- ICU
- nephrology
- respiratory medicine for non-invasive ventilation.

Refer patients who have COVID-19 but are not at immediate risk of requiring ventilatory support and have AKI to nephrology when:
- stage 2 or 3 AKI is present
- hyperkalaemia (K ≥6.0mmol/L) if not responsive to medical intervention
- AKI is worsening despite initial management
- AKI is suspected due to systemic disease (eg vasculitis, connective tissue disease, multiple myeloma) or interstitial nephritis (drugs).
Advance care planning is also essential to identify those who would not benefit or who would prefer not to receive escalation of care to ICU. All patients with COVID-19 and AKI should have a clear escalation plan, including individualised treatment limits agreed and reviewed as necessary depending on the clinical situation.
1. Assessing AKI risk

One or more of the following risk factors present?

1. Those undergoing treatments that increase risk of AKI:
   - diuretic therapy
   - non-invasive ventilation.

2. Those with significant pre-existing risk factors for AKI in the setting of any acute illness:
   - chronic kidney disease (CKD) stage 3B or higher (eGFR <45mL/min/1.73m²)
   - diabetes mellitus
   - age >65
   - cardiac failure
   - history of AKI
   - drugs that increase the risks of AKI in the setting of hypovolaemia [non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists (ARBs)].

Suggested monitoring:

No

1. Measure U/Es every 24-48h
2. Standard hydration charts

Yes

Suggested monitoring:

1. Assess volume status daily with clinical examination.
2. Fluid balance monitoring (fluid balance chart/and or daily weights). If ambulant, measure lying and standing BP.
3. Measure U/Es daily.

Reduce AKI risk:

- Review medications and withhold those that may increase risk of AKI.
- Individualise volume status targets and avoid excessive volume depletion.
2. Responding to those who develop AKI

- Follow local AKI guidelines for investigation and management of AKI.
- Identify and manage sepsis as per local guidelines.

Clinical assessment consistent with volume depletion as the main cause of AKI?

- **No**
  - 3. Investigate for other causes of AKI, and perform urinalysis
  - 4. Renal imaging (ultrasound or non-contrast CT KUB) if following are present:
    - i) lower urinary tract symptoms
    - ii) previous renal calculi
    - iii) single kidney
    - iv) long-term urethral catheter
    - v) prostatic disease
    - vi) pelvic malignancy
    - vii) progressive AKI, non-responsive to first-line management strategies and without obvious cause.
  - 6. Do not administer IV fluids if blood pressure maintained and patient is not volume depleted.

- **Yes**
  - 5. Consider fluid challenge if respiratory function allows.

7. Review medications and withhold/avoid those that may worsen AKI.
3. Referral

Is it appropriate to refer patient for escalation of care?

Respiratory compromise plus AKI stage 2 or 3.

- ICU referral

Respiratory compromise plus AKI stage 1 or less and not considered at immediate risk of requiring invasive ventilation.

- Respiratory referral

No immediate risk of respiratory deterioration and one or more of:
- AKI stage 2-3 is present
- hyperkalaemia (K ≥6.0mmol/L)
- AKI is worsening despite initial management
- AKI with ≥1+ of blood and protein on urinalysis
- AKI is suspected due to systemic disease.

- Nephrology referral

AKI stage 1 alone does not normally require referral