Acute kidney injury: prevention, detection and management of acute kidney injury up to the point of renal replacement therapy

NICE guideline

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If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.

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Introduction

Acute kidney injury, previously known as acute renal failure, encompasses a wide spectrum of injury to the kidneys, not just kidney failure. The definition of acute kidney injury has changed in recent years, and diagnosis is now mostly based on monitoring creatinine levels, with or without urine output. Acute kidney injury is increasingly being seen in primary care in people without any acute illness, and awareness of the condition needs to be raised among primary care health professionals.

Acute kidney injury is seen in 13–18% of all people admitted to hospital, with older adults being particularly affected. These patients are usually under the care of healthcare professionals practising in specialties other than nephrology, who may not always be familiar with the optimum care of patients with acute kidney injury. The number of inpatients affected by acute kidney injury means that it has a major impact on the use of healthcare resources. The costs to the NHS of acute kidney injury (excluding costs in the community) are estimated to be between £434 million and £620 million per year, which is more than the costs associated with breast cancer, or lung and skin cancer combined.

There have been concerns that suboptimal care may contribute to the development of acute kidney injury. In 2009, the National Confidential Enquiry into Patient Outcome and Death (NCEPOD)[1] reported the results of an enquiry into the deaths of a large group of adult patients with acute kidney injury. This described systemic deficiencies in the care of patients who died from acute kidney injury: only 50% of these patients had received ‘good’ care. Other deficiencies in the care of patients who died of acute kidney injury included failures in acute kidney injury prevention, recognition, therapy and timely access to specialist services. This report led to the Department of

[1] National Confidential Enquiry into Patient Outcome and Death (2009) Acute kidney injury: adding insult to injury.

Health's request for NICE to develop its first guideline on acute kidney injury in adults and also, importantly, in children and young people.

This guideline emphasises early intervention and stresses the importance of risk assessment and prevention, early recognition and treatment. It is primarily aimed at the non-specialist clinician, who will care for most patients with acute kidney injury. The recommendations aim to address known and unacceptable variations in recognition, assessment, initial treatment and referral for renal replacement therapy. The inpatient mortality of acute kidney injury varies considerably, depending on its severity, setting (intensive care or not), and many other patient-related factors, but in the UK might typically be 25–30% or more. In view of its frequency and mortality rate, prevention or amelioration of just 20% of cases of acute kidney injury would prevent a large number of deaths and substantially reduce complications and their associated costs.

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations.

Patient-centred care

This guideline offers best practice advice on the care of adults, children and young people with or at risk of acute kidney injury.

Patients and healthcare professionals have rights and responsibilities as set out in the NHS Constitution for England – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If someone does not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent, the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.

If the patient is under 16, healthcare professionals should follow the guidelines in the Department of Health's Seeking consent: working with children. Families and carers should also be given the information and support they need to help the child or young person in making decisions about their treatment.

NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in Patient experience in adult NHS services.

If a young person is moving between paediatric and adult services, care should be planned and managed according to the best practice guidance described in the Department of Health's Transition: getting it right for young people.

Adult and paediatric healthcare teams should work jointly to provide assessment and services to young people with or at risk of acute kidney injury. Diagnosis and management should be reviewed throughout the

transition process, and there should be clarity about who is the lead clinician to ensure continuity of care.

Strength of recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also 'Patient-centred care').

Interventions that must (or must not) be used

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions that should (or should not) be used – a 'strong' recommendation

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer…') when we are confident that an intervention will not be of benefit for most patients.

Interventions that could be used

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values

and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

Identifying acute kidney injury in patients with acute illness

- Investigate for acute kidney injury, by measuring serum creatinine and comparing with baseline, in adults with acute illness if any of the following are likely or present:
  - chronic kidney disease (eGFR less than 60 ml/min/1.73 m^2)
  - heart failure
  - liver disease
  - diabetes
  - history of acute kidney injury
  - oliguria (urine output less than 0.5 ml/kg/hour)
  - limited access to fluid because of neurological or cognitive impairment or disability
  - hypovolaemia
  - use of drugs with nephrotoxic potential (such as non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycosides, angiotensin-converting enzyme [ACE] inhibitors, angiotensin II receptor antagonists [ARBs] and diuretics) within the past week, especially if hypovolaemic
  - use of iodinated contrast agents within the past week
  - symptoms or history of urological obstruction, or conditions that may lead to obstruction
  - sepsis
  - deteriorating early warning scores
  - age 65 years or over. **[1.1.1]**

- Investigate for acute kidney injury, by measuring serum creatinine and comparing with baseline, in children and young people with acute illness if any of the following are likely or present:
  - chronic kidney disease
  - heart failure

- liver disease
- history of acute kidney injury
- oliguria (urine output less than 0.5 ml/kg/hour)
- limited access to fluid because of young age, neurological or cognitive impairment or disability
- hypovolaemia
- use of drugs with nephrotoxic potential (such as NSAIDs, aminoglycosides, ACE inhibitors, ARBs and diuretics) within the past week, especially if hypovolaemic
- symptoms or history of urological obstruction, or conditions that may lead to obstruction
- sepsis
- deteriorating paediatric early warning score (PEWS)
- bloody diarrhoea
- symptoms or signs of nephritis (such as oedema or haematuria)
- haematological malignancy
- hypotension. **[1.1.2]**

Assessing risk factors in adults having iodinated contrast agents

- Before offering iodinated contrast agents to adults for emergency or non-emergency imaging, assess their risk of acute kidney injury. Be aware that increased risk is associated with:
  - chronic kidney disease (eGFR less than 60 ml/min/1.73 m^2)
  - diabetes but only with chronic kidney disease (eGFR less than 60 ml/min/1.73 m^2)
  - heart failure
  - renal transplant
  - age 65 years or over
  - hypovolaemia
  - increasing volume of contrast agent
  - intra-arterial administration of contrast agent.

  Ensure that risk assessment does not delay emergency imaging. **[1.1.6]**

Assessing risk factors in adults having surgery

- Assess the risk of acute kidney injury in adults having surgery. Be aware that increased risk is associated with:
  - emergency surgery, especially when the patient has sepsis or hypovolaemia
  - intraperitoneal surgery
  - chronic kidney disease (eGFR less than 60 ml/min/1.73 m^2)
  - diabetes
  - heart failure
  - age 65 years or over
  - liver disease
  - use of drugs with nephrotoxic potential in the perioperative period (in particular, NSAIDs after surgery). **[1.1.8]**

Ongoing assessment of the condition of patients in hospital

- When adults are at risk of acute kidney injury, ensure that systems are in place to recognise and respond to oliguria (urine output less than 0.5 ml/kg/hour) if the track and trigger system does not use urine output. **[1.2.2]**

Detecting acute kidney injury

- Monitor serum creatinine regularly[2] in all patients with or at risk of acute kidney injury. **[1.3.2]**
- Identify the cause of acute kidney injury and record the details in the patient's notes. **[1.3.3]**

Ultrasound

- Offer urgent ultrasound of the urinary tract to patients with acute kidney injury who:
  - have no identified cause of acute kidney injury, or
  - are at risk of urinary tract obstruction.

[2] The GDG did not wish to define 'regularly' because this would vary according to clinical need but recognised that daily measurement was typical.

Ensure that the imaging is performed within 24 hours of assessment. **[1.4.5]**

Referring to nephrology

- Discuss the management of acute kidney injury with a nephrologist or paediatric nephrologist as soon as possible and within 24 hours of diagnosis when one or more of the following is present:
  - a possible diagnosis that may need specialist treatment (for example, vasculitis, glomerulonephritis, tubulointerstitial nephritis, myeloma)
  - acute kidney injury with no clear cause
  - inadequate response to treatment
  - complications associated with acute kidney injury
  - stage 3 acute kidney injury
  - a renal transplant
  - chronic kidney disease stage 4 or 5. **[1.5.15]**

Information and support for patients and carers

- Give information about long-term treatment options, monitoring, self-management and support to people who have had acute kidney injury (and/or their parent or carer, if appropriate) in collaboration with a multidisciplinary team appropriate to the person's individual needs. **[1.6.2]**

1 Recommendations

The following guidance is based on the best available evidence. The full guideline [hyperlink to be added for final publication] gives details of the methods and the evidence used to develop the guidance.

All recommendations relate to adults, children and young people unless otherwise specified. In this guideline the term 'adults' is used to describe people who are aged 18 years or older, and 'children' those who are aged 11 years or younger (excluding neonates less than 1 month old). 'Young people' describes those who are aged 12 to 17 years.

1.1 Assessing risk of acute kidney injury

Identifying acute kidney injury in patients with acute illness

1.1.1 Investigate for acute kidney injury, by measuring serum creatinine and comparing with baseline, in adults with acute illness if any of the following are likely or present:

- chronic kidney disease (eGFR less than 60 ml/min/1.73 m^2)
- heart failure
- liver disease
- diabetes
- history of acute kidney injury
- oliguria (urine output less than 0.5 ml/kg/hour)
- limited access to fluid because of neurological or cognitive impairment or disability
- hypovolaemia
- use of drugs with nephrotoxic potential (such as non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycosides, angiotensin-converting enzyme [ACE] inhibitors, angiotensin II receptor antagonists [ARBs] and diuretics) within the past week, especially if hypovolaemic
- use of iodinated contrast agents within the past week

- symptoms or history of urological obstruction, or conditions that may lead to obstruction
- sepsis
- deteriorating early warning scores
- age 65 years or over.

1.1.2 Investigate for acute kidney injury, by measuring serum creatinine and comparing with baseline, in children and young people with acute illness if any of the following are likely or present:

- chronic kidney disease
- heart failure
- liver disease
- history of acute kidney injury
- oliguria (urine output less than 0.5 ml/kg/hour)
- limited access to fluid because of young age, neurological or cognitive impairment or disability
- hypovolaemia
- use of drugs with nephrotoxic potential (such as NSAIDs, aminoglycosides, ACE inhibitors, ARBs and diuretics) within the past week, especially if hypovolaemic
- symptoms or history of urological obstruction, or conditions that may lead to obstruction
- sepsis
- deteriorating paediatric early warning score (PEWS)
- bloody diarrhoea
- symptoms or signs of nephritis (such as oedema or haematuria)
- haematological malignancy
- hypotension.

Identifying acute kidney injury in patients with no obvious acute illness

1.1.3 Be aware that in people with chronic kidney disease and no obvious acute illness, a rise in serum creatinine may indicate acute kidney injury rather than a worsening of their chronic disease.

1.1.4 Ensure that acute kidney injury is considered as a possible diagnosis when a patient presenting with an illness with no clear acute component has any of the following:

- chronic kidney disease, especially stage 3B, 4 or 5, or urological disease
- new onset or significant worsening of urological symptoms
- symptoms suggesting complications of acute kidney injury
- symptoms or signs of disease affecting the kidneys and other organ systems (suggesting multi-system illness).

Assessing risk factors in adults having iodinated contrast agents

1.1.5 Before offering iodinated contrast agents to adults for non-emergency imaging, investigate for chronic kidney disease by measuring eGFR or by checking an eGFR result obtained within the past 3 months.

1.1.6 Before offering iodinated contrast agents to adults for emergency or non-emergency imaging, assess their risk of acute kidney injury. Be aware that increased risk is associated with:

- chronic kidney disease (eGFR less than 60 ml/min/1.73 m^2)
- diabetes but only with chronic kidney disease (eGFR less than 60 ml/min/1.73 m^2)
- heart failure
- renal transplant
- age 65 years or over
- hypovolaemia

- increasing volume of contrast agent
- intra-arterial administration of contrast agent.

Ensure that risk assessment does not delay emergency imaging.

1.1.7 Include the risks of developing acute kidney injury in the routine discussion of risks and benefits of the imaging procedure with the patient and/or their carer. Follow the recommendations on shared decision-making in Patient experience in adult NHS services (NICE clinical guidance 138).

Assessing risk factors in adults having surgery

1.1.8 Assess the risk of acute kidney injury in adults having surgery. Be aware that increased risk is associated with:

- emergency surgery, especially when the patient has sepsis or hypovolaemia
- intraperitoneal surgery
- chronic kidney disease (eGFR less than 60 ml/min/1.73 m^2)
- diabetes
- heart failure
- age 65 years or over
- liver disease
- use of drugs with nephrotoxic potential in the perioperative period (in particular, NSAIDs after surgery).

1.1.9 Include the risks of developing acute kidney injury in the routine discussion of risks and benefits of surgery with the patient and/or their carer. Follow the recommendations on shared decision-making in Patient experience in adult NHS services (NICE clinical guidance 138).

1.2 Preventing acute kidney injury

Ongoing assessment of the condition of patients in hospital

1.2.1 Follow the recommendations in Acutely ill patients in hospital (NICE clinical guideline 50) on the use of track and trigger systems to identify adults who are at risk of acute kidney injury because their clinical condition is deteriorating or is at risk of deteriorating.

1.2.2 When adults are at risk of acute kidney injury, ensure that systems are in place to recognise and respond to oliguria (urine output less than 0.5 ml/kg/hour) if the track and trigger system does not use urine output.

1.2.3 Use PEWS to identify children and young people admitted to hospital who are at risk of acute kidney injury because their clinical condition is deteriorating or is at risk of deteriorating:

- Record physiological observations at admission and then according to local protocols for given PEWS.
- Increase the frequency of observations if abnormal physiology is detected.

1.2.4 Use PEWS with multiple-parameter or aggregate weighted scoring systems that allow a graded response and:

- define the parameters to be measured and the frequency of observations
- include a clear and explicit statement of the parameters, cut-off points or scores that should trigger a response.

1.2.5 Use PEWS with multiple-parameter or aggregate weighted scoring systems that measure:

- heart rate
- respiratory rate
- systolic blood pressure

- level of consciousness
- oxygen saturation
- temperature
- capillary refill time.

1.2.6 When children and young people are at risk of acute kidney injury because of risk factors in recommendation 1.1.2, think about additional monitoring such as:

- measuring urine output
- recording weight twice daily to determine fluid balance
- performing biochemical analyses (lactate, blood glucose, urea, creatinine, electrolytes and blood gases).

Preventing acute kidney injury in adults having iodinated contrast agents

1.2.7 Offer intravenous volume expansion to adults having iodinated contrast agents if:

- they are at risk of contrast-induced acute kidney injury, or
- they have an acute illness.

Offer either isotonic sodium bicarbonate or 0.9% sodium chloride.

1.2.8 Consider oral or intravenous N-acetylcysteine[3] for adults having iodinated contrast agents and intravenous volume expansion.

1.2.9 Consider temporarily stopping ACE inhibitors and ARBs in adults having iodinated contrast agents if:

- they have chronic kidney disease, or

[3] Although this use is common in UK clinical practice, at the time of consultation (March 2013), N-acetylcysteine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

- they have heart failure.

1.2.10 Discuss care with a nephrology team before offering iodinated contrast agent to adults with contraindications to intravenous fluids if:

- they are at risk of contrast-induced acute kidney injury, or
- they have an acute illness, or
- they are on renal replacement therapy.

Monitoring and preventing deterioration in patients with or at high risk of acute kidney injury

1.2.11 Consider electronic systems to support clinical decision-making and prescribing, but ensure they do not replace clinical judgement.

1.2.12 When acquiring any new electronic clinical decision support systems (CDSS) or systems for electronic prescribing, ensure that any systems considered:

- can interact with laboratory systems
- can recommend drug dosing and frequency
- can obtain data on patient history and characteristics, including age, weight and renal replacement therapy
- can include alerts that are mandatory for the healthcare professional to acknowledge.

1.2.13 Seek advice from a pharmacist about optimising medicines and drug dosing.

1.2.14 Consider temporarily stopping ACE inhibitors and ARBs in patients with diarrhoea, vomiting or sepsis until their clinical condition has improved and stabilised.

1.3 Detecting acute kidney injury

1.3.1 Diagnose acute kidney injury, in line with (p)RIFLE[4], AKIN[5] or KDIGO[6], using any of the following criteria:

- a rise in serum creatinine (of 26 µmol/l or greater within 48 hours)
- a 50% or greater rise in serum creatinine known or presumed to have occurred within the past 7 days
- a fall in urine output (to less than 0.5 ml/kg/hour for more than 6 hours in adults and more than 8 hours in children and young people)
- a 25% or greater fall in eGFR in children and young people.

1.3.2 Monitor serum creatinine regularly[7] in all patients with or at risk of acute kidney injury.

1.3.3 Identify the cause of acute kidney injury and record the details in the patient's notes.

1.4 Identifying the cause of acute kidney injury

Urinalysis

1.4.1 Perform urine dipstick testing for blood, protein, leucocytes, nitrites and glucose in all patients as soon as acute kidney injury is suspected or diagnosed. Document the results and ensure that appropriate action is taken when results are abnormal.

1.4.2 Think about a diagnosis of acute nephritis and referral to the nephrology team when a patient with no obvious cause of acute kidney injury has urine dipstick results showing haematuria and

[4] Risk, Injury, Failure, Loss, End stage renal disease, (p) refers to the paediatric classification
[5] Acute Kidney Injury Network
[6] Kidney Disease: Improving Global Outcomes
[7] The GDG did not wish to define 'regularly' because this would vary according to clinical need but recognised that daily measurement was typical.

proteinuria, without urinary tract infection or trauma due to catheterisation.

Ultrasound

1.4.3 Do not routinely offer ultrasound of the urinary tract when the cause for the acute kidney injury has been identified.

1.4.4 Offer immediate ultrasound of the urinary tract to patients with acute kidney injury when pyonephrosis (infected and obstructed kidney[s]) is suspected. Ensure that the imaging is performed within 6 hours of assessment.

1.4.5 Offer urgent ultrasound of the urinary tract to patients with acute kidney injury who:

- have no identified cause of acute kidney injury, or
- are at risk of urinary tract obstruction.

Ensure that the imaging is performed within 24 hours of assessment.

1.5 Managing acute kidney injury

Relieving urological obstruction

1.5.1 Refer all patients with upper tract urological obstruction to a urologist. Refer immediately when one or more of the following is present:

- pyonephrosis
- an obstructed solitary kidney
- complications of acute kidney injury caused by urological obstruction.

1.5.2 When nephrostomy or stenting is used to treat upper tract urological obstruction in patients with acute kidney injury, undertake as soon as possible and within 12 hours of diagnosis.

Pharmacological management

1.5.3 Do not routinely offer loop diuretics to treat acute kidney injury.

1.5.4 Consider loop diuretics for treating fluid overload or oedema while:

- the patient is awaiting renal replacement therapy, or
- renal function is recovering in a patient not receiving renal replacement therapy.

1.5.5 Do not offer low-dose dopamine to treat acute kidney injury.

Referring for renal replacement therapy

1.5.6 Discuss any potential indications for renal replacement therapy with a nephrologist and/or critical care specialist immediately to ensure that the therapy is started as soon as needed.

1.5.7 When a patient has significant comorbidities, discuss with the patient and/or their parent or carer and within the multidisciplinary team whether renal replacement therapy would be suitable. Follow the recommendations on shared decision-making in Patient experience in adult NHS services (NICE clinical guidance 138).

1.5.8 Refer patients for renal replacement therapy immediately if any of the following are not responding to medical management:

- hyperkalaemia
- metabolic acidosis
- symptoms or complications of uraemia (for example, pericarditis, encephalopathy)
- fluid overload
- pulmonary oedema.

1.5.9 Base the decision to start renal replacement therapy on the patient's condition as a whole and not on an isolated urea, creatinine or potassium value.

1.5.10 When there are indications for renal replacement therapy, the nephrologist and/or critical care specialist should discuss the treatment with the patient and/or their parent or carer as soon as possible and before starting treatment. Follow the recommendations on shared decision-making in Patient experience in adult NHS services (NICE clinical guidance 138).

Referring to nephrology

1.5.11 Refer patients with acute kidney injury to a nephrologist, paediatric nephrologist or critical care specialist immediately if they meet criteria for renal replacement therapy in recommendation1.5.8.

1.5.12 Do not refer patients to a nephrologist when there is a clear cause for acute kidney injury and the condition is responding promptly to medical management, unless they have a renal transplant.

1.5.13 Consider discussing management with a nephrologist when a patient with severe illness might benefit from treatment, but there is uncertainty as to whether they are nearing the end of their life.

1.5.14 Refer patients in intensive care to a nephrology team when there is uncertainty about the cause of acute kidney injury or when specialist management of kidney injury might be needed.

1.5.15 Discuss the management of acute kidney injury with a nephrologist or paediatric nephrologist as soon as possible and within 24 hours of diagnosis when one or more of the following is present:

- a possible diagnosis that may need specialist treatment (for example, vasculitis, glomerulonephritis, tubulointerstitial nephritis, myeloma)
- acute kidney injury with no clear cause
- inadequate response to treatment
- complications associated with acute kidney injury
- stage 3 acute kidney injury
- a renal transplant

- chronic kidney disease stage 4 or 5.

1.5.16 Consider referral to a nephrologist for patients who have recovered from an acute kidney injury when eGFR is 30 ml/min/1.73 m^2 or less.

1.5.17 Consider referral to a paediatric nephrologist for children and young people who have recovered from an episode of acute kidney injury but have hypertension, impaired renal function or 1+ or greater proteinuria on dipstick testing of an early morning urine sample.

1.6 Information and support for patients and carers

1.6.1 Discuss immediate treatment options, monitoring, prognosis and support options with the patient with acute kidney injury and/or their parent or carer if appropriate. Follow the recommendations on patient views and preferences and shared decision-making in Patient experience in adult NHS services (NICE clinical guidance 138).

1.6.2 Give information about long-term treatment options, monitoring, self-management and support to people who have had acute kidney injury (and/or their parent or carer, if appropriate) in collaboration with a multidisciplinary team appropriate to the person's individual needs.

1.6.3 Give information about future care to patients needing renal replacement therapy after discharge following acute kidney injury. This should include information about the frequency and length of dialysis sessions and the preparation needed (such as having a fistula or peritoneal catheter).

1.6.4 Discuss the risk of developing acute kidney injury, particularly the risk associated with conditions leading to dehydration (for example, diarrhoea and vomiting) and with drugs with nephrotoxic potential (including over-the-counter NSAIDs), with people who have:

- chronic kidney disease (eGFR less than 60 ml/min/1.73 m^2)
- limited access to fluid because of neurological or cognitive impairment or disability.

Involve parents and carers in the discussion if appropriate.

2 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in appendix L of the full guideline

2.1 Long-term outcomes of acute kidney injury

What are the long-term outcomes of acute kidney injury in adults, children and young people?

Why this is important

Long-term follow-up studies, predominantly from North America, have shown that acute kidney injury is associated with an increased risk of chronic kidney disease or exacerbation of underlying chronic kidney disease. This can lead to end-stage renal disease (ESRD) and long-term dialysis. About a quarter to a third of the costs associated with acute kidney injury in adults are due to ESRD. Older adults with comorbidities are at particular risk.

Although acute kidney injury is traditionally regarded as reversible, the psychological effects are not well studied. Some studies of adults who have recovered from acute kidney injury suggest a reduced quality of life, including higher levels of depression. People also often need more social care or discharge to institutional care.

The factors associated with the long-term complications of acute kidney injury are poorly understood. A large, prospective epidemiological or cohort study is needed with a control group (for example, patients admitted to hospital as an emergency with an acute illness, but without acute kidney injury). In adults follow-up should be for at least 2–3 years, and the study should be adequately powered to detect factors predictive of the two most costly outcomes in adults, new ESRD and new need for institutional care or the inability to live independently in the community. In children and young people, longer follow-up beyond puberty is needed. Important long-term complications for children

and young people include hypertension, proteinuria and reduced renal function.

2.2 Rapid referral to nephrology services for moderate to severe acute kidney injury

What is the clinical and cost effectiveness of rapid referral (within 12 hours) to nephrology services for adults with moderate to severe (stage 2 to 3) acute kidney injury not needing critical care?

Why this is important

There is national variation in referral of patients with moderate to severe acute kidney injury to nephrology services. Evidence is lacking on the effect of rapid referral (within 12 hours) on major outcomes, including the need for renal replacement therapy, mortality, length of hospital stay and health-related quality of life at 6 months. In most patients acute kidney injury is managed by correcting volume depletion and hypotension and avoiding further renal insults, including nephrotoxic drugs. This does not usually require specialist input from nephrology or critical care services.

In a proportion of patients, renal function may deteriorate further because of primary renal diseases needing specialist treatment (for example, immunosuppressive therapy), progressive organ failure needing treatment with adverse effects on the kidneys (for example, high-dose diuretics in congestive heart failure) or inadequate correction of volume depletion and hypotension.

The optimal timing for referral to nephrology services is not known. Rapid referral of all patients with stage 2 to 3 acute kidney injury may allow earlier detection of primary renal diseases and avoid delay in starting appropriate therapy. It may also ensure more rapid correction of volume depletion and hypotension and initiation of targeted investigations. Potential benefits also include prevention of progressive acute kidney injury, avoidance of renal replacement therapy, avoidance of a delayed transfer to critical care, improved chances of renal recovery, a shorter hospital stay and better long-term outcomes.

The challenge would be to provide rapid referral (within 12 hours) out of hours. This would be a particular problem in hospitals without a renal unit on site. Another downside of rapid referral of all patients with stage 2 to 3 acute kidney injury would be the costs associated with referring patients whose renal function recovers quickly with basic general management alone.

A randomised controlled trial is needed to evaluate the clinical and cost effectiveness of rapid referral (within 12 hours) to nephrology services for all adult patients with moderate to severe (stage 2 to 3) acute kidney injury compared with referral based on clinical judgement (that is, standard care). Outcomes should include need for renal replacement therapy, mortality, length of hospital stay and health-related quality of life at 6 months.

2.3 Definition of acute kidney injury – system for staging and diagnosis

Can a simplified definition and staging system, based on Système International (SI) units, be used to predict short- to medium-term outcomes in acute kidney injury?

Why this is important

Definitions of acute kidney injury have evolved fairly rapidly in recent years, from RIFLE (2004), through AKIN (2007), to KDIGO (2012) (a merger of RIFLE and AKIN, but with less rigorous requirements for diagnosis in those with chronic kidney disease). All three are complex and rely on non-SI units for creatinine.

Absolute creatinine rises have been shown to be independently associated with mortality, but the evidence comes from US studies that used non-SI units for creatinine. Stage 1 acute kidney injury is currently defined by a rise in creatinine of 0.3 mg/dl within 48 hours, which translates awkwardly to 26.4 µmol/l in SI units (note that laboratories report creatinine as an integer value only). The current definitions are complex and difficult to use for non-specialists in healthcare systems that use SI units for creatinine measurement (including the UK).

A large, prospective epidemiological or cohort study is needed to investigate whether a simplified system, derived from KDIGO, would be useful for detecting and staging acute kidney injury in the NHS. The study should investigate the relationship of acute kidney injury, as defined by creatinine rise in SI units, with outcomes, adjusted for comorbidity. It also needs to investigate whether the same absolute rise in creatinine equally reflects outcomes among patients with and without chronic kidney disease. The study should include a control group (for example, patients admitted to hospital as an emergency with an acute illness, but without acute kidney injury) and be adequately powered to show the effect of acute kidney injury on mortality, length of stay and dialysis for acute kidney injury at 6 months.

2.4 Introducing renal replacement therapy

What is the clinical and cost effectiveness of early versus later introduction of renal replacement therapy in patients with acute kidney injury stages 2 and 3, when there is no urgent need for such therapy?

Why this is important

In some patients renal replacement therapy is a lifesaving intervention (for example, in those with hyperkalaemia). For other patients, there may be no clear indicators of when renal replacement therapy should be started because oliguria, fluid overload and uraemia are common and ill-defined indications. An early introduction of renal replacement therapy might reduce the incidence of uraemic or other complications of acute kidney injury, but might also expose the patient to more risks from the therapy itself. Later introduction might increase the incidence of uraemic or other complications of acute kidney injury, but might also reduce the risks associated with renal replacement therapy.

A prospective study is needed of adult inpatients with acute kidney injury AKIN stages 2 and 3, who are likely to need renal replacement therapy within a given timeframe (for example, 72 hours), but have no urgent need for therapy. Units participating in the study should be logistically capable of providing early or later dialysis for these patients. Mortality, length of stay, incidence of complications of acute kidney injury, incidence of complications

of renal replacement therapy and usage of dialysis should be compared in patients having early therapy and those having later renal replacement therapy. Possible indicators for early renal replacement therapy could be weight gain less than 10%, urea less than 25 mmol/l and oliguria 0.5 ml/kg/hour or less for at least 24 hours.

2.5 Preventing deterioration

What is the clinical and cost effectiveness of continuing ACE inhibitor or ARB treatment, versus stopping treatment 24 hours before cardiac surgery and resuming 24 hours after, in people with chronic kidney disease and an eGFR of less than 30 ml/min/1.73 m^2?

Why this is important

People who need cardiac surgery are often receiving ACE inhibitors or ARBs for their cardiac disease. It is unclear whether these people should stop ACE inhibitors or ARBs around the time of cardiac surgery when their blood pressure will be most unstable. Stopping ACE inhibitors or ARBs might cause deterioration of cardiac disease, which is often a concern for cardiology clinicians, but trials of ACE inhibitors and ARBs in cardiac disease have typically excluded patients undergoing cardiac surgery whose condition is unstable. Stopping ACE inhibitors or ARBs at the time of surgery may prevent exacerbation of acute kidney injury in patients whose condition is unstable.

A randomised controlled trial is needed in patients on ACE inhibitors or ARBs undergoing cardiac surgery to compare continuing treatment with stopping treatment for 48 hours (24 hours before and after surgery). Outcomes should include the incidence of acute kidney injury, cardiovascular events, all-cause mortality, number of patients needing renal replacement therapy and length of hospital stay.

3 Other information

3.1 Scope and how this guideline was developed

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover.

How this guideline was developed

NICE commissioned the National Clinical Guideline Centre to develop this guideline. The Centre established a Guideline Development Group (see section 4), which reviewed the evidence and developed the recommendations.

The methods and processes for developing NICE clinical guidelines are described in The guidelines manual.

3.2 Related NICE guidance

Details are correct at the time of consultation on the guideline (March 2013). Further information is available on the NICE website.

Published

General

- Patient experience in adult NHS services. NICE clinical guidance 138 (2012).
- Medicines adherence. NICE clinical guideline 76 (2009).
- Acutely ill patients in hospital. NICE clinical guideline 50 (2007).

Condition-specific

- Hypertension. NICE clinical guideline 127 (2011).
- Peritoneal dialysis. NICE clinical guideline 125 (2011).
- Anaemia management in people with chronic kidney disease. NICE clinical guideline 114 (2011).
- Chronic heart failure. NICE clinical guideline 108 (2010).

- Chest pain of recent onset. NICE clinical guideline 95 (2010).
- Unstable angina and NSTEMI. NICE clinical guideline 94 (2010).
- Critical illness rehabilitation. NICE clinical guideline 83 (2009).
- Type 2 diabetes. NICE clinical guideline 66, partially updated by CG87 (2008).
- Type 1 diabetes. NICE clinical guideline 15 (2004).

Under development

NICE is developing the following guidance (details available from the NICE website):

- Intravenous fluids therapy in children. NICE clinical guideline. Publication expected November 2015.
- Acute heart failure. NICE clinical guideline. Publication expected September 2014.
- Chronic kidney disease (update). NICE clinical guideline. Publication expected July 2014.
- Type 1 diabetes (update). NICE clinical guideline. Publication expected July 2014.
- Diabetes in children and young people. NICE clinical guideline. Publication expected June 2014.
- Management of hyperphosphataemia. NICE clinical guideline. Publication expected March 2013.
- Intravenous fluid therapy. NICE clinical guideline. Publication expected November 2013.
- Myocardial infarction with ST-segment-elevation. NICE clinical guideline. Publication expected July 2013.
- Anaemia management in chronic kidney disease (update). NICE clinical guideline. Publication date to be confirmed
- Type 2 diabetes (update). NICE clinical guideline. Publication date to be confirmed
- Clinitek Microalbumin 9 reagent strips for the early detection and monitoring of kidney disease. NICE technology appraisal guidance. Publication date to be confirmed.

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