Northern Ireland Guidelines for Acute Kidney Injury

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Foreword

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These guidelines have been published by the Guidelines & Audit Implementation Network (GAIN), which is a team of health and social care professionals established under the auspices of the Department of Health, Social Services & Public Safety in 2008. The aim of GAIN is to promote quality in the Health Service in Northern Ireland, through audit and guidelines, while ensuring the highest possible standard of clinical practice is maintained.

This guideline was developed by GAIN and the Northern Ireland Nephrology Forum and was chaired by Professor Peter Maxwell, Consultant Nephrologist, Renal Unit, Belfast Health & Social Care Trust.

GAIN wishes to thank all those who contributed in any way to the development of these guidelines.

Dr T Trinick
Chairman of GAIN

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Introduction

Acute kidney injury (AKI) is a common clinical problem, expensive to manage and associated with a high mortality. Prompt recognition of the risk factors for AKI, accurate clinical assessment of patients with kidney injury and avoidance of further nephrotoxic insults can help to prevent or reverse AKI.

Normal kidney function depends on having an adequate blood pressure and fluid volume to perfuse the kidneys. The kidney itself must have a sufficient number of intact nephrons (glomeruli and tubules) to achieve normal glomerular filtration and electrolyte balance. Finally there must be free drainage of the urinary tract.

AKI can develop at home in people who become dehydrated e.g. from vomiting and diarrhoea and are hypotensive e.g. associated with sepsis or poor cardiac function. Fluid depletion and hypotension compromise the normal perfusion of the kidney. This problem can be further exacerbated by commonly prescribed drugs e.g. ACE inhibitors or NSAIDs that impair how the kidneys respond to hypotension. AKI, developing in this community setting, will respond to fluid replacement and temporary withdrawal of drugs affecting kidney function.

AKI in hospitalized patients may be present on admission and be responsive to prompt fluid resuscitation, coupled with temporary withdrawal of drugs e.g. ACE inhibitors or NSAIDs and avoidance of further nephrotoxins such as radiocontrast. This “volume sensitive” or “pre-renal” form of AKI often precedes the development of AKI characterized by pathological damage to kidney tissues. Once established, this more severe form of AKI takes much longer to resolve and will not respond to vigorous intravenous fluid volume replacement. This “renal” AKI (also known as acute tubular necrosis or ATN) is associated with prolonged hospitalization and higher mortality both during the hospital stay and following discharge. Over 75% of all AKI in hospitalized patients is due to the volume sensitive and ATN forms of AKI. Of the remaining causes of AKI, urinary tract obstruction is the most important to rapidly exclude as early drainage of obstructed kidneys improves the longer term renal function.

Clinically, AKI is easily recognised by decreasing urine volume (oliguria or anuria) and a rise in serum creatinine. AKI, if unrecognised and allowed to deteriorate, will result in

uraemia, metabolic acidosis, hyperkalaemia, an increased risk of prolonged hospitalization and much higher mortality.

Published studies of AKI suggest a large percentage of episodes are preventable, or potentially reversible through simple interventions such as fluid volume replacement, discontinuing and/or avoiding potentially nephrotoxic agents, relief of urinary tract obstruction and earlier recognition of conditions causing rapid progression of AKI.

Recognition of Acute Kidney Injury

Acute Kidney Injury (AKI) has traditionally been defined as the abrupt loss of kidney function resulting in the retention of urea and other nitrogenous waste products and in the dysregulation of extracellular volume and electrolytes. This can occur in the setting of previously normal renal function or in patients with pre-existing renal disease (acute on chronic renal failure)

More recently it has been recognised that even very small changes in serum creatinine are associated with adverse outcomes.

How to diagnose AKI in Hospitalised Patients:

This involves clinical assessment of the vital signs of the patient together with accurate interpretation of changes in urine output. This is coupled with measurement of kidney function (U&E) and recognition of significant changes in serum creatinine.

An abrupt (within 48 hours) reduction in kidney function is associated with

-
- with an absolute increase in serum creatinine of either ≥ 30 μmol/L

- or a serum creatinine percentage increase ≥ 50% (1.5 fold from baseline)

- or a reduction in urine output (documented oliguria of <0.5 mL/kg/h for > 6 hours).

Accurate measurement of urine output may not be routine outside of the intensive care unit (ICU). Urine output may be influenced by the use of diuretics or the presence of urinary tract obstruction. Nevertheless, a reduction in urine output is a sensitive indicator of renal dysfunction and often precedes a rise in serum creatinine in critically ill patients.

Persons at higher risk of Acute Kidney Injury

Individuals are more likely to develop AKI if they have any of the following risk factors.

- Pre-existing chronic kidney disease (CKD) - (eGFR < 60 mL/min/1.73m^2)
- Older age (> 60 years old)
- Sepsis
- Co-existing illness including: cardiac failure, liver disease diabetes mellitus
- Use of NSAIDs or COX II inhibitor drugs
- Use of ACE inhibitors or angiotensin receptor blocker (ARB) medication particularly in the setting of hypovolaemia
- Hypotension (systolic blood pressure < 100 mmHg)
- Symptoms and signs of hypovolaemia (vomiting, diarrhoea, tachycardia, hypotension)
- Urinary tract symptoms (especially reduced urine output or anuria)
- Those receiving intravenous contrast for diagnostic and therapeutic procedures
- Patients in the peri-operative period

Prevention of Acute Kidney Injury

In hospitalized patients a strategy for prevention of AKI should include the following management principles.

1. All patients, both on admission and during their hospital stay, need to be assessed for their risk for developing AKI.

2. Patients admitted as an emergency should have their baseline renal function established on admission. Patients with an eGFR < 60 mL/min/1.73m^2 have a higher risk for AKI and need closer monitoring of their renal function (serum creatinine and record of daily urine output).

3. Hydration state should be carefully assessed paying attention to symptoms and signs of both dehydration and fluid overload. Where patients are at risk of dehydration (poor oral intake, fasting for procedures) then consideration should be given to prescription of maintenance IV fluids.

4. Fluid balance and U&E should be carefully monitored especially during periods of antibiotic therapy, episodes of clinical deterioration and the peri-operative period.

5. Hypotension (systolic blood pressure < 100 mmHg) needs urgent assessment and treatment with the use of appropriate IV fluid challenges and vasopressor agents where indicated.

6. Care should be taken prescribing NSAIDs in patients at risk of developing AKI. Regular monitoring of renal function (serum creatinine and record of daily urine output) should occur in patients taking these medications during their inpatient stay.

7. Temporary cessation of ACE inhibitors (and ARBs) should be considered in patients with dehydration, hypotension (systolic blood pressure < 100 mmHg) and or deteriorating renal function. Alteration of timing of prescription to 6pm would allow for time during the working day to assess clinical state and renal function in case of the need to hold these medications.

8. Where clinically indicated aminoglycosides can continue to be used in AKI. However, renal function and levels of potentially nephrotoxic antibiotics (including gentamicin, vancomycin, teicoplanin) must be carefully monitored during their administration.

Diagnosis

For patients with hospital-acquired AKI the cause is frequently associated with several risk factors. Assessment of the patient with AKI therefore starts with a careful history and examination, including a thorough review of the patient's notes and drug treatment records where available.

Any evidence of previous chronic kidney disease (CKD) should be sought from either previous hospital attendances/admissions or the patient's GP.

A focused history can identify pre-existing risk factors and potential causes for AKI including reduced fluid intake and/or increased fluid losses, urinary tract symptoms and recent drug ingestion.

AKI secondary to systemic disease may be associated with other clinical features such as fever, rash and joint pains.

Clinical examination includes assessment of volume status which is guided by clinical signs including core temperature, peripheral perfusion, heart rate, blood pressure and jugular venous pressure. The abdomen must be examined carefully for the presence of a palpable bladder.

Urine output should be measured with consideration of urinary catheterisation in patients with no demonstrated urine output within 4 hrs, hypotension, sepsis and pulmonary oedema.

Reagent strip urinalysis should be performed on all emergency admissions. Positive protein values of 3+ and 4+ on reagent strip testing of the urine suggests intrinsic glomerular disease.

The laboratory evaluation should include a U&E (with particular reference to concentrations of urea creatinine, sodium, potassium and bicarbonate), full blood count, CRP, liver function tests, glucose and bone profile. Where there is clinical suspicion of muscle injury or pancreatitis, creatinine kinase and amylase levels should be checked.
Measure of urine sodium concentration may be helpful in identifying volume sensitive pre-renal AKI (urine sodium < 20 mmol/L)

Ultrasound of kidneys is ideally undertaken within 4 hrs when upper tract renal obstruction is suspected and within 24 hrs where there is failure of improvement in renal function following treatment of the underlying condition.

A less common cause for AKI may be considered if

- clinical features such as fever, rash, joint pains or pulmonary infiltrates are present
- there is no obvious cause for AKI (e.g. hypotension, dehydration, sepsis, nephrotoxins, obstruction)
- abnormal urinalysis (proteinuria +/- haematuria) is found
- thrombocytopenia and haemolytic anaemia are present (suggestive of haemolytic uraemic syndrome)

This should prompt investigation for rarer causes for AKI such as systemic vasculitis (ANCA, C3, C4), anti-GBM nephritis (anti-GBM antibody), lupus nephritis (auto-antibody screen) and myeloma (serum immunoglobulins, plasma protein electrophoresis, urine for Bence-Jones protein)

NB: It should be stressed that “volume responsive” AKI and acute tubular necrosis are much more common forms of AKI in community and hospital settings than AKI due to intrinsic glomerular disease.

Treatment Principles

There is no specific pharmacological treatment for AKI. There is no evidence to support the use of loop diuretics or dopamine as treatments for AKI.

Loop diuretics may have a limited role in managing fluid overload in some patients.

The focus of therapy should be:

1. To correct those conditions causing or contributing to the kidney injury

2. Where indicated to support kidney function by means of renal replacement therapy (dialysis) until recovery of independent renal function has occurred.

It is critical that the volume status of patients with AKI is accurately assessed. This is usually accomplished by clinical assessment and dynamic response to appropriate fluid replacement. Where there is clinical uncertainty of fluid and volume status then patients should be considered for invasive haemodynamic monitoring (CVP) of fluid status in a high dependency unit (HDU) setting.

Special consideration should be given to:

1. Urgent relief of urinary tract obstruction

2. Adequate fluid resuscitation to restore an effective circulating blood volume

3. Prompt restoration of effective blood pressure

4. Avoidance of fluid overload

5. Stopping potentially nephrotoxic drugs

Restoration of kidney perfusion

Correct dehydration

- In ill patients, fluid replacement is best achieved through the rapid infusion of repeated small volumes (e.g. 250 mls of intravenous crystalloid or colloid) to achieve clinical evidence of adequate perfusion (capillary refill time < 3 seconds, systolic blood pressure of > 100 mmHg, visible JVP).

- Where there are clinical uncertainties consider CVP monitoring in an HDU setting - aiming for a CVP of 6 – 8 mmHg.

- Once dehydration has been corrected prescribe maintenance fluids at an hourly rate according to total losses + 50 mls/hour

- Avoid potassium containing fluids (Hartman's, Pentastarch) where the serum potassium is above 5.5 mmol/L.

- Care should be taken to avoid fluid overload. In particular once the patient is haemodynamically stable, if the urine output remains poor (< 50 mls/hr) then further fluid boluses should not be specifically targeted to try and improve urine output. This practice often results in fluid overload with a worse outcome in AKI.

STOP drugs that interfere with kidney function

- In hypotensive and/or hyovolaemic patients stop ACE inhibitors, angiotensin receptor blockers, diuretics, other anti-hypertensive agents and NSAIDs.

- These drugs will exacerbate the hypoperfusion of kidneys and should be withheld until the patient is stabilized and the AKI has resolved.

Restore an effective blood pressure

- Sepsis is a common cause of AKI.

- Where the patient is hypotensive (systolic blood pressure < 100 mmHg) a fluid challenge is appropriate using 250 – 500 mls of intravenous crystalloid or colloid.

- Where the systolic blood pressure remains labile (< 100 mmHg) despite 1.5 L of intravenous fluid administered over 1 hour then consideration should be given to HDU/ICU referral for invasive haemodynamic monitoring and administration of vasopressor therapy (e.g. noradrenaline) in an HDU - ICU setting.

Medication Review

Medications commonly contribute to the development of AKI. In addition, with a sudden reduction in kidney function many drugs require dose modification to avoid hazardous side effects e.g. oral hypoglycaemic drugs have a much longer duration of action in kidney failure.

Patients with AKI are by definition in a clinically unstable condition and all medication including “usual” prescriptions should be reviewed as soon as AKI is identified.

The following list is not exhaustive but will provide a useful start.

Drugs interfering with renal perfusion

- ACE inhibitors and ARBs
- NSAIDs
- All antihypertensives
- Nitrates
- Nicorandil
- Diuretics (loop and thiazide)

Common drugs requiring dose reduction or cessation

- Low molecular weight heparins
- Opiates
- Penicillin based antibiotics
- Metformin (risk of lactic acidosis)
- Sulphonylurea-based hypoglycaemic agents
- Aciclovir

Drugs requiring close monitoring

- Warfarin
- Aminoglycosides

Drugs aggravating hyperkalaemia

- Digoxin
- Beta blockers
- Trimethoprim
- Potassium sparing diuretics e.g. spironolactone, amiloride

Preventing Contrast Nephropathy

Acute kidney injury secondary to radiological contrast media classically occurs within 72 hours of receiving such agents. There is no specific treatment.

Prevention involves identifying those patients at risk and avoiding dehydration before, during and after the radiological procedure. The incidence of radiocontrast nephropathy increases significantly in patients with the following risk factors

Who is at risk?

- Estimated GFR ≤30 mL/min/1.73m^2
- Estimated GFR between 31 and 60 mL/min/1.73m^2 and "AT RISK" patients (see page 4)

Management: Five point plan

- Recommended for all patients with an eGFR of ≤ 30 mL/min/1.73m^2
- Consider for all patients with an eGFR of ≤ 60 mL/min/1.73m^2 and risk factors listed in page 4.

1. Adequate hydration is of paramount importance to the patient's management prior to the procedure. If at risk of developing contrast nephropathy the patient should receive intravenous 0.9% sodium chloride or 1.4% sodium bicarbonate at a rate of 3mL/kg/hour for 1 hour pre-procedure and 1 mL/kg/hour for 6 hours post-procedure.

2. Potentially nephrotoxic medications should be avoided.

- Omit ACE/ARBs for 12 hrs pre and do not restart post procedure until U&E stable (back to baseline at 24 hrs and 48 hrs).
- Omit NSAIDs for 12 hrs pre and do not restart post procedure until U&E stable (back to baseline at 24 hrs and 48 hrs.
- Metformin should be stopped on or prior to the day of study and not restarted until renal function has been demonstrated to be stable because of the risk of lactic acidosis.

3. Low osmolar agents are associated with a decreased risk of nephrotoxicity as compared to the high osmolar agents, particularly in those at risk from contrast media-associated AKI. Patients with CKD should receive the iso-osmolar non-ionic contrast agent iodixanol which has been shown to reduce the risk of contrast induced nephropathy in this patient group.

4. The dose of contrast media should be minimised and further exposure to contrast media should be delayed until full recovery of renal function unless absolutely necessary.

5. Renal function should be checked up to 48-72 hours following the procedure if in a high risk group to ensure stable renal function.

Currently there is no compelling evidence for the routine use of N-acetylcysteine.

Indications for AKI Referral to a Nephrology Team

Early contact with a nephrology team is advisable for those patients who are likely to need renal replacement therapy (dialysis) or for whom intrinsic renal disease is considered to be a cause of their AKI.

In particular referral to a nephrology team is appropriate if a patient with AKI has:

- Hyperkalaemia (> 6.5 mmol/L) refractory to medical management
- Pulmonary oedema refractory to medical management
- Refractory metabolic acidaemia pH ≤ 7.2
- Progressive renal failure (creatinine ≥ 300 umol/L, rise in serum creatinine of >100 umol/L/day)
- Patients suspected of intrinsic renal disease (vasculitis, primary glomerulonephritis, interstitial nephritis)

Nephrology - ICU Interface

Many patients who develop AKI do so in the context of multiple organ dysfunction. This is often manifest by hypotension, lactic acidosis and respiratory compromise.

Such patients require invasive monitoring and multi-organ support which may include mechanical ventilation, vasopressor / inotropic support to facilitate their optimal clinical care. There are several modes of renal replacement therapy (dialysis) that are appropriate for critically ill patients with AKI in the setting of multiple organ failure. The critical care team will decide on the choice of dialysis modality in ICU and HDU environments with input as required from the nephrology service. Liaison between nephrologist and critical care staff is essential to help plan for AKI management during and after ICU admission

Early involvement with the ICU team in assessment of ill and clinically deteriorating patients with AKI is to be encouraged.

Nephrology – Conservative Care Interface

It should be recognised that AKI may be just part of a terminal illness in a hospitalized patient. The terminal nature may reflect the severity of the clinical event or the progression of advanced untreatable co-morbidity.

In such patients provision of renal replacement therapy (dialysis) is futile and may prolong suffering of a dying patient and lead to false hopes in relatives for the expected survival of a family member

Such patients should be identified by their senior medical staff early in the course of their deterioration to decide on ceilings of care for both resuscitation (invasive monitoring, vasopressor therapy) and appropriateness of a referral to a nephrology team.

Acute Kidney Injury (AKI) Protocol

PREVENTION

1. Monitor serum creatinine and fluid balance closely in "at risk patients"
2. Avoid dehydration
3. Avoid hypotension (systolic BP<100 mmHg)
4. Caution in use of NSAIDs
5. ACE - ARBs
   - 5.1. Evening prescription
   - 5.2. Stop if dehydrated / hypotensive or deteriorating renal function
6. Monitor aminoglycosides closely

Contrast Nephropathy

(GFR < 30 or GFR < 60 + risk factors)

- 6.1. Omit ACE-ARB / NSAID 12hrs pre-procedure
- 6.2. 0.9% saline OR 1.4% NaHCO3 @ 3mls/kg/hr x 1 hr pre procedure then 1ml/kg/hr x 6 hrs post-procedure
- 6.3. Check U+E 24 hrs post procedure.

AT RISK PATIENTS

1. Pre-existing chronic kidney disease (CKD)
2. Older age (> 60 years old)
3. Sepsis
4. Co-existing illness including: Cardiac failure, Liver disease, Diabetes mellitus
5. Use of NSAIDs or COX II inhibitor drugs)
6. Use of ACE inhibitor or ARB medication particularly in the setting of hypovolaemia
7. Hypotension (systolic blood pressure < 100 mmHg)
8. Symptoms and signs of hypovolaemia (vomiting, diarrhoea, tachycardia hypotension)
9. Urinary tract symptoms (especially reduced urine output or anuria)
10. Those receiving intravenous contrast for diagnostic and therapeutic procedures)

RECOGNITION

Creatinine ↑ by ≥ 30 µmol/L or ↑ from baseline by 50%
and / or
Urine output < 30mls / hr for > 6 hr

TREATMENT - 5 points to consider

1. Correct Dehydration

1. Rapid infusion repeated small volumes (250mls) to achieve Cap. Refill time < 3 secs / SBP > 100, visible JVP)
2. Consider CVP if uncertain of volume status
3. When dehydration corrected prescribe maintenance fluids @ hourly rate (total losses + 50 mls/hr)
4. Avoid K^+ containing fluids if K^+ > 5.5 mmol/L

2. Review All Drugs

1. Stop drugs which interfere with renal function (NSAID / ACE/ARB)
2. Stop BP lowering medication in hypotensive / hypovolaemic patients.
3. Review doses of all other drugs

3. Restore Effective BP

- Fluid challenges (250 - 500mls crystalloid or colloid to achieve systolic BP > 100 mmHg)
- If SBP < 100 mmHg despite 1.5L IV fluid over 1 hr consider vasopressor therapy in HDU - ICU

4. Relieve Obstruction

5. Treat Hyperkalaemia

INDICATIONS FOR NEPHROLOGY REFERRAL

- Refractory hyperkalaemia (> 6.5)
- Refractory pulmonary oedema
- Refractory metabolic acidosis (pH < 7.2)
- Progressive renal failure (creatinine > 300 umol/L or rise of > 100 umol/L/day
- Possible intrinsic renal disease

INTRINSIC RENAL DISEASE

- Absence of obvious cause of AKI
- 3 - 4+ Protein ± Blood on Urinalysis
- ? Vasculitis (rash, arthralgia, pulmonary infiltrates - request urgent ANCA + anti GBM titres
- Thrombocytopenia + haemolytic anaemia (HUS)

Appendix 1

Membership of GAIN Acute Kidney Injury Guideline Development Group

The Acute Kidney Injury Guidelines were developed by the Northern Ireland Nephrology Forum, a collegial network of nephrologists, in consultation with colleagues in other specialties. The guideline development was led by Dr John Harty and Prof Peter Maxwell with valuable input from Dr Emma Borthwick, Dr Michael Quinn and Dr Joanne Shields

For further advice on Acute Kidney Injury contact your local nephrologist as listed below

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Appendix 2

Additional Sources of Guidance

National Confidential Enquiry into Patient Outcome and Death (NCEPOD) “Acute Kidney Injury: Adding Insult to Injury (2009)” http://www.ncepod.org.uk/2009aki.htm

Renal Association Clinical Practice Guidelines: Module 5: Acute Kidney Injury, 4th edition, 2008. http://www.renal.org/Clinical/GuidelinesSection/AcuteKidneyInjury.aspx

British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients http://www.ics.ac.uk/intensive_care_professional/standards_and_guidelines/

Northern Ireland Guidelines and Audit Implementation Network (GAIN) guidelines www.gain-ni.org/Guidelines/index.asp

Northern Ireland Guidelines for Management of Chronic Kidney Disease, 2010 http://www.gain-ni.org/Guidelines/Chronic%20Kidney%20Disease.pdf

Hyponatraemia in Adults on or after 16th birthday, 2010 http://www.gain-ni.org/Guidelines/Hyponatraemia_guideline.pdf

Guidelines for the Treatment of Hyperkalaemia in Adults, 2009 http://www.gain-ni.org/Guidelines/hyperkalamia_guidelines.pdf