Guidelines and protocol for the prevention of contrast-induced acute kidney injury

Heart Division

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Signed by:
Chairman –

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Target audience: All clinical staff

Disclaimer: Information provided within this guideline is with respect to the use at the Royal Brompton and Harefield NHS Foundation Trust. This Guideline is for reference only and for interpretation by clinical healthcare professionals. The authors do NOT accept any responsibilities in any form in relation to the use and interpretation of this document when used outside of the Royal Brompton & Harefield NHS Foundation Trust.
SUMMARY

These guidelines describe measures to reduce the risk of developing renal impairment (Contrast-induced Acute Kidney Injury; CI-AKI) following the use of iodinated radiographic contrast media by physicians other than radiologists. It is intended that these guidelines apply principally to practice in adult cardiology throughout the Royal Brompton & Harefield NHS Foundation Trust, but the principles also will apply as appropriate to critical care and transplant medicine. These guidelines do not apply to the use of radiographic contrast media in children aged 16 or under.

The Heart Divisions (RBH & HH) are responsible for implementing these guidelines and establishing a local protocol across the Royal Brompton & Harefield NHS Foundation Trust in line with these guidelines. The local protocol will be effective on both sites from June 2012.

These guidelines should be read in conjunction with the guidelines for radiographers and radiologists ('Intravenous cannulation and administration of intravenous contrast medium').

TIMETABLE

The authorised policy will be distributed to all relevant clinical areas in paper format and posted on Trust Intranet – Policies & Guidelines/Policies and Procedures/Patient Related.

Dissemination: Heart Divisions, including Imaging
Directorate of Anaesthesia & Critical Care

Review: To commence

Reissue date: Anticipated
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1. INTRODUCTION

1.1 Context

These guidelines describe measures to reduce the risk of developing renal impairment (Contrast-induced Acute Kidney Injury; CI-AKI) following the use of iodinated radiographic contrast media by physicians other than radiologists.

1.2 Scope of these guidelines

It is intended that these guidelines will apply principally to practice in adult cardiology throughout the Royal Brompton & Harefield NHS Foundation Trust, but the principles also will apply as appropriate to critical care and transplant medicine. These guidelines do not apply to the use of radiographic contrast media in children aged 16 or under.

These guidelines should be read in conjunction with the guidelines for radiographers and radiologists ‘Intravenous cannulation and administration of intravenous contrast medium’.

1.3 Implementation of these guidelines

The Heart Division is responsible for implementing these guidelines and establishing a local protocol across the Royal Brompton & Harefield NHS Foundation Trust in line with these guidelines. The local protocol is shown in Appendix I. It is expected that the local protocol will be effective as from June 2012.

1.4 Audit of effectiveness of local protocol

The Heart Division, in consultation with the Quality and Safety team is responsible for ensuring that the local protocol is effective in identifying the risk of patients developing contrast-induced acute kidney injury (CI-AKI) and in ensuring that appropriate measures are taken to reduce these risks. It is expected that there will be appropriate local clinical audit following the introduction of the local protocol. The Heart Division will be responsible for ensuring that appropriate changes to the local protocol are made at the review date for this document.
2. GUIDELINES

2.1 Measurement of serum creatinine and estimation of GFR before undergoing angiography. Except in emergencies, all patients should have their serum creatinine measured and GFR estimated before undergoing angiography using iodinated contrast. For clinically stable outpatients the measurement should have been done in the last 2 months and a strategy for CI-AKI prevention planned in advance. For patients attending the pre-admission clinic this assessment will take place in the clinic 1-2 weeks prior to admission. For inpatients, the latest measurement, obtained during the current admission, should be used (see Appendix II for estimating GFR).

2.2 Pre-procedure hydration. When pre-procedural hydration is indicated to reduce the risk of developing CI-AKI (see appendix 1), intravenous sodium bicarbonate 1.26% should be administered at 3 ml/kg/hr for 1 hour prior to the procedure and 1 ml/kg/hr for 6 hours afterwards. In patients where this volume cannot be administered safely (e.g. heart failure), less vigorous hydration (e.g. 1 ml/kg/hr for 1 hour before procedure and 6 hours afterwards) may provide some protection. N-acetylcysteine (NAC) is no longer recommended.

2.3 Discontinuation of nephrotoxic drugs and metformin
Nephrotoxic drugs such as NSAIDs and aminoglycosides should be withheld on the day of the procedure wherever possible. Patients with eGFR > 60ml/min can continue taking metformin. In patients with eGFR < 60ml/min, metformin should be discontinued 48 hours prior to the procedure and for 48hrs afterwards.

2.4 Use of haemofiltration. Prophylactic haemofiltration may be considered in patients who are receiving treatment in intensive care who require angiography.

2.5 Use of contrast agents. Minimise the volume of contrast used where possible. A low-osmolarity contrast agent other than iohexol should be used and in high-risk situations, iodixanol (Visipaque) should be considered in addition to pre-hydration with Sodium Bicarbonate.

2.6 Assessment of the risk of CI-AKI. Measures to prevent CI-AKI should be planned prior to the procedure based on the risk profile of the patient and the procedure as described in the Trust’s current guideline and recorded in the patient notes.

2.7 Emergency procedures. For emergency procedures when the patient’s renal function is unknown and there are high risk features for CI-AKI (see table 1), the same measures apply to those with eGFR<60 ml/min (see appendix I). However a bolus dose of 0.5 ml/kg sodium bicarbonate 1.26% is recommended in place of the pre-procedure one hour infusion of 3ml/kg/hour used for planned procedures. Either iopromide (Ultravist 300) or iodixanol (Visipaque) should be considered.
2.8 **Post-procedure monitoring of renal function.** For patients at significant risk of CI-AKI, renal function should be monitored 48-72 hours after the procedure. In many cases this will need to be checked by the GP post discharge and arrangements to do this must be documented in the notes and communicated to the GP (see appendix III for GP letter).

3. **BACKGROUND INFORMATION**

3.1 **Contrast-Induced Acute Kidney Injury (CI-AKI)**

The administration of iodinated radiographic contrast media is often associated with a mild, transient and clinically benign decline in renal function. However, overt renal failure may occur and this is associated with considerable morbidity, a risk of mortality and a worsening of the patient’s long-term prognosis.

Fortunately, overt renal failure is a relatively infrequent event after contrast administration. CI-AKI is defined as a rise of serum creatinine of 44 μmol/l (0.5 mg/dL) or a 25% relative rise from baseline at 48 hrs following contrast.

The pathogenesis of CI-AKI is not completely understood. A decrease in glomerular filtration and renal blood flow play a role along with ischaemia in the renal medullar, generation of reactive oxygen species (ROS) and direct cellular toxicity from the contrast agent.

![CI-AKI: pathogenesis](image)

Most cases of CI-AKI are self-limiting with renal function returning to normal within 7 days of the procedure. However, severe renal impairment can necessitate renal replacement therapy and can lead to permanent renal injury.

When renal function deteriorates significantly, the pharmacokinetics of drugs that are excreted by the kidney will be changed. This is particularly important when the drug has a narrow therapeutic range (e.g. digoxin).
3.2 Clinical risk factors

A number of patient-related risk factors for CI-AKI have been defined (Table 1). In practice, the most important factors are advanced age, pre-existing renal dysfunction, diabetic kidney disease and heart failure.

<table>
<thead>
<tr>
<th>Table 1: Risk factors for Contrast-Induced Acute Kidney Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Advanced age (&gt; 75 years)</td>
</tr>
<tr>
<td>• Pre-existing renal impairment</td>
</tr>
<tr>
<td>• Diabetes with renal impairment</td>
</tr>
<tr>
<td>• Congestive heart failure</td>
</tr>
<tr>
<td>• Hypotensive or low cardiac output state</td>
</tr>
<tr>
<td>• Hypovolaemia</td>
</tr>
<tr>
<td>• Dehydration</td>
</tr>
<tr>
<td>• Diuretic therapy</td>
</tr>
<tr>
<td>• Nephrotoxic drug therapy (e.g. ciclosporin, tacrolimus,</td>
</tr>
<tr>
<td>aminoglycosides, NSAIDs)</td>
</tr>
<tr>
<td>• Proteinuria and nephrotic syndrome</td>
</tr>
<tr>
<td>• Multiple myeloma</td>
</tr>
<tr>
<td>• Sepsis</td>
</tr>
</tbody>
</table>

3.3 Procedural risk factors

The procedural risk should be considered high when it is anticipated that more than 150ml contrast will be used or when angiography must be repeated within 5 days (or a CT scan performed), or before the patient’s serum creatinine has returned to its baseline value.

3.4 Assessment of renal function to evaluate the clinical risk

Serum creatinine is an imperfect measure of renal function because it is affected by the patient’s muscle mass and therefore by factors such as age, sex, nutritional state and racial group. Glomerular filtration rate (GFR) is the best summary measure of renal function but direct measurement of GFR by clearance techniques is impractical for routine clinical use. GFR can be estimated using the Cockcroft and Gault formula (Appendix II), bearing in mind some of the limitations using this formula.

The National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative (KDOQI) classifies chronic kidney disease (CKD) according to the GFR (Table 2). There are five stages but kidney function is normal in Stage 1, and minimally reduced in Stage 2.
### Table 2: Stratification of chronic kidney disease by GFR

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>GFR ml/min/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

For the purpose of the trust guidelines and to enable identification of high risk patients and implementation of preventative measures, patients with eGFR > 60 ml/min are considered to have normal renal function, where as patients with eGFR < 60 ml/min are considered to have abnormal renal function and therefore high risk of CI-AKI.

### 3.5 Strategies for Prevention

Prevention is important as there is no specific treatment for CI-AKI. This involves the evaluation of potential risk factors and clinical assessment of the patient's volume status. It should also be considered whether alternative imaging could be utilised whenever a patient with CKD needs investigation, (e.g. magnetic resonance).

### 3.6 Discontinuation of nephrotoxic drugs

Nephrotoxic medications such as non-steroidal anti-inflammatory drugs and aminoglycosides should be withheld or avoided on the day of the procedure wherever possible. Currently there is insufficient evidence to support the routine discontinuation of angiotensin-converting enzyme inhibitors (ACE-I) or angiotensin receptor blockers (ARBs) in stable outpatients.

### 3.7 Pre-hydration

Pre-procedure hydration with intravenous fluids is the most effective method for reducing the risk of CI-AKI. Sodium chloride 0.9% or isotonic sodium bicarbonate 1.26% may be used and given peripherally. However sodium bicarbonate has the advantage that it can be given one hour before the procedure eliminating the need for admission the night before. Sodium bicarbonate is given at a rate of 3 ml/kg/hr for 1 hour prior to the procedure and 1 ml/kg/hr for 6 hours afterwards. If the first hour is completed and the patient has not had the procedure, the 6 hour post procedure infusion should be commenced. This can be continued in the lab during the procedure. The nursing staff should inform the lab and update the iplan accordingly. Patients prone to fluid overload such as those with decompensated heart failure (HF) may require slower infusion rate or less volume (e.g. 1 ml/kg/hr for 1 hour before procedure and 6 hours afterwards).
3.8 Haemofiltration

Haemofiltration is a complex therapy with major resource implications that has its own side effects and complications. It should not be used routinely for CI-AKI prevention. However, prophylactic haemofiltration may be considered in patients who are already receiving treatment in intensive care who require angiography.

3.9 Choice of contrast agent

Currently a low-osmolarity agent, iopromide (Ultravist 300) is the standard agent used for contrast angiography within the Trust. Iodixanol (Visipaque) is available for high-risk cases.

In all cases, volume of contrast used should be limited to that necessary to obtain the diagnostic information. Where multiple angiographic procedures are needed, the procedures should be separated as much as possible (ideally until the serum creatinine has returned to baseline after the first procedure).

3.10 Diabetics on metformin

Metformin is not nephrotoxic but it increases the risk of lactic acidosis in patients with CI-AKI. Patients with eGFR > 60ml/min can continue taking metformin\textsuperscript{14}.

In patients with eGFR < 60ml/min, metformin should be discontinued 48 hours prior to the procedure and for 48hrs afterwards. Renal function should be checked prior to restarting. The dose of metformin may need to be adjusted if eGFR remains low; for patients with eGFR 30-45ml/min the maximum recommended dose is 500mg BD and for patients with eGFR < 30ml/min, metformin should be discontinued and alternative therapy arranged.

3.11 Approach for emergency procedures

Whenever safe and practical, renal function should be assessed before the procedure and the precautions outlined above should be used.

When a procedure must be performed immediately (e.g. primary angioplasty) and the patient’s renal function is unknown, a blood sample should be taken to measure the patient’s serum creatinine retrospectively. In this circumstance, either iopromide (Ultravist 300) or iodixanol (Visipaque) should be used. If large volumes of intravenous fluids are required for maintaining stable haemodynamics, sodium chloride 0.9% or colloids should be used in preference to sodium bicarbonate. When the patient’s renal function is unknown and there are high risk features for CI-AKI a bolus dose of 0.5 ml/kg sodium bicarbonate 1.26% can be given instead of 3 ml/kg/hr for 1 hour. Following the bolus dose, a maintenance dose of 1 ml/kg/hr for 6 hours post procedure can be given.
3.12 Post procedure monitoring and care

High risk patients (eGFR < 60ml/min and/or multiple risk factors for CI-AKI – see table 1) should have post procedure measurement of serum creatinine between days 2 and 5. If the patient is to be discharged from hospital, the GP may do the test but the arrangements made must be clearly documented in the patient’s notes and communicated to the GP (see appendix III).

If the serum creatinine has not risen by more than 44 μmol/L or 25% relative rise from baseline at 48 hrs following the procedure, no further monitoring is required.

When drug therapy has been changed (metformin) arrangements for further treatment must be documented and communicated to the GP.
4. REFERENCES


APPENDIX I

Prevention of Contrast-Induced Acute Kidney Injury (CI-AKI) – Cardiology Protocol

The recommendations below are a summary of the Trust Guidelines for the Prevention of Contrast Induced Acute Kidney Injury (CI-AKI).

- All patients undergoing contrast studies should have their serum creatinine and eGFR calculated.
- Metformin – Discontinue 48 hours prior to procedure (patients with normal renal function (eGFR > 60ml/min) can continue taking metformin). Restart 48 hours post procedure, providing there is no evidence of CI-AKI.
- Avoid diuretics on the day of the procedure (if no CHF) and avoid NSAIDs and aminoglycosides wherever possible.

<table>
<thead>
<tr>
<th></th>
<th>eGFR &gt; 60ml/min</th>
<th>eGFR &lt; 60ml/min</th>
<th>eGFR unknown and high risk features for CI-AKI (Emergency procedure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid dehydration, encourage oral fluids</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Include risk of CI-AKI in consent</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Minimise volume of contrast used</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>IV hydration with Sodium Bicarbonate 1.26% as per protocol below</td>
<td>✓</td>
<td>✓</td>
<td>✓ (if large volumes are required, Sodium Chloride 0.9% or colloids should be used)</td>
</tr>
<tr>
<td>Consider use of Iodixanol (Visipaque®)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Check U&amp;E’s prior to discharge</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Where appropriate arrange repeat U&amp;E’s after 48-72 hours (at hospital or via GP)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Protocol for IV hydration pre-and-post procedure

Prescribe Sodium Bicarbonate 1.26% (500ml polyfusor) as below – inform the cath lab and record on iplan

- 3ml/kg/hr for 1 hour pre-procedure (for emergency procedures 0.5 ml/kg bolus)
- 1ml/kg/hr for 6 hours post procedure

If the first hour is completed, and the lab are not ready to receive the patient, then commence the 6 hour post-procedure infusion and patients can have their procedure with the infusion in situ.
## Methods for estimating Glomerular Filtration Rate (GFR)

### Formula

**Cockcroft and Gault equation**

\[
CrCl \text{ (ml/min)} = (140 - \text{age}) \times \text{weight (kg)} \times \text{constant (1.23 for men / 1.04 women)}
\]

Serum Creatinine

<table>
<thead>
<tr>
<th>Web Calculators</th>
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<tbody>
<tr>
<td><a href="http://www.renal.org/eGFRcalc/GFR.pl">http://www.renal.org/eGFRcalc/GFR.pl</a></td>
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<th>Mobile phone apps</th>
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<tr>
<td>MedCalc</td>
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<td>QxMD</td>
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Please note that all these formulas are inaccurate in patients with UNSTABLE renal function.
**APPENDIX III**

**Advice for patients discharged following a procedure requiring the administration of radiocontrast media**

**Additional monitoring of renal function required post discharge**

<table>
<thead>
<tr>
<th>U&amp;Es on admission</th>
<th>Na+</th>
<th>K+</th>
<th>Urea</th>
<th>Cr</th>
<th>eGFR</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>U&amp;Es on discharge</th>
<th>Na+</th>
<th>K+</th>
<th>Urea</th>
<th>Cr</th>
</tr>
</thead>
</table>

**Consultant:**

**Date of procedure:**

**Ward:**

Dear Doctor,

Your patient has been discharged from Harefield Hospital / Royal Brompton Hospital following a procedure which required the administration of radiocontrast media.

A record of pre and post procedure U&E’s are recorded above for your information. We would be grateful if you could arrange repeat U&E’s on …………………………… and alert the relevant consultant if there is a significant deterioration in renal function.

Many thanks,

…………………………

Signed

Date

…………………………

Name / Grade