



Prevention of Contrast Induced Acute Kidney Injury (CI-AKI) In Adult Patients

on behalf of

**The Renal Association,
British Cardiovascular Intervention Society and
The Royal College of Radiologists**

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Foreword

These guidelines have been developed by an intercollegiate working party of health professionals from The Renal Association, The Royal College of Radiologists and The British Cardiovascular Intervention Society to outline what is considered best practice for the administration of intravascular iodinated contrast agents to adults. We would like to thank the authors, Dr Andrew Lewington, Dr Robert MacTier, Dr Richard Hoefield, Dr Mark Downes, Dr Andrew Sutton and Dr David Smith.

These joint guidelines have been developed with direct input from The Royal College of Radiologists to ensure compliance with the *RCR Standards for intravascular contrast agent administration to adult patients, Second edition*.

Please note at the time of publication, NICE (The National Institute for Health and Clinical Excellence) are in the process of developing national clinical guidelines on acute kidney injury at present, which are due for publication in August 2013.

Introduction

The use of intravascular iodinated contrast agents has continued to increase over recent years. It is recognised that there are potential risks associated with the intravascular administration of iodinated contrast agents. It is, therefore, essential for the safe administration of iodinated contrast media, that those persons administering iodinated contrast media and those performing the imaging procedures have an understanding of the indications for use of iodinated contrast media as well as the potential side effects and their management.

We would encourage practitioners, wherever practicable, to adopt the current trend towards reduced doses of intravenous iodinated contrast media due to the benefit of modern dual-head pumps and fast CT scanners. At the time of publishing these guidelines, investigations into the potential of low-kVp, low iodinated contrast dose CT technique, were in progress.

These guidelines address the issues associated with administering iodinated contrast agents to adult patients only. For children and neonates a paediatric radiologist should be consulted.

1. Definition and Staging of Contrast Induced Acute Kidney Injury (CI-AKI)

Guideline 1.1 – Definition and Staging of CI-AKI

We suggest that the international Kidney Disease: Improving Global Outcomes (KDIGO) *definition* of contrast induced - acute kidney injury (CI-AKI) should be adopted. (Not Graded)

Contrast induced - acute kidney injury is defined when one of the following criteria is met

- Serum creatinine rises by $\geq 26\mu\text{mol/L}$ within 48 hours **or**
- Serum creatinine rises ≥ 1.5 fold from the baseline value, which is known or presumed to have occurred within one week **or**
- urine output is $< 0.5\text{ml/kg/hr}$ for >6 consecutive hours

If a baseline serum creatinine is not available within 1 week the lowest serum creatinine value recorded within 3 months of the episode of AKI can be used

If a baseline serum creatinine value is not available within 3 months and AKI is suspected

- repeat serum creatinine within 24 hours
- a reference serum creatinine value can be estimated from the nadir serum creatinine value if patient recovers from AKI

Rationale

Acute kidney injury following receipt of iodinated contrast (CI-AKI) has previously been referred to as contrast induced nephropathy (CIN) defined as a rise in serum creatinine by 25% or $44\mu\text{mol/L}$ from the baseline value. It is uncommon in the general population, with an incidence of 1-2%, and occurs within 72 hours of receiving contrast media, usually recovering over the following five days.¹ It is important to exclude other causes of AKI as small rises in serum creatinine have been demonstrated to occur in 8-35% of patients admitted to hospital without exposure to contrast media.² Its incidence increases significantly in patients with risk factors and is associated with increased mortality.³

The adoption of the Kidney Disease: Improving Global Outcomes (KDIGO) international guideline definition will provide the opportunity to standardise the nomenclature used to define AKI and stage its severity.⁴ The definition will rely predominantly on rises in serum creatinine rather than reductions in urine output in a phenomenon that is rarely oliguric in nature. A universal definition will allow the collection of epidemiological data and the standardisation of future research on the prevention and treatment of CI-AKI.

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Guideline 1.2 – Definition and Staging of CI-AKI

We suggest that the international Kidney Disease: Improving Global Outcomes (KDIGO) *staging classification** of acute kidney injury (AKI) should be adopted. (Not Graded)

Stage	Serum creatinine (Cr) criteria	Urine output criteria
1	increase $\geq 26 \mu\text{mol/L}$ within 48hrs <u>or</u> increase ≥ 1.5 - to 1.9 X baseline Cr	<0.5 mL/kg/hr for > 6 consecutive hrs
2	increase ≥ 2 to 2.9 X baseline Cr	<0.5 mL/kg/ hr for > 12 hrs
3	increase ≥ 3 X baseline Cr <u>or</u> * increase $\geq 354 \mu\text{mol/L}$ <u>or</u> commenced on renal replacement therapy (RRT) irrespective of stage	<0.3 mL/kg/ hr for > 24 hrs or anuria for 12 hrs

* must have met initial criteria for definition of AKI

Audit measure

1. Incidence and severity of patients developing contrast induced AKI (CI-AKI)

Rationale

The application of both the Acute Dialysis Quality Initiative (ADQI) RIFLE and Acute Kidney Injury Network (AKIN) staging systems to patient populations have demonstrated that as the stage of AKI increases so does the risk of mortality.¹⁻³ Acute kidney injury staging can be performed using serum creatinine or urine output criteria (Table 1). Patients should be staged according to whichever criteria (serum creatinine or urine output) gives them the highest stage and only after they have been identified as meeting the criteria for the definition of AKI.

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2. Risk Assessment for Contrast Induced Acute Kidney Injury (CI-AKI)

Guideline 2.1 – Risk Assessment for CI-AKI

We suggest that prior to any imaging using iodinated contrast media baseline kidney function and presence of other risk factors for CI-AKI should be identified. The exception to this is when the benefit of very early imaging outweighs the risk of delaying the procedure. (Not Graded)

Guideline 2.2 – Risk Assessment for CI-AKI

We suggest that estimated glomerular filtration rate (eGFR) should only be used to assess kidney function in stable outpatients. (Not Graded)

Guideline 2.3 – Risk Assessment for CI-AKI

We suggest that serum creatinine is used to assess kidney function in acutely ill patients or patients with acute kidney injury. All such patients should be considered as at increased risk of CI-AKI. (Not Graded)

Guideline 2.4 – Risk Assessment for CI-AKI

We suggest that patients identified to be at high risk of CI-AKI may be discussed with a renal physician to assess whether the potential benefit from the iodinated contrast study outweighs the increased risk of CI-AKI. (Not Graded)

Audit measure

1. Proportion of patients developing contrast induced AKI (CI-AKI) who did not have baseline kidney function assessed

Rationale

The risk of CI-AKI is low in patients with normal kidney function, estimated at 1-2% even in patients with diabetes.¹ However prior exposure to iodinated contrast media has been identified as the third most common aetiological factor for AKI in hospital after renal hypoperfusion and nephrotoxic medication.² The risk of CI-AKI has been reported to be as high as 25% in patients with a combination of chronic kidney disease (CKD) and diabetes, cardiac failure, older age and exposure to nephrotoxic drugs.³ The CI-AKI Consensus Working Panel has recommended that the risk of CI-AKI becomes clinically important with an eGFR < 60 ml/min/1.73m².⁴ Acutely ill patients with sepsis and/or hypotension are particularly vulnerable to injury following iodinated contrast exposure. There is a general consensus that the risk of CI-AKI is higher after arterial compared to venous administration of iodinated contrast media although this has not been proven convincingly.

Risk factors for patients developing CI-AKI include

- chronic kidney disease (CKD) eGFR < 60 ml/min/1.73m²
- older age (> 75 years old)
- cardiac failure
- nephrotoxic medication
 - aminoglycosides
 - NSAIDs
 - Amphotericin B
- hypovolaemia
- sepsis
- volume (dose) of contrast
- intra-arterial administration

It should be appreciated that often a number of these risk factors will be present together in a patient, and that there is currently no validated CI-AKI risk assessment available to recommend. The use of the estimated glomerular filtration rate (eGFR) to quantify kidney function should only be applied to patients with stable kidney function and should not be used in patients with AKI. Patients identified as at high risk of CI-AKI may be discussed with a renal physician to assess the individual risk/benefit associated with a specific contrast procedure. In some patients the risk of CI-AKI is outweighed by the potential benefit from

the contrast study. It is recommended that these risks are explained to the patient in the context of the potential benefit of proceeding with the study. Imaging should not be delayed where the benefit of early imaging clearly outweighs the risk of waiting.

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3. Strategies to Prevent Contrast Induced Acute Kidney Injury (CI-AKI)

Guideline 3.1 – Strategies to Prevent CI-AKI

We suggest that unenhanced scanning or alternative imaging techniques should be considered in patients with risk factors for developing CI-AKI. (Not Graded)

Guideline 3.2 – Strategies to Prevent CI-AKI

We recommend intravenous volume expansion with 0.9% sodium chloride or isotonic sodium bicarbonate in patients identified as at high risk of CI-AKI (Grade 1A)

Guideline 3.3 – Strategies to Prevent CI-AKI

We suggest that the lowest possible volume of a low or iso-osmolar iodinated contrast medium should be used in patients with risk factors for developing CI-AKI. (Not Graded)

Guideline 3.4 – Strategies to Prevent CI-AKI

We recommend that there is no convincing benefit for prescribing oral or intravenous N-acetylcysteine or any other pharmacological agents to prevent CI-AKI. (Grade 2D)

Audit measure

- Proportion of patients receiving iodinated contrast that did not have risk factors for contrast induced AKI (CI-AKI) assessed

Rationale

Contrast induced - AKI results from a combination of afferent arteriolar vasoconstriction and direct toxicity of the contrast media to the tubular epithelial cells. Prevention is important as there is no specific treatment and involves identification of patients at increased risk of CI-AKI.¹ It should also be considered whether alternative imaging could be utilised such as ultrasound or whether carbon dioxide can be used to reduce the amount of iodinated contrast agent required.²

Magnetic resonance angiography (MRA) may be considered as an alternative but the use of gadolinium (Gd) in MRA is associated with the risk of developing Nephrogenic Systemic Fibrosis (NSF). Nephrogenic Systemic Fibrosis is a severe fibrosis of the skin resulting in extensive limitation in mobility. The condition has been reported rarely in patients usually with dialysis requiring CKD or AKI who have received Gd-

containing contrast agents. The European Society of Urogenital Radiology has produced NSF guidelines with further advice issued from the European Medicines Agency.^{3,4}

Potentially nephrotoxic medications such as non-steroidal anti-inflammatory drugs and aminoglycosides should be withheld or avoided. 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.⁵ However in acutely ill patients at an increased risk of developing AKI it is suggested that withholding ACE-I and ARBs should be considered on an individual patient basis.

Metformin is not nephrotoxic but is exclusively excreted via the kidneys. Therefore patients on metformin who develop AKI following contrast are at risk of developing lactic acidosis due to the accumulation of the drug. The Royal College of Radiologists recommends that there is no need to stop metformin after receiving iodinated contrast if the serum creatinine is within the normal range and/or eGFR > 60 ml/min/1.73m². If serum creatinine is above the normal reference range or eGFR is < 60 ml/min/1.73m², any decision to stop it for 48 hours should be made in consultation with the referring clinician.⁶

Acutely ill patients and patients who are identified at high risk of CI-AKI should have an assessment of their volume status and receive appropriate volume expansion prior to the procedure. Intravenous 0.9% sodium chloride at a rate of 1 mL/kg/hour for 12 hours pre- and post- procedure has been shown to be more effective than 0.45% sodium chloride in reducing CI-AKI.⁷ More recently it has been demonstrated that intravenous isotonic sodium bicarbonate significantly reduces the risk of CI-AKI.^{8,9} Subsequently there have been a number of studies that have compared intravenous isotonic sodium bicarbonate to intravenous 0.9% sodium chloride.^{10,11} Systematic reviews and meta-analyses have provided conflicting conclusions and have recognised a significant degree of heterogeneity and publication bias. It is currently recommended that either intravenous 0.9% sodium chloride or isotonic sodium bicarbonate should be used for volume expansion in patients at risk of CI-AKI.^{12,13} Oral volume expansion has not been shown to be as effective as intravenous volume expansion.

It is generally accepted that high osmolar contrast media should be avoided in patients at risk of CI-AKI.¹⁴ More controversial is the debate regarding whether iso-osmolar contrast media is safer than low-osmolar contrast media in patients at risk of CI-AKI. Currently there is only one type of iso-osmolar media which has failed to demonstrate any clear benefit compared to different low-osmolar media in preventing CI-AKI¹⁵. There is a need for better designed head to head studies between the different contrast media to allow any clear recommendations in the future.

The volume of contrast media should be minimised and further exposure to contrast media should be delayed until full recovery of renal function unless absolutely necessary.¹⁶ Renal function should be checked up to 48-72 hours following the procedure in a high risk group to ensure stable renal function.

Following the seminal paper demonstrating the beneficial effects of N-acetylcysteine in preventing CI-AKI there has been a multitude of publications which have been subject to a number of meta-analyses.¹⁷ These meta-analyses have commented on the heterogeneity of the studies making a definitive conclusion difficult.^{18,19} Most recently a large randomized trial found that acetylcysteine does not reduce the risk of contrast-induced acute kidney injury or other clinically relevant outcomes in at-risk patients undergoing coronary and peripheral vascular angiography.²⁰ Currently there is no compelling evidence for the routine use of N-acetylcysteine to prevent CI-AKI.

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