



Standards for intravascular contrast administration to adult patients

Third edition

Faculty of Clinical Radiology

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RCR Standards

The Royal College of Radiologists (RCR), a registered charity, exists to advance the science and practice of radiology and oncology.

It undertakes to produce standards documents to provide guidance to radiologists and others involved in the delivery of radiological services with the aim of improving the service for the benefit of patients by defining best practice, and promoting advances in practice.

The standards documents cover a wide range of topics. All have undergone an extensive consultation process to ensure a broad consensus, underpinned by published evidence where applicable. Each is subject to review four years after publication or earlier if appropriate.

The RCR has committed to reviewing all relevant publications in line with the recommendations of the Francis report and, where appropriate, applying the category of standard defined by Francis (fundamental, enhanced or developmental).¹ This document contains standards that fall within the enhanced category.

The standards are not regulations governing practice but attempt to define the aspects of radiological services and care which promote the provision of a high-quality service to patients.

All of the standards produced by the RCR can be found on the College website www.rcr.ac.uk/standards

Francis classification of RCR Standards

- Fundamental standards of minimum safety and quality in respect of which non-compliance should not be tolerated. Failures leading to death or serious harm should remain offences for which prosecution can be brought against organisations. There should be a defined set of duties to maintain and operate an effective system to ensure compliance.
- Enhanced quality standards: such standards could set requirements higher than the fundamental standards, but would be discretionary matters for commissioning and subject to availability of resources.
- Developmental standards which set longer term goals for providers: these would focus on improvements in effectiveness and are more likely to be the focus of commissioners.¹

Foreword

These revised guidelines are necessary because of the ever-changing literature about both iodinated contrast media and gadolinium-based contrast agents (GBCAs). The RCR would like to thank the original authors, Professors Sameh Morcos and Peter Dawson, along with Dr Mark Downes, Dr Giles Roditi, Dr Andrew Lewington (Renal Association) and Dr Grant Baxter, who were largely responsible for this revision. The RCR would also like to thank the members of the Professional Support and Standards Board (PSSB) who made significant contributions.

This document replaces *Standards for intravascular contrast administration to adult patients, second edition* (BFCR[10]4) and *Gadolinium-based contrast media and nephrogenic systemic fibrosis* (BFCR[07]14) which have been withdrawn. These standards fall within the enhanced category as defined by the Francis report, see RCR Standards (page 2).¹

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Current standards documents

Standards for the provision of an ultrasound service

Standards of practice of computed tomography coronary angiography (CTCA) in adult patients

Cancer multidisciplinary team meetings – standards for clinical radiologists, Second edition

Standards for Learning from Discrepancies meetings

Standards for radiofrequency ablation (RFA), Second edition

Standards for patient confidentiality and PACS and RIS

Standards for the communication of critical, urgent and unexpected

significant radiological findings, Second edition

Standards for patient consent particular to radiology, Second edition

Standards of practice and guidance for trauma radiology in severely injured patients

Standards and recommendations for the reporting and interpretation of imaging investigations by non-radiologist medically qualified practitioners and teleradiologists

Standards for the NPSA and RCR safety checklist for radiological interventions

Standards for the provision of teleradiology within the United Kingdom

Standards for the recording of second opinions or reviews in radiology departments

Standards for a results acknowledgement system

Standards for providing a 24-hour diagnostic radiology service

Standards for providing a 24-hour interventional radiology service

Standards for Self-assessment of Performance

Standards for the Reporting and Interpretation of Imaging investigations

Standards for Ultrasound Equipment

Recommended standards

Standard 1

An individual trained in recognising and treating severe contrast reactions, including anaphylaxis, should be immediately available in the department where contrast is administered.

Standard 2

A formal record of the decision to inject intravascular contrast should be made before administration.

Standard 3

The individual administering the contrast must check that there are no contraindications to its use and ensure that the patient understands that it is to be given and agrees to the procedure.

Standard 4

In cases where there is a previously reported moderately severe or severe reaction to intravascular contrast, caution should be exercised and the need for the use of contrast should be re-examined with respect to an unenhanced study or other potential methods of investigation.

Standard 5

For elective examinations in patients who have a history of previous contrast reaction, consideration should be given to referral to a specialist drug allergy service for assessment and testing against a panel of contrast compounds to determine the safety of administration.

Standard 6

The dose of non-ionic iodine-based contrast medium should be minimised, taking into consideration the indication and the patient's body weight.

Standard 7

GBCAs deemed to be high-risk in regard to their association with the development of nephrogenic systemic fibrosis (NSF) are contraindicated in patients with severe chronic or acute renal impairment, patients in the peri-operative liver transplantation period and in neonates.

Standard 8

When using GBCAs, renal function must be known for all patients receiving agents deemed as high risk. Knowledge of renal functional status is also generally advisable for patients receiving agents classed as medium risk.

Standard 9

Significant suspected contrast reactions should be formally documented with full details, investigated appropriately with advice given to the patient and referral made to a specialist drug allergy service to help guide future management.

1. Introduction

The use of intravascular contrast in radiology continues to increase. The potential risks of intravascular administration of contrast must be weighed against the potential benefits. Withholding contrast may deprive patients of the benefits of valuable diagnostic information or necessary therapy. This document aims to provide guidance on how intravascular contrast may be used as safely as possible.

This document deals with administration of intravascular contrast to adult patients. For children and neonates, a paediatric radiologist should be consulted.

2. General safety issues

Non-ionic, low or iso-osmolar iodinated media are five to ten times safer than the older, high osmolar ionic contrasts.²

Both low osmolar iodinated media and GBCAs are associated with a very low rate of adverse events (0.15% for low osmolar iodine contrast and 0.04% for gadolinium contrast).³

Most adverse events are mild and can be managed in the radiology department.³

A major life-threatening contrast reaction is rare. The incidence of severe reactions with non-ionic contrast media is 0.04% and very serious reactions is 0.004%.^{2,3} For GBCAs, the severe adverse reaction rate is even lower, estimated to be 0.0025%.⁴

To minimise risk, it is important to identify individuals at an increased risk of an adverse event.

Appropriate steps to reduce the risk of contrast reactions should always be taken.

3. Practical safety issues

An individual trained in recognising and treating severe contrast reactions, including anaphylaxis, should be immediately available in the department. This could be a registered nurse or radiographer or other appropriately trained healthcare professional.

There should be systems in place to call an appropriately trained doctor who can deal immediately with a severe contrast reaction. If required, this may include a crash team.

In the presence of risk factors, the decision about contrast administration should only be taken by the radiologist responsible for the procedure. This decision process should include the location of the proposed examination with reference to resuscitation capability.

In view of the risk of contrast nephrotoxicity, dehydration of patients before contrast administration is undesirable and should be avoided.

Facilities for the treatment of acute adverse reactions should be readily available and regularly checked within the department.

A patient should not be left alone or unsupervised in the first five minutes after an injection of any intravascular contrast.

It is advisable that the patient remains on the premises for at least 15 minutes following the injection. Most severe reactions occur during this time. In patients at increased risk of a reaction, this should be increased to 30 minutes.

All contrast reactions, with details of their nature, severity and the specific compound used, should be included in the radiological report, updated in the patient's hospital notes and on the radiology information system (RIS).

Standard 1

An individual trained in recognising and treating severe contrast reactions, including anaphylaxis, should be immediately available in the department where contrast is administered.

4. Prescribing contrast

A formal record of the decision to inject intravascular contrast should be made before administration. How this is achieved will depend on local circumstances, but may include:

- Setting up a patient group directive to cover specific scan protocols
- A formal written record by the radiologist, signed and dated on the request and either filed in the radiology department or scanned into the RIS
- Recording the decision electronically, directly into the RIS as part of the vetting and protocol assignment process
- A formal prescription on the patient's drug chart.

Standard 2

A formal record of the decision to inject intravenous contrast should be made before administration.

5. Patient information and consent

The patient should always be fully informed about any procedure and understand what it will involve. Appropriate patient information leaflets should be available in the department. The individual administering the contrast must check that there are no contraindications to its administration and ensure that the patient understands that it is to be given and agrees to proceed.

Standard 3

The individual administering the contrast must check that there are no contraindications to its use and ensure that the patient understands that it is to be given and agrees to the procedure.

6. Identifying patients at increased risk from contrast administration

The ultimate responsibility for intravascular contrast administration rests with the person who prescribes it, although delivery of the injection is frequently delegated to others under local rules and protocols.

Essential information which should be sought from the patient before a contrast injection includes history of:

- Previous contrast reaction
- Asthma
- Renal problems
- Diabetes mellitus
- Metformin therapy.

Ideally, this information will be available when the examination is requested but should always be checked in the department before injection.

7. Recommendations for contrast use in patients at increased risk

History of previous contrast reaction

Caution should be exercised when there is a previously reported moderately severe (such as bronchospasm or urticaria requiring treatment) or severe reaction (for example, laryngeal or angioneurotic oedema, severe bronchospasm or collapse) to intravascular contrast.^{5,6}

Advice

Determine:

- The exact nature of the previous reaction
- The specific compound used on that occasion.

Re-examine the need for the use of contrast, with respect to an unenhanced study or other potential methods of investigation.

Assess the risk–benefit ratio of the procedure, bearing in mind that a non-diagnostic examination may be as or more detrimental to the patient than the perceived risk from contrast exposure.

For elective examinations, consider referral to a specialist drug allergy service for assessment and testing of the patient against a panel of contrast compounds to determine the safety of administration.

If the injection is deemed necessary:

- Use a different contrast compound to that previously used (preferably one that has been tested and shown to be safe)
- Maintain close medical supervision

- Leave the cannula in place and keep the patient under observation for 30 minutes after the procedure
- Be ready to treat any adverse reaction promptly and ensure that emergency drugs and equipment are available.

Asthma

Asthmatics are at an increased risk of severe contrast reactions by a factor of six with low or iso-osmolar non-ionic contrast and by a factor of ten with high osmolar contrast.²

Advice

Determine:

- Whether the patient has true asthma or chronic obstructive pulmonary disease (COPD)
- Whether the asthma is currently well controlled.

If the patient is wheezy or reports that their asthma is currently not well controlled, and the examination is not urgent, it should be deferred and the patient referred back for appropriate medical therapy.

If the asthma is well controlled, reassess the need for intravascular contrast with respect to an unenhanced study or other potential methods of investigation.

If the injection is deemed necessary:

- For iodine contrast, use a non-ionic low or iso-osmolar compound
- Maintain close medical supervision
- Leave the cannula in place and observe the patient for 30 minutes after the procedure
- Be ready to treat any adverse reaction promptly and ensure that emergency drugs and equipment are available.

Multiple allergies or a documented severe allergy requiring therapy

Individuals with multiple well-documented allergies or a single very severe allergy are at increased risk.^{2,5,6}

Advice

Determine the nature of the allergies and their sensitivity. (NB: there is no specific cross reactivity with shellfish or topical iodine in acute contrast reactions.)

In those with multiple or severe allergies, re-examine the need for contrast administration with respect to an unenhanced study or other potential methods of investigation. For elective examinations, consult with a specialist drug allergy service for testing the patient against a panel of contrast compounds to determine safety of administration.⁷

The potential risks of intravascular administration of contrast must be weighed against the potential benefits.

If the injection is deemed necessary:

- For iodine contrast, use a non-ionic low or iso-osmolar compound
- Maintain close medical supervision
- Leave the cannula in place and observe the patient for 30 minutes after the procedure
- Be ready to treat any adverse reaction promptly and ensure that emergency drugs and equipment are available.

There is no conclusive evidence of benefit for the prophylactic use of steroids in the prevention of severe reactions to contrast.^{5,6}

Renal disease, diabetes mellitus and conditions associated with renal impairment

In the presence of renal impairment, all contrast – including non-ionic low osmolar, iso-osmolar media and high-volumes of GBCAs – are nephrotoxic.

Previous terminology such as contrast nephrotoxicity, contrast-induced nephropathy (CIN) or radiocontrast nephropathy (RCN) have been replaced by contrast-induced acute kidney injury (CI-AKI), in line with other causes of acute kidney injury.^{8,9} (See Appendix 1 for a definition of CI-AKI).

Risk factors for acute kidney injury in adults receiving iodinated contrast media

Increased risk is associated with:

- Chronic kidney disease (adults with an estimated glomerular filtration rate [eGFR] of less than 40 millilitres [ml]/minute [min]/1.73 m² are at particular risk)
- Heart failure
- Renal transplant
- Age 75 years or older
- Hypovolaemia
- Increasing dose of contrast or repeated administration of contrast
- Intra-arterial administration of contrast.^{8,9}

To minimise the risk of CI-AKI, joint guidance from the Renal Association, British Cardiovascular Intervention Society (BCIS) and the RCR recommends that eGFR should be available for all non-emergency patients.¹⁰ For patients who are in a stable clinical condition, an eGFR within the previous three months is satisfactory.

In practice, many units ask patients under the age of 70 the question 'Do you have diabetes, high blood pressure, heart failure or any kidney problems, kidney failure or have you ever been on dialysis?' If the patient's answer is anything other than an unequivocal 'no', and for all patients due to receive intra-arterial contrast, an eGFR is mandated. However, asking such a question allows a busy unit to proceed with contrast without recourse to blood results if the patient replies 'no' to all these points.

Patients who have an acute illness or who are known to have renal disease should have an eGFR or, preferably, serum creatinine estimations obtained from the previous seven days, which can be assessed against a baseline.

Particular care should be taken in patients who are acutely or severely unwell, such as with hypotension or hypovolaemia. In these cases, scans are likely to be carried out on an urgent or emergency basis and the potential risks of contrast use must be weighed against the potential benefits.

Further preventative strategies should include offering intravenous volume expansion to patients at risk of CI-AKI.

In the presence of acute illness, volume expansion regimes can include the use of isotonic sodium bicarbonate or 0.9% sodium chloride.

Consideration should be given to temporarily stopping angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) in the presence of chronic kidney disease with an eGFR less than 40 ml/min/1.73 m² (see Appendix 2 for chronic kidney disease stages).¹¹

Early involvement by a nephrology team has been shown to be

beneficial in patients at significant risk of CI-AKI.

There is insufficient evidence at this stage to advocate any pharmacological treatment attempting to reduce the incidence of CI-AKI prophylactically.

The dose of non-ionic iodine-based contrast medium should be minimised, taking into consideration the indication and the patient's body weight.

For computed tomography (CT) angiographic studies, the efficiency of the iodine-based contrast medium should be maximised by using a saline flush (this aids peak enhancement and also helps volume expansion/hydration) and minimising applied tube kilovoltage (this also minimises radiation dose).¹²

A hydration regime should be maintained post contrast administration.

Metformin

Metformin is not recommended for use in diabetics with renal impairment because it is excreted exclusively via the kidneys. Accumulation of metformin may result in the development of lactic acidosis – a serious complication. There is a lack of any valid evidence that lactic acidosis is really an issue after administration of iodinated contrast media in patients taking metformin. The problems caused to patients and clinicians by stopping the drug and its increasing use in poorly controlled diabetic patients regardless of renal function have been considered when formulating this advice. It does, however, remain the case that renal function should be known in patients taking metformin who require intravenous or intra-arterial iodinated contrast medium administration.

Advice

There is no need to stop metformin after contrast in patients with serum creatinine within the normal reference range and/or eGFR >60 ml/min/1.73 m². If serum creatinine is above the normal reference range or eGFR is below 60, any decision to stop metformin for 48 hours following contrast medium administration should be made in consultation with the referring clinic.

Standard 4

In cases where there is a previously reported moderately severe or severe reaction to intravascular contrast, caution should be exercised and the need for the use of contrast should be re-examined with respect to an unenhanced study or other potential methods of investigation.

Standard 5

For elective examinations in patients who have a history of previous contrast reaction, consideration should be given to referral to a specialist drug allergy service for assessment and testing against a panel of contrast compounds to determine the safety of administration.

Standard 6

The dose of non-ionic iodine-based contrast medium should be minimised, taking into consideration the indication and the patient's body weight.

8. Other special cases

Pregnancy

Where iodinated contrast is administered during pregnancy, due to the small theoretical risk of thyroid suppression in the fetus, thyroid function should be measured in the first week after birth.¹³

Lactation

A very small percentage of the injected dose enters the breast milk and virtually none is absorbed across the normal gut, hence no special precaution or cessation of breastfeeding is required.¹³

Thyroid

Intravascular contrast should not be administered if the patient is hyperthyroid. In patients with thyroid cancer, the use of iodinated contrast media will preclude therapeutic radio-iodine treatment for two months.¹⁴ Magnetic resonance imaging (MRI) is the preferred staging method in these patients.

Isotope thyroid imaging should also be avoided for two months after intravascular administration of iodinated contrast.¹⁵

Interleukin-2 treatment

A specific risk of delayed skin rash is associated with interleukin-2 therapy. Oncologists should be informed that they should always indicate if the patient is on this drug when referring them for a contrast injection.¹⁶

9. Gadolinium-based contrast agents

GBCAs are remarkably safe, with a lower adverse event rate for both allergic type reactions and nephrotoxicity. However, their administration in patients with severe renal failure has been associated with the development of the very rare condition nephrogenic systemic fibrosis (NSF). See advice below to minimise this risk from GBCAs in the following vulnerable groups:

- Patients with renal impairment
- Patients in the perioperative liver transplantation period
- Infants, neonates and the elderly
- Women who are pregnant or breastfeeding.

NSF is an extremely rare but serious and potentially life-threatening condition characterised by the deposition of collagen in the skin which becomes thickened, coarse and hard, sometimes leading to contractures and joint immobility. Patients with NSF can have systemic involvement of other organs, including the lungs, liver, muscles and heart. The cause of NSF is not fully understood but the consensus is that it is associated with the administration of gadolinium contrast agents (particularly linear chelates) in patients with severe renal impairment. A diagnosis of NSF is based on a combination of clinical and pathological criteria (see Appendix 3).¹⁷ The RCR published guidance on GBCAs and NSF soon after this association was first identified in 2007.¹⁸ While in most instances of NSF, the onset of symptoms can be identified to be from the day of exposure to two or

three months later, it is now recognised that clinical manifestations may present years later, the reasons for and mechanisms underlying this are not understood currently.¹⁹

Some GBCAs have been much more associated with the development of NSF than others. The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has classified these as low, medium and high risk (see Appendix 4 for details).^{20,21}

The EMA's Scientific Advisory Group on Diagnostics concluded that the cyclic products (the three products with the lowest risk) can be used for patients with severely reduced renal function when a contrast enhanced MRI scan is clearly the best method of examination. They did not recommend contraindicating the use of these GBCAs in patients with renal impairment because, in some cases, there are no alternatives, although dose should be limited to the minimum consistent with the investigation being carried out. This classification has not been revised since initial publication but remains appropriate as research continues to reinforce the association of cases of NSF, both unconfounded and confounded in nature, with the use of the high-risk classified linear chelates (see Appendix 5 for definitions of confounded and unconfounded cases).^{11,22,23}

High-risk GBCAs are contraindicated in patients with severe chronic or acute renal impairment, patients in the perioperative liver transplantation period and in neonates.

Advice

The following risk minimisation measures should be used for GBCAs. This advice is adapted from the current Medicines and Healthcare products Regulatory Agency (MHRA) advice.²⁴

Renal function monitoring

Renal function should be tested in all patients receiving high-risk agents and is generally advisable for patients receiving medium-risk agents. It is particularly important to screen patients aged 65 years or older and patients with chronic diseases, such as diabetes, which are associated with renal failure.

Renal impairment

For patients with severe chronic renal impairment (eGFR <30 ml/min/1.73 m²) or acute renal impairment, use of a high-risk agent is contraindicated. If, after clinical review, use of a low-risk agent is appropriate or if it is necessary to use a medium-risk agent, a single lowest dose possible can be used (a dose not exceeding 0.1 millimoles [mmol]/kilogram [kg] body weight) and should not be repeated for at least seven days.

Avoid administering GBCAs in acute kidney injury while creatinine is rising.²⁵

For patients with moderate chronic renal impairment (eGFR 30–59 ml/min/1.73 m²), if, after clinical review, it is necessary to use a high-risk agent, a single lowest dose possible should be used and should not be repeated for at least seven days.

Perioperative liver transplantation period

Use of a high-risk agent is contraindicated for patients in the perioperative liver transplantation period. If the use of a low-risk agent is required, or if it is necessary to use a medium-risk agent, a single lowest dose possible can be used and should not be repeated for at least seven days.

Breastfeeding

Breastfeeding should be discontinued for at least 24 hours after use of a high-risk agent. The decision as to whether to continue or suspend breastfeeding for 24 hours after use of a medium-risk or low-risk agent should be at the clinician's discretion in consultation with the mother.

Pregnancy

Use of any GBCA is not recommended during pregnancy unless absolutely necessary.

Haemodialysis

There is no evidence to support the initiation of haemodialysis for prevention or treatment of NSF in patients not already undergoing haemodialysis, as emergency initiation of dialysis entails significant risks. However, those patients already established on dialysis should be dialysed promptly after contrast administration (certainly within 24 hours).²⁶

Recording of the agent used

When they are available, 'peel-off' tracking labels found on the vials, syringes or bottles should be stuck onto or scanned into the patient record to maintain an accurate note of the name and batch of the gadolinium contrast agent used. The dose used should also be documented.

Suspected adverse reactions should be reported on a Yellow Card to the MHRA.²⁷

Standard 7

GBCAs deemed to be high-risk in regard to their association with the development of NSF are contraindicated in patients with severe chronic or acute renal impairment, patients in the perioperative liver transplantation period and in neonates.

Standard 8

When using GBCAs, renal function must be known for all patients receiving agents deemed as high risk. Knowledge of renal functional status is also generally advisable for patients receiving agents classed as medium risk.

10. The treatment of reactions

Simple guidelines for the treatment of reactions are presented below.^{28,29}

Nausea/vomiting

- *Transient*: supportive treatment
- *Severe, protracted*: appropriate anti-emetic drugs should be considered.

Urticaria

- *Scattered, transient*: supportive treatment, including observation
- *Scattered, protracted*: appropriate H1-antihistamine orally or intramuscularly should be considered. Drowsiness and/or hypotension may occur
- *Profound*: consider adrenaline 1:1000, 0.1–0.3 ml (0.1–0.3 milligrams [mg]) intramuscularly. Repeat, as needed.

Bronchospasm

- Oxygen by mask (6–10 litre [l]/min)
- β -2-agonist metered dose inhaler (2–3 deep inhalations)
- Adrenaline:
 - Elevate patient's legs
 - *Normal blood pressure*: adrenaline 1:1000, 0.1–0.3 ml (0.1–0.3 mg) intramuscularly. Use smaller dose in a patient with coronary artery disease or elderly patient

- Decreased blood pressure: adrenaline 1:1000, 0.5 ml (0.5 mg) intramuscularly.

Laryngeal oedema

- Oxygen by mask (6–10 l/min)
- Adrenaline 1:1000, 0.5 ml (0.5 mg) intramuscularly. Repeat as needed.

Hypotension

- Isolated hypotension
 - Oxygen by mask (6–10 l/min)
 - Intravenous fluid: rapidly, normal saline or lactated Ringer's solution
 - If unresponsive: adrenaline 1:1,000, 0.5 ml (0.5 mg) intramuscularly. Repeat as needed.
- Vagal reaction (hypotension and bradycardia)
 - Elevate patient's legs
 - Oxygen by mask (6–10 l/min)
 - Atropine 0.6–1.0 mg intravenously, repeat if necessary. After 3–5 min, to 3 mg total (0.04 mg/kg)
 - Intravenous fluids: rapidly, normal saline or lactated Ringer's solution.

Generalised anaphylactic reaction

- Call for resuscitation team
- Suction airway if needed
- Elevate patient's legs if hypotensive
- Oxygen by mask (6–10 l/min)
- Adrenaline: 1:1000, 0.5 ml (0.5 mg) intramuscularly
- H1 blocker, for example, diphenhydramine 25–50 mg intravenously.

Recording and investigation of significant suspected contrast reactions

- For anaphylaxis (severe multisystem reaction) or for severe urticaria or angioedema without systemic features, record details of the incident with a description in the report and notes, including generic and proprietary names of the contrast used plus batch number
- For anaphylaxis, take blood samples for mast cell tryptase in line with recommendations in *Anaphylaxis: assessment to confirm an anaphylactic episode and the decision to refer after emergency treatment for a suspected anaphylactic episode*³⁰
- Discuss the patient's suspected contrast reaction with them and their carers, if appropriate, and provide written information
- Arrange referral to a specialist drug allergy service to help guide future management
- Suspected adverse reactions should be reported on a Yellow Card to the MHRA.²⁷

Contrast medium extravasation

- Record details of the incident with management advice in the report and notes
- Elevate the affected limb
- Apply ice packs to the affected area
- If symptoms resolve such that an outpatient can be allowed home, supply the patient with an appropriate advice leaflet
- If symptoms do not resolve quickly, admit and monitor

- Skin blistering, paraesthesiae, altered tissue perfusion and increasing or persistent pain for more than four hours suggest severe injury. In this case, seek surgical advice (plastic surgeon).^{31–33}

Delayed skin reactions

- Skin reactions have been reported up to a week after the administration of contrast medium, more commonly with dimeric iodine-based contrast media.¹⁵ Symptomatic treatment only is required. The reaction should be noted in the patient's record, but it is the case that the status and significance of these reactions are uncertain.

Standard 9

Significant suspected contrast reactions should be formally documented with full details, investigated appropriately with advice given to the patient and referral made to a specialist drug allergy service to help guide future management.

11. Conclusion

The use of intravascular contrast has become fundamental to modern radiology and the compounds used in daily practice are extremely safe. However, as our knowledge expands regarding the potential to prevent and risk manage adverse events associated with the use of intravascular contrast, so it is appropriate that guidance is revised and standards are set for safe administration. This most recent revision to the RCR guidance builds upon earlier work. The main areas of change are:

- The nomenclature and definitions in relation to contrast-induced acute kidney injury (CI-AKI)
- A focus on maintaining hydration of patients at risk of CI-AKI and minimising the dose of intravascular contrast used for any individual patient taking into account patient factors, the indication for the examination and technical scan parameters
- Clearer identification of patients at risk and explicit documentation of adverse events when they occur (preferably with the use of electronic record systems such as RIS/picture archiving and communication systems [PACS]) such that patients are better prepared for future imaging investigations.

The intention of this standards document is to clarify those factors that should be taken into account for the prevention and treatment of adverse events related to the use of intravascular contrast. Compliance with the proposed standards should translate directly into high-quality care for the many patients referred to departments of radiology for diagnostic imaging and image guided intervention.

Approved by the Clinical Radiology Faculty Board: 30 October 2014.

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Appendix 1. Contrast-induced acute kidney injury

CI-AKI is defined when one of the following criteria is met.

- Serum creatinine rises by ≥ 26 micromoles (μmol)/l within 48 hours
- Serum creatinine rises ≥ 1.5 fold from the baseline value, which is known or presumed to have occurred within one week
- Urine output is <0.5 ml/kg/hour for more than six consecutive hours.

If a baseline serum creatinine is not available within one week, the lowest serum creatinine value recorded within three months of the episode of AKI can be used.

If a baseline serum creatinine value is not available within three 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 the patient recovers from AKI.

Appendix 2. Chronic kidney disease stages¹¹

Chronic kidney disease (CKD) stage	GFR ml/min/1.73 m ²	Description
1	90+	Normal kidney function but urine findings or structural abnormalities or genetic trait point to kidney disease
2	60–89	Mildly reduced kidney function, and other findings (as for stage 1) point to kidney disease
3A 3B	45–59 30–44	Moderately reduced kidney function
4	15–29	Severely reduced kidney function
5	<15 or on dialysis	Very severe or end-stage kidney failure (sometimes called established renal failure)

Appendix 3. Clinical features and clinicopathological definition of NSF

Clinical features of NSF

Initial presentation

- Pain
- Pruritus
- Swelling
- Erythema
- Usually starts in the legs.

Later results

- Thickened skin and subcutaneous tissues – ‘woody’ texture and brawny plaques
- Fibrosis of internal organs; for example, muscle, diaphragm, heart, liver, lungs
- Contractures
- Cachexia
- Death, in a proportion of patients.

At-risk patients

Higher risk

- Patients with chronic kidney disease (CKD) 4 and 5 (Appendix 2) (glomerular filtration rate [GFR] <30 ml/min/1.73 m²)
- Acute renal failure
- Patients on dialysis
- Patients with reduced renal function who have had or are awaiting liver transplantation.

Lower risk

- Patients with CKD 3 (GFR 30–59 ml/min/1.73 m²)
- Children under one year (immature renal function).

Notes:

1. No cases of NSF have been reported in patients with GFR greater than 60 ml/min/1.73 m² and it appears that those few cases reported with estimated GFR above 30 were actually in acute renal failure in which estimated GFR is inappropriate.
2. The role of various possible co-factors in the pathogenesis of NSF is not proven but there are suspicions that both hyperphosphataemia and the use of erythropoietin may have a bearing.
3. In the absence of specific information, it remains wise to manage pregnant patients, whatever their renal function, in the same way as children aged less than one year, to protect the fetus.

Clinicopathological definition of NSF (Girardi criteria)¹⁷

The diagnosis of NSF is made with a combination of clinical and pathological scoring. For the clinical score there are major criteria (patterned plaques, joint contractures, cobblestoning and marked induration/peau d'orange) and minor criteria (skin puckering/banding, superficial NSF, dermal papules and scleral plaque in patients aged over 45). A clinical score is then summated with:

>1 Major – Highly consistent = 4

1 Major – Consistent = 3

>1 Minor – Suggestive = 2

0–1 – Minor = 1

Another diagnosis = 0

The pathology score follows a similar system for which the interested reader can find details in the referred original article.²⁷

Pathology/clinical	0	1	2	3	4
0	Alternative diagnosis (Dx)				
1		Not NSF	Not NSF		Inconsistent
2			Suggestive	Consistent	
3			Consistent	NSF	
4		Inconsistent			

Appendix 4. European Medicines Agency classification of gadolinium-based contrast agents^{20,21}

NSF risk category	Generic name	Trade name	T1 specific relaxivity in blood at 1.5 T – mmol ⁻¹ s ⁻¹	Notes
High	Gadodiamide	Omniscan	4.6	Non-ionic linear chelate, contraindicated when GFR <30ml/min/1.73 m ² . Incidence of NSF – triggering agent, estimated 3–7% in at-risk subjects (624 unconfounded cases – 2009 data).
	Gadopentate dimeglumine	Magnevist	4.3	Ionic linear chelate, contraindicated when GFR <30 ml/min/1.73 m ² . Incidence of NSF – triggering agent, estimated to be 0.1–1% in at risk subjects (221 unconfounded cases – 2014 data).
	Gadoversetamide	Optimark	5.2	Non-ionic linear chelate, contraindicated when GFR <30 ml/min/1.73 m ² . Incidence of NSF – triggering agent, no clear data but five reported cases, likely similar incidence to gadodiamide to which it is chemically related. Limited use in European Union (EU).
Medium	Gadobenate dimeglumine	MultiHance	6.7	Ionic linear chelate, 2–3% protein binding, significant hepatic excretion. Incidence of NSF – no unconfounded cases with MultiHance criteria.
	Gadofosveset trisodium	Ablavar (previously Vasovist)	19.0	Ionic linear chelate, strong albumin binding for blood-pool contrast, significant hepatic excretion, not currently commercially available in EU. Incidence of NSF – one unconfounded report unclear as to whether meets Girardi criteria.
	Gadoxetate disodium	Primovist	8.7	Ionic linear chelate, 10% protein binding and 50% hepatic excretion. Incidence of NSF – no reports of NSF.
Low	Gadobutrol	Gadovist	5.3	Non-ionic cyclic chelate. Incidence of NSF – four unconfounded reports unclear as to whether meet Girardi criteria.
	Gadoterate meglumine	Dotarem	4.2	Ionic cyclic chelate. Incidence of NSF – no unconfounded reports.
	Gadoteridol	Prohance	4.4	Non-ionic cyclic chelate. Incidence of NSF – single unconfounded report unclear as to whether meets Girardi criteria.

Appendix 5. Definitions of confounded and unconfounded cases of contrast reaction

Unconfounded:	In 'unconfounded' cases only one GBCA had been given before development of NSF.
Confounded:	If two different GBCAs had been injected within eight weeks of each other (maybe longer), it is impossible to determine with certainty which agent triggered the development of NSF and the situation is described as 'confounded'. However, the agent that is most likely responsible is the one which has triggered NSF in other unconfounded situations.
Triggering agent:	To be described as an NSF triggering agent, there must be at least 5–10 NSF cases, validated by adequate documentation including deep skin biopsy, following exposure to a GBCA.

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