RANZCR GUIDELINES FOR

IODINATED CONTRAST ADMINISTRATION

March 2009
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1. Introduction

This document contains guidelines for radiologists using iodinated contrast media and may be used by such radiologists in performing imaging examinations and associated procedures requiring the use of iodinated contrast.

These guidelines were developed by the Standards of Practice and Accreditation Committee of The Royal Australian and New Zealand College of Radiologists (‘RANZCR’). The RANZCR acknowledges with appreciation the advice received from the Australian and New Zealand Society of Nephrologists and Kidney Health Australia in the development of these guidelines.

These guidelines are general guidelines. In developing the guidelines the RANZCR has not considered the specific medical requirements of individual patients or the practise of individual radiologists in administering or supervising iodinated contrast.

The RANZCR recommends that each radiologist:

1. administering or supervising the administration of iodinated contrast should consider each patient’s individual situation and clinical requirements;
2. should review and consider the specific contrast or pharmaceutical manufacturer’s recommendations in regard to dose and clinical contraindications; and
3. should review and consider any other relevant information available.

The RANZCR does not assume liability for patient management decisions by individual radiologists resulting from the use of the information contained in this guide.

Feedback

The RANZCR welcomes feedback on these guidelines. If you wish to provide feedback, please send this in writing to:

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2. General Safety Issues

Any radiological examination requiring administration of iodinated contrast involves the risk of an adverse contrast reaction. While most reactions are minor, life-threatening and fatal reactions may occur without warning. It is essential to minimize the risk of contrast reactions and to be prepared to appropriately treat any reactions which may occur. The risk of a contrast reaction should always be carefully weighed against the benefit expected to be obtained from a contrast enhanced imaging examination.

a. Intravenous Access and Contrast Administration

The task of obtaining intravenous access for administering intravenous contrast can be performed by a medical practitioner, or delegated to a radiographer or nurse who is trained in venepuncture and the administration of contrast.

Written protocols may be used to identify when intravenous contrast is to be administered. If written protocols are used, these shall identify the dose and type of iodinated contrast to be administered, and determine the situations when the radiologist supervising the procedure is to be contacted.

Equipment used for administering iodinated contrast should be appropriate for its use.

A medical practitioner must be immediately available to attend to the patient in the event of an emergency or complication of contrast injection.

A patient should not be left alone or unsupervised in the first ten minutes after injection of the iodinated contrast agent.

It is advisable that the patient remains on the premises for at least 15 minutes after iodinated contrast administration as most severe reactions occur within this time period. This should be increased to 30 minutes in patients at increased risk of a reaction.

b. Emergency Equipment

Resuscitation equipment and medications for the treatment of complications of iodinated contrast administration shall be immediately available.

c. Training

Nurses and radiographers who perform venepuncture for contrast administration shall be trained in venepuncture, and have received certification of their competence. This training and certification may be performed by the radiology practice.

Nurses, radiographers and medical practitioners who administer intravenous contrast shall be trained in the recognition of contrast reactions, the procedures for treating these reactions, and resuscitation procedures.

Nurses, radiographers and medical practitioners who administer intravenous contrast shall also be trained in CPR.
3. Patient Information and Consent

The doctor has a duty to warn the patient of material risks inherent in the injection of contrast. The patient must be provided with sufficient information to allow them to make an informed choice of whether or not to accept the risks of proposed iodinated contrast administration. This enables the patient to make an informed decision regarding their future.

The doctor bears the burden of deciding whether the patient is capable of understanding. A patient who is not legally competent cannot give valid consent. This applies to several categories of patients including children, intellectually disabled, mentally ill and the obtunded or unconscious.

Children over the age of sixteen are able to consent to iodinated contrast administration, and may likewise refuse contrast administration.

Unconscious patients, and those in emergency situations where urgent diagnosis or treatment are needed to save life or avoid serious harm, are a special category. In these situations the interests of the patient are paramount. It would be advisable that the doctor obtain a second opinion where possible.

The doctor is entitled to delegate the responsibility of obtaining consent, but in doing so must ensure the patient is properly advised.

Documentation of the risks discussed and the patient’s consent is advisable. This may consist of a standard information and consent form which is signed by the patient.
4. Contrast Reactions

a. Acute contrast reactions
Acute adverse reactions to iodinated contrast manifest within 60 minutes of injection of contrast medium.

The majority of acute, non-renal, adverse contrast reactions are thought to be idiosyncratic (anaphalactoid) or "pseudoallergic". They are not dose dependant and do not involve antibodies to contrast media. Histamine release, along with other active biological mediators such as serotonin, prostaglandins, bradykinin, leukotrienes, adenosine and endothelin has been implicated. They may be classified as mild, moderate or severe.

Mild reactions include flushing, nausea, pruritus, vomiting, headache and mild urticaria. They are usually self limited and resolve without specific treatment. Mild reactions may be seen in up to 3% of patients after non-ionic low-osmolality contrast agent administration.

Moderate contrast reactions include severe vomiting, marked urticaria, bronchospasm, facial/laryngeal oedema and vasovagal attacks.

Severe contrast reactions include hypovolaemic shock, respiratory arrest, cardiac arrest, pulmonary oedema and convulsions. Severe reactions are uncommon, occurring in 0.04% to 0.004% of non-ionic low omolar iodinated contrast injections. (i.e. 1 in 2,500 to 1 in 25,000 contrast injections). The risk of death is rare (1 in 170,000).

The current non-ionic, low osmolar iodinated contrast agents are in the order of 5 to 10 times safer, in terms of mild to moderate reactions, than the older, high osmolar ionic agents. There is not sufficient data available to assess the relative risk of severe reactions).

b. Delayed contrast reactions
Late adverse contrast reactions occur between one hour and one week after intravascular iodinated contrast administration. These are typically skin reactions with a maculopapular rash being most common. Less frequent skin reactions include angioedema, urticaria and erythema. Delayed contrast reactions are not typically associated with bronchospasm or laryngeal oedema.

The incidence of reported late adverse reactions varies in the literature but is likely to be 4% or less. There is an increased incidence of late reactions to iodinated contrast in patients who have received interleukin-2 (IL-2). The effectiveness of premedication with corticosteroids in reducing the incidence of recurrent delayed contrast reaction is unknown.

c. Patients at increased risk for an adverse reaction to iodinated contrast
In order to minimize the risk of iodinated contrast administration, the medical imaging department should have systems in place to identify individuals at increased risk for adverse reactions to iodinated contrast.

Information which should be obtained before contrast administration includes:

- History of a previous reaction to iodinated contrast agents or history of allergy requiring medical treatment
- History of asthma
• History of renal disease or conditions predisposing to renal impairment such as:
  − Previous renal surgery
  − Diabetes Mellitus
  − Proteinuria
  − Hypertension
  − Gout
  − Recent nephrotoxic drugs (eg. Aminoglycosides, NSAIDs, etc)
  − Dehydration, Cardiac Failure

• Current drugs which may cause adverse reactions in association with iodinated contrast:
  − Metformin
  − β-adrenergic blockers

• Other medical conditions which are associated with adverse reactions to iodinated contrast
  − Hyperthyroidism
  − Sickle cell disease (homozygous) may develop crisis although the risk is very low with nonionic contrast.
  − Myasthenia Gravis symptoms may be worsened with ionic contrast but the risk with nonionic contrast is thought to be low.

This information may be obtained by specific questions on the radiology request form, at the time of booking the examination, or by a specific questionnaire completed prior to the examination. The information should also be checked with the patient immediately prior to contrast administration.

The medical imaging request form should include space for the referring clinician to document the patient’s most recent eGFR (or serum creatinine) if this information is available.

i. Previous moderate or severe reaction to iodinated contrast agents.

There is a six fold increase in reactions to both ionic and non-ionic contrast media following a previous adverse reaction. The likelihood of a recurrent reaction has been reported to be in the order of 8% to 60%.

Guideline
• Evaluate the nature of any previous contrast reaction and the contrast agent used at the time of the reaction.
• Consider performing a non-contrast study or use of alternative imaging modalities which do not require administration of iodinated contrast (e.g. ultrasound, MRI). In some situations an alternative contrast agent (e.g. gadolinium for CT arthrography or carbon dioxide for angiography) may be useful.

If, after considering the risks of a recurrent contrast reaction and the potential benefits of the procedure, it is decided to proceed with the contrast-enhanced study -

• Use a non-ionic contrast agent
• Use a different, non-ionic low or iso-osmolar agent to that previously used.
Maintain close medical supervision
Leave the cannula in place and keep the patient under observation for 30 minutes after contrast administration
Ensure emergency drugs and equipment for resuscitation are readily available
Be prepared to treat any adverse reaction promptly.
Consider use of premedication

While safe for the majority of patients, the medical literature supporting the routine use of premedication in patients with a prior contrast reaction is limited.

Several older studies have shown premedication with steroids and antihistamines reduce the risk of anaphylactoid reactions to ionic contrast media. There is as yet no convincing evidence that premedication with corticosteroids or antihistamines reduces the incidence of severe acute reactions to non-ionic contrast.

If premedication is used, it must be administered at least 6 hours prior to the contrast study.

A typical premedication regime for adults is:

− Prednisolone 50mg orally, given at 13 hours and 1 hour before contrast administration.
− Diphenhydramine 50mg orally given 1 hour before contrast.

Because Diphenhydramine (or alternative antihistamines) can cause drowsiness, the patient should make arrangements to be driven to and from the examination.

ii. Multiple allergies

A history of multiple allergies requiring medical treatment is associated with a 3 to 5 fold increase in the risk of an acute reaction to iodinated contrast. Most such reactions are mild.

Shellfish allergy is not associated with an increased risk of adverse reaction to intravenous iodinated contrast agents, over and above the 3-fold increased risk associated with other food allergies.

Skin irritation or “allergy” to topical iodine antiseptic solutions is not associated with an increased risk of adverse reaction to intravenous iodinated contrast.

Guideline

Consider performing a non-contrast study or use of alternative imaging modalities which do not require administration of iodinated contrast (e.g. ultrasound, MRI).

If, after considering the risks of a contrast reaction and the potential benefits of the procedure, it is decided to proceed with the contrast enhanced study -

− Use a non-ionic low or iso-osmolar contrast agent.
− Maintain close medical supervision
− Leave the cannula in place and keep the patient under observation for 30 minutes after contrast administration
− Ensure emergency drugs and equipment for resuscitation are readily available
− Be prepared to treat any adverse reaction promptly.
• Consider use of premedication

iii. Asthma

Patients with a history of asthma experience a 6 to 10 times increased risk of severe contrast reactions.

**Guideline**

*If, after considering the risks of a contrast reaction and the potential benefits of the procedure, it is decided to proceed with the contrast enhanced study:*

• Use a non-ionic low or iso-osmolar contrast agent.
• Maintain close medical supervision
• Leave the cannula in place and keep the patient under observation for 30 minutes after contrast administration
• Ensure emergency drugs and equipment for resuscitation are readily available
• Be prepared to treat any adverse reaction promptly.
5. Treatment of contrast reactions

Mild

**Nausea / Vomiting**
Supportive measures (antiemetics if prolonged vomiting)

**Urticaria (mild)**
Supportive measures

**Urticaria (protracted)**
Antihistamine (oral or intramuscular depending on severity)

Moderate

**Marked Urticaria**
- Antihistamines
- Consider use of Adrenaline 1:1000
  - In adults 0.1-0.25ml (0.1-0.25mg) intramuscularly – repeat as necessary
  - In children 0.01 mg/kg intramuscularly up to 0.3mg maximum dose

**Bronchospasm**
1. Oxygen by mask (6-10 l/min)
2. β-2-agonist (e.g. Salbutomol or Terbutaline) metered dose inhaler (2-3 deep inhalations).
   - In more severe cases, give Salbutamol or Terbutaline by nebuliser.
3. Consider Adrenaline
   - Normal blood pressure
     - In adults: 1:1,000, 0.1-0.25 ml (0.1-0.25 mg) intramuscularly
     - [use smaller dose in patients with coronary artery disease or elderly patients]
     - In paediatric patients: 0.01 mg/kg up to 0.3 mg max intramuscularly
   - Decreased blood pressure
     - In adults: 1:1,000, 0.5 ml (0.5 mg) intramuscularly
     - In paediatric patients: 0.01 mg/kg intramuscularly

**Hypotension**
- Isolated hypotension
  1. Elevate patient’s legs
  2. Oxygen by mask (6-10 l/min)
  3. Intravenous fluid: rapidly, normal saline or lactated Ringer’s solution
  4. If unresponsive: adrenaline: 1:1,000 , 0.5 ml (0.5 mg) intramuscularly, repeat as needed
- Vaso-vagal reaction (hypotension and bradycardia)
  1. Elevate patient’s legs
  2. Oxygen by mask (6-10 l/min)
  3. Atropine
    - In adults 0.6-1.0 mg intravenously, repeat if necessary after 3-5 min, to 3 mg total (0.04 mg/kg).
– In paediatric patients give 0.02 mg/kg intravenously (max. 0.6 mg per dose) repeat if necessary to 2 mg total.
4. Intravenous fluids: rapid infusion of normal saline or Hartmann’s solution 20 ml/kg, repeat as necessary.

**Severe**

**Generalized anaphylactoid reaction**

1. Stop contrast injection
2. Call for resuscitation team
3. Suction and maintain airway as needed
4. Oxygen by mask (6 – 10 l/min)
5. Intramuscular adrenaline, intramuscularly into the lateral thigh

In adults (and in children >25 kgs), Adrenaline 1:1,000

- < 50 kg give 0.25 – 0.5 mL
- > 50 kg give 0.5 mL

In children, Adrenaline 1:1,000

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>10 kg</td>
<td>0.1 mL</td>
</tr>
<tr>
<td>3 years</td>
<td>15 kg</td>
<td>0.15 mL</td>
</tr>
<tr>
<td>5 years</td>
<td>20 kg</td>
<td>0.2 mL</td>
</tr>
<tr>
<td>8 years</td>
<td>25 kg</td>
<td>0.25 mL</td>
</tr>
</tbody>
</table>

- If necessary, repeat intramuscular dose every 5 minutes.
- Large doses of adrenaline may be needed, up to a maximum of 5 mL (5 mg).
- If the patient remains shocked after two intramuscular doses, consider an adrenaline infusion to restore blood pressure. (See notes 3,4).

6. Intravenous fluids (e.g. normal saline or Hartmann’s solution 20mL/kg). Continue as necessary
7. Ventilate patient if severe respiratory and circulatory collapse
8. Additional measures:

<table>
<thead>
<tr>
<th>Bronchodilators</th>
<th>Corticosteroids</th>
<th>Nebulised adrenaline</th>
</tr>
</thead>
<tbody>
<tr>
<td>For bronchospasm, give salbutamol or terbutaline by nebuliser, or aerosol with spacer device.</td>
<td>Hydrocortisone 2-6mg/kg or Dexamethasone 0.1-0.4 mg/kg intravenously</td>
<td>May be tried for laryngeal oedema (5ml of 1:1,000)</td>
</tr>
</tbody>
</table>
9. Supportive measures

Observe vital signs frequently, and, if possible, monitor ECG and pulse oximetry.

Arrange for transfer to hospital if reaction occurs in an outpatient facility.

Keep under observation for at least 4-6 hours after complete resolution of signs and symptoms, as biphasic reactions may occur.

Notes:

1. Adrenaline is life-saving and must be used promptly. Withholding adrenaline due to misplaced concerns of possible adverse effects can result in deterioration and death of the patient.

2. Adrenaline 1:1000 contains 1000 microgram in 1 mL (1 mg/mL). The volumes of adrenaline recommended for adults and children approximate to 5 to 10 microgram/kg. Children's weights are approximate for age.

3. If critical care facilities are not immediately available, give the following adrenaline infusion:
   - Mix 1 mg adrenaline (1 ampoule) in 1000 mL of normal saline
   - Start infusion at 5 mL/kg/hour (approx. 0.1 microgram/kg/minute)
   - Titrate rate up or down according to response.

4. Some cases are resistant to adrenaline, especially if the patient is taking beta blocking drugs. If adequate doses of adrenaline are not improving the situation, give glucagon 1 to 2 mg intravenously over 5 minutes.

5. Drug-assisted intubation for impending airway obstruction is a very high-risk procedure and should only be attempted by an expert.

6. Corticosteroids may modify the overall duration of a reaction and may prevent relapse. However, onset of action will be delayed. Never use these to the exclusion of adrenaline.
6. Contrast Extravasation

Extravasation of contrast material into the subcutaneous tissues is uncommon, occurring in less than 1% of intravenous injections. It occurs more frequently in association with power injectors in comparison to hand injection of contrast. There is no correlation between the rate of contrast injection and the frequency of extravasation.

Risk factors include use of small veins, fragile or previously damaged veins, obesity, high osmolar contrast agents and large volume contrast injections.

Guideline:
- The risk of contrast extravasation may be reduced by:
  - Use of an appropriately sized vein in relation to contrast injection rate (flow rate)
  - Use of appropriate plastic cannula rather than scalp vein needle
  - Testing of the cannula with saline to ensure it is satisfactorily located within the vein prior to contrast administration
  - Direct visual monitoring of the injection site during the injection where possible
  - Use of non-ionic contrast

Most contrast extravasation injuries are minor. Uncommonly, severe injury may occur including cutaneous ulceration, tissue necrosis or compartment syndrome

Guideline:
- Conservative treatment is adequate for most cases of contrast extravasation. This includes:
  - Limb elevation
  - Cold or warm compresses
  - Monitor for complications including compartment syndrome
  - Surgical review if serious injury or developing compartment syndrome
7. Renal disease

Contrast induced nephropathy (CIN) is usually defined as impairment in renal function (measured by an increase in serum creatinine of more than 25%) occurring within 3 days following intravascular administration of a contrast agent, in the absence of an alternative etiology. In most patients with CIN, renal impairment is maximal 3 days following contrast administration, and spontaneously recovers over a period of 14 days. A few patients progress to established renal failure and dialysis dependence (this proportion is much higher in those with multiple pre-existing risk factors and/or severe renal impairment).

Risk factors for contrast induced nephropathy include:

- pre-existing CKD (chronic kidney disease), particularly secondary to diabetic nephropathy
- dehydration
- sepsis or hypotension
- cardiovascular disease (including congestive heart failure, hypertension)
- age over 60 years (18% of patients > age 60 have GFR < 60)
- nephrotoxic drugs (e.g. aminoglycosides, loop diuretics, ACE inhibitors, angiotensin II antagonists, NSAIDS, cyclosporine and cisplatin etc)
- organ transplantation, chemotherapy
- multiple myeloma, proteinuria, hyperuricaemia

Contrast induced nephropathy is more likely to occur with large doses of contrast (greater than 125mls), repeated doses within 72 hours, high osmolality agents, and with intra-arterial (rather than intravenous) administration.

The medical imaging department must have in place a protocol to identify patients at increased risk for contrast-induced nephropathy prior to performing contrast enhanced examinations.

It is not practical to routinely measure serum creatinine or eGFR levels in all patients prior to injection of iodinated contrast. Most patients at risk for developing CIN can be identified by clinical assessment of the risk factors listed above.

This information may be obtained by specific questions on the radiology request form, at the time of booking the examination, or by a specific questionnaire completed prior to the examination. The information should also be checked with the patient immediately prior to contrast administration.

Serum creatinine measurement is an imperfect tool for identifying patients with renal impairment as the level of serum creatinine is dependent on muscle mass and is not normally raised until the glomerular filtration rate has fallen by more than 50%. Estimated glomerular filtration rate (eGFR) is a better measure of renal function as it takes into account patient age and sex.
The MDRD formula is one of many formulas used to estimate eGFR and is currently used by pathology labs in Australia and NZ:

\[
eGFR = 175 \times ([SCR/88.4]^{1.154} \times (age)^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African-American})
\]

\(eGFR\) = estimated glomerular filtration rate (mL/min/1.73m\(^2\)), \(SCR\) = serum creatinine concentration (μmol/L)

An automated calculator for MDRD-based eGFR can be found at <http://www.kidney.org.au>.

Australian pathology laboratories routinely provide an eGFR figure whenever a serum creatinine level is reported. Formula based eGFR’s are not valid at extremes of body weight, in patients with liver disease and in patients with a changing creatinine. The MDRD formula has not been validated in children and in some ethnic groups including indigenous Australians, Maori and Pacific Islanders.

The following classification of chronic kidney disease from the USA National Kidney Foundation K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease describes the relationship between eGFR levels and chronic kidney disease stages.

<table>
<thead>
<tr>
<th>eGFR (mL/min)</th>
<th>Chronic Kidney Disease (CKD) Stage</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 90</td>
<td>1</td>
<td>Kidney damage (albuminuria, haematuria or abnormal kidney imaging)</td>
</tr>
<tr>
<td>60 - 90</td>
<td>2</td>
<td>Kidney damage</td>
</tr>
<tr>
<td>30 – 59</td>
<td>3</td>
<td>Moderate kidney failure</td>
</tr>
<tr>
<td>15 - 29</td>
<td>4</td>
<td>Severe kidney failure</td>
</tr>
<tr>
<td>&lt; 15</td>
<td>5</td>
<td>End stage kidney disease requiring dialysis or transplant</td>
</tr>
</tbody>
</table>

In the general Australian community, about 16% of adults aged over the age of 25 have at least one indicator of CKD (proteinuria or reduced kidney function).

Patients with an eGFR >60 mL/min are at very low risk of CIN. The risk is low to moderate for patients with an eGFR between 30–60 mL/min and is greatest for patients with an eGFR < 30mL/min. Patients with an eGFR < 15 have end-stage renal failure and are usually on dialysis.

In patients with a history of renal impairment, and in those with one or more risk factors, a recent eGFR measurement is recommended.

This should be obtained -
- within the previous 3 months in stable outpatients
- within the previous 7 days in inpatients with stable renal function
- In patients where the serum creatinine is rising, GFR cannot be estimated from a serum creatinine level and nephrology advice should be sought regarding assessment and management prior to contrast administration. Serum creatinine may take 7-10 days to stabilize after renal injury.
A recent eGFR measurement is also recommended within the previous 7 days for examinations requiring intra-arterial contrast administration or high volumes (greater than 125mls) of contrast.

**Guideline:**
- The decision to administer iodinated contrast to a patient with renal disease should be made in consultation with the patient’s referring doctor or renal physician.
- For patients in stage 3 CKD (eGFR 30-60mL/min), consider performing a noncontrast study or use of alternative imaging modalities which do not require administration of iodinated contrast (e.g. ultrasound, MRI).
- For patients in stage 4 CKD (eGFR 15-29mL/min), consider ultrasound as a noncontrast –requiring imaging modality. MR may also be appropriate provided the guidelines for MR use in advanced CKD are adhered to in order to minimize the risk of the development of nephrogenic systemic fibrosis.

If, after considering the risks of contrast induced nephropathy and the potential benefits of the procedure, it is decided to proceed with the contrast enhanced study:
- Ensure the patient is well hydrated before and after the procedure. Fluid volume loading is the most important protective measure. This is best achieved in high risk patients with intravenous fluids (e.g. normal saline infusion at 1ml/kg body weight/hr or 100 mls/hour for 6 hours pre and post-procedure). Oral fluid loading of 1 litre pre-procedure is appropriate in lower risk outpatients. Those with cardiac failure and those on dialysis should not receive fluid loading.
- Nephrotoxic medications should be discontinued 48 hours prior to the study.
- Use the smallest volume of contrast possible while still maintaining diagnostic image quality. Avoid repeat contrast injections within 72 hours.
- Use iso-osmolar or low-osmolar contrast. High osmolar contrast should be avoided in patients with renal impairment.
  - For **intravenous** injections, there is currently no convincing evidence of lower risk with iso-osmolar agents, compared to low-osmolar agents.
  - For **intra-arterial injection in high-risk patients**, iso-osmolar agents appear to carry a lower risk than some low-osmolar agents, but it has not been established that this applies to all low-osmolar agents; available evidence suggests no difference in risk between iso-osmolar and several low osmolar agents.
- Monitor renal function 48hrs after contrast administration.
- Communication between the radiologist and referring doctor, or the patient’s general practitioner, is recommended to assist with management of fluid loading, withholding of nephrotoxic drugs prior to contrast administration and to arrange reassessment of renal function 48 hours following contrast administration.
- Consider consulting renal physician, particularly for patients with eGFR < 30 mL/min.
- Consider use of N-acetylcysteine. There are mixed reports regarding the benefits of N-acetylcysteine in preventing contrast induced nephropathy; but as yet, the evidence is not convincing. Currently there are no proven pharmacological agents that have been consistently shown to reduce the risk of CIN and some strategies (e.g. mannitol and frusemide) have been shown to
increase risk. The only strategy that has been definitively proven to reduce the risk of CIN is IV hydration.

**Dialysis**

Iodinated contrast agents are readily cleared by dialysis. In patients on haemodialysis, fluid overloading should be avoided by limiting the dose of contrast, and by the use of low osmolar or iso-osmolar agents. Unless there is significant underlying cardiac dysfunction, or very large volumes of contrast used, there is no need to schedule dialysis to immediately follow contrast administration.
8. Drugs which may cause adverse reactions in association with iodinated contrast

Metformin

Metformin is an oral hypoglycaemic drug used in the treatment of Type II diabetes mellitus. It is excreted unchanged by the kidneys and is not metabolized by the liver. It is recommended that the dose of metformin should be reduced when the GFR is between 30-60mL/min and its use is not recommended when the GFR is <30ml/min.

Lactic acidosis is a rare but serious metabolic complication which can occur due to metformin accumulation in patients with renal impairment. The risk of lactic acidosis increases with the degree of renal dysfunction and the patient's age. Lactic acidosis is a medical emergency and must be treated in hospital immediately. Symptoms include vomiting, somnolence, nausea, epigastric pain, anorexia, hyperpnea, lethargy, diarrhea and thirst. The diagnosis is confirmed by demonstration of acidosis and an elevated lactate level on biochemical testing.

Patients receiving intravascular iodinated contrast may experience an acute deterioration in renal function leading to metformin accumulation and potential lactic acidosis. There is no evidence for a direct interaction between metformin and iodinated contrast agents. The absolute risk of lactic acidosis is low but when it occurs, it is fatal in approximately 50% of cases.

Guideline

- Communication between the radiologist and referring doctor, or the patient’s general practitioner, is required to arrange reassessment of renal function, management of diabetic control and recommencement of Metformin.
- In diabetic patients taking metformin, consider the risks of lactic acidosis and the potential benefits of the procedure.
- In patients with normal renal function (see Section 7 of these Guidelines), Metformin does not need to be stopped providing that a moderate amount of contrast is used (≤100ml) which would be unlikely to result in contrast induced nephropathy in the patient. There is no need to retest the renal function.
- In patients with renal impairment, Metformin should be withheld for at least 48hrs commencing on the day of the contrast study. Renal function should be reassessed before recommencing Metformin.

B-adrenergic blockers

The incidence of anaphylactoid reactions to iodinated contrast, particularly bronchospasm, is increased in patients taking β-blockers.

These reactions may also be more difficult to treat as Adrenaline is less effective in patients receiving β-blockers.
9. Pregnancy

There is no evidence that iodinated contrast agents are teratogenic in humans. On the other hand, there is very limited evidence to conclude that they are entirely safe. It is therefore wise to avoid administering iodinated contrast agent to women who are pregnant (particularly in the first trimester). It is appropriate, however, to use contrast agents when the procedure requiring them is considered to be essential and the diagnostic information obtained from the study will have substantial impact on the management of the patient and foetus during the pregnancy. The risks, as always, must be balanced against the possible benefits. It is likely that the risks of radiation exposure in this situation are greater than those resulting from administration of an iodinated contrast agent.

A concern regarding the use of iodinated contrast agents in both pregnant women is the theoretical effect of free iodine within these agents on the foetal thyroid gland.

**Guideline:**

- *Iodinated contrast should only be administered during pregnancy when deemed clinically essential and the information obtained from the study will have substantial impact on the management of the patient and foetus during the pregnancy.*

- *The potential risks of iodinated contrast and radiation exposure and the potential benefits of the examination should be discussed with the patient along with any diagnostic alternatives. Informed consent should be obtained.*

- *Because of the theoretical risk of thyroid suppression in the foetus, thyroid function should be measured in the first week after birth.*
10. Breast Feeding

In breast-feeding women, the risks to the mother and to her infant must be weighed against any possible benefits. If an iodinated contrast agent is administered, the infant is likely to receive a very small amount orally and then absorb only a very small percentage of this. There is no evidence of iodinated contrast agent induced toxicity in newborns. On the other hand, there is limited information confirming the safety of these medications in infants.

Guideline:

• If iodinated contrast must be administered to a patient who is breast-feeding, there is no need for special precautions or cessation of breastfeeding.
11. Thyroid Disease

Iodinated contrast agents contain small amounts of free iodine.

Iodinated contrast injections do not have a significant effect in patients with normal thyroid function.

Iodinated contrast induced thyrotoxicosis is rare, but may occur in patients with Graves’ disease or multinodular goiter with autonomous nodules. This typically manifests within 3 to 8 weeks after contrast administration.

**Guideline:**
- **Iodinated contrast should not be administered to patients with overt hyperthyroidism. Patients with Graves disease and multinodular goiter are at increased risk of developing thyrotoxicosis following iodinated contrast injection and should be warned regarding this possibility. Thyroid function should be monitored in this group by the patient’s medical practitioner or endocrinologist.**

**Thyroid Isotope Studies:**
Free iodine from an iodinated contrast agent causes reduced uptake of radioactive tracer in nuclear medicine thyroid isotope studies

**Guideline:**
- **Diagnostic thyroid isotope studies should be avoided within 8 weeks after an injection of iodinated contrast.**
- **Patients with suspected or known thyroid carcinoma should not receive iodinated contrast media if therapeutic radioactive iodine treatment is planned, because this may delay treatment with radioactive iodine for up to 8 weeks.**
12. Phaeochromocytomas and Paragangliomas

Phaeochromocytomas and paragangliomas may secrete catecholamines and can induce life threatening episodes of hypertension.

Intravenous non-ionic iodinated contrast has not been demonstrated to produce a statistically significant elevation in catecholamine levels in comparison to injection of normal saline.

While it may be prudent to administer oral alpha- and beta-adrenoceptor antagonists in patients with a biochemically proved pheochromocytoma to control symptoms and to prevent a spontaneous adrenergic crisis, specific blockade is not required prior to administration of iodinated contrast.

**Guideline:**
- No specific preparation is required prior to administration of iodinated contrast in patients with an incidental adrenal mass, or in patients with a biochemically demonstrated catecholamine producing tumour.
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