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Anaphylactic Reactions in Radiology Procedures

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Abstract

Reactions to contrast agents are uncommon but range from mild urticaria to life threatening anaphylactic reactions. Majority of these reactions occur due to intravenous administration of iodinated contrast media. Acute reactions to MRI gadolinium-based contrast are much less common but they do occur and thus have to be managed. Usual presentations include urticaria, nausea, vomiting, angioedema, bronchospasm, laryngospasm and systemic hypotension. Majority of these reactions occur within the first twenty minutes after administration of contrast. Therefore, their recognition and prompt treatment are critical for good patient outcome. Attendant to this the radiology department must be adequately prepared to handle these emergencies as and when they do occur. This means an up to date emergency tray must be checked regularly before the start of the procedure, ensure there is epinephrine, antihistamines, beta-2-agonists metered dose inhalers, IV fluids, and ready supply of oxygen. Close collaboration of radiology staff with the hospital emergency response team is critical since severe reactions will need the intervention of this team.

Keywords: anaphylaxis, iodinated contrast, bronchospasm, hypotension, diagnosis, treatment

1. Introduction

Contrast media is a substance that is used to enhance the differentiation of tissues within the body in medical imaging. They are administered either intravenously, intraarterially, orally or into body cavities, majority being administered intravenously. Over the past few years there has been an increase in the number of radiographic examinations that use contrast media for better lesion characterization, more so in CT and MRI examinations [1]. Although contrast media has become progressively safer over time, especially with the use of low osmolar contrast media (LOCM), anaphylactic reactions still do occur. It is estimated that 0.6% of iodinated and 0.12% of gadolinium contrast cause anaphylactic reactions [2–4]. Reactions to contrast media range from mild reactions to life threatening severe reactions. Most acute reactions occur within 1 hour of contrast media administration, with majority occurring within the first 20 minutes. Therefore, it is important to be aware of these reactions, to monitor the patient closely in this period and to manage the reactions when they do occur [5].

There are two main types of iodinated contrast comprising high osmolar (HOCM) or ionic contrast that dissociates in solution to form particles and low

Types of contrast media				
Contrast	Trade name	Ionic/Non-ionic	Iodine content	Osmolarity
Diatrizoate	Gastrografin	Ionic	300mg/ml	1550
Ioxaglate	Hexabrix	Ionic	320mg/ml	580
Ultravist	Iopromide	Non-ionic	300mg/ml	607
Optiray	Ioversal	Non-ionic	300mg/ml	651
Isovue 370	Iopamidol	Non-ionic	370mg/ml	796
Omnipaque 300	Iohexol	Non-ionic	300mg/ml	672
Ioxilan 350	Oxilan	Non-ionic	350mg/ml	695
Iotrol 300	Iotrolan	Non-ionic	300mg/ml	310
Visipaque 320	Iodixanol	Non-ionic	320mg/ml	290

Table 1.
Types of iodine based contrast media and osmolarity.

osmolar or non-ionic that does not dissociate in solution. Contrast media osmolality is determined by the number of particles formed in solution. Ionic contrast media dissociates into osmotically active ions in solution and therefore have a higher osmolality. Non-ionic agents do not dissociate to ions when dissolved in solution and hence have a lower osmolality. In recent years there has been a shift to using the LOCM because of associated fewer reactions therefore making contrast administration safer. Nevertheless, acute anaphylactic reactions can still occur unpredictably and therefore must be recognized and managed promptly. Some of the commonly used iodine-based contrast agents and their osmolality are listed in **Table 1** above.

2. Gadolinium based contrast

Gadolinium based MRI contrast agents have been shown to be safe for intravenous administration, and actually a better safety profile than iodinated contrast for CT and other radiographic examinations. However acute reactions do occur and include urticaria, nausea and vomiting, and rarely anaphylaxis. In a study of 141,623 doses of MRI contrast administered Jae-woo et al. identified 0.079% immediate hypersensitivity reactions including urticaria, angioedema, bronchospasm and anaphylaxis and one fatality giving a mortality rate of 0.007% [6].

3. Presentation and management of contrast reactions

3.1 Clinical presentation

Reactions can be categorized as mild, moderate and severe as well as immediate and delayed. Mild reactions are usually self-limiting and require just supportive treatment, whereas moderate to severe reactions require prompt treatment. Delayed reactions such as abdominal pains, joint pains, fever and chills, diarrhea, headache, rashes and dizziness may be seen within two weeks from the date of contrast administration. Renal toxicity is also a commonly encountered side effect of contrast reactions manifesting as impaired renal function within two weeks of contrast administration.

Table 2 below shows the different types of reactions seen.

Severity	Reaction
Mild reactions	Urticaria
	Hives
	Nausea
	Vomiting
Moderate reactions	Facial oedema
	Severe vomiting
	Bronchospasm
	Laryngeal oedema
Severe reactions	Pulmonary oedema
	Cardiac arrhythmia
	Cardiovascular collapse
	Respiratory collapse

Table 2.
Classification of contrast media reactions.

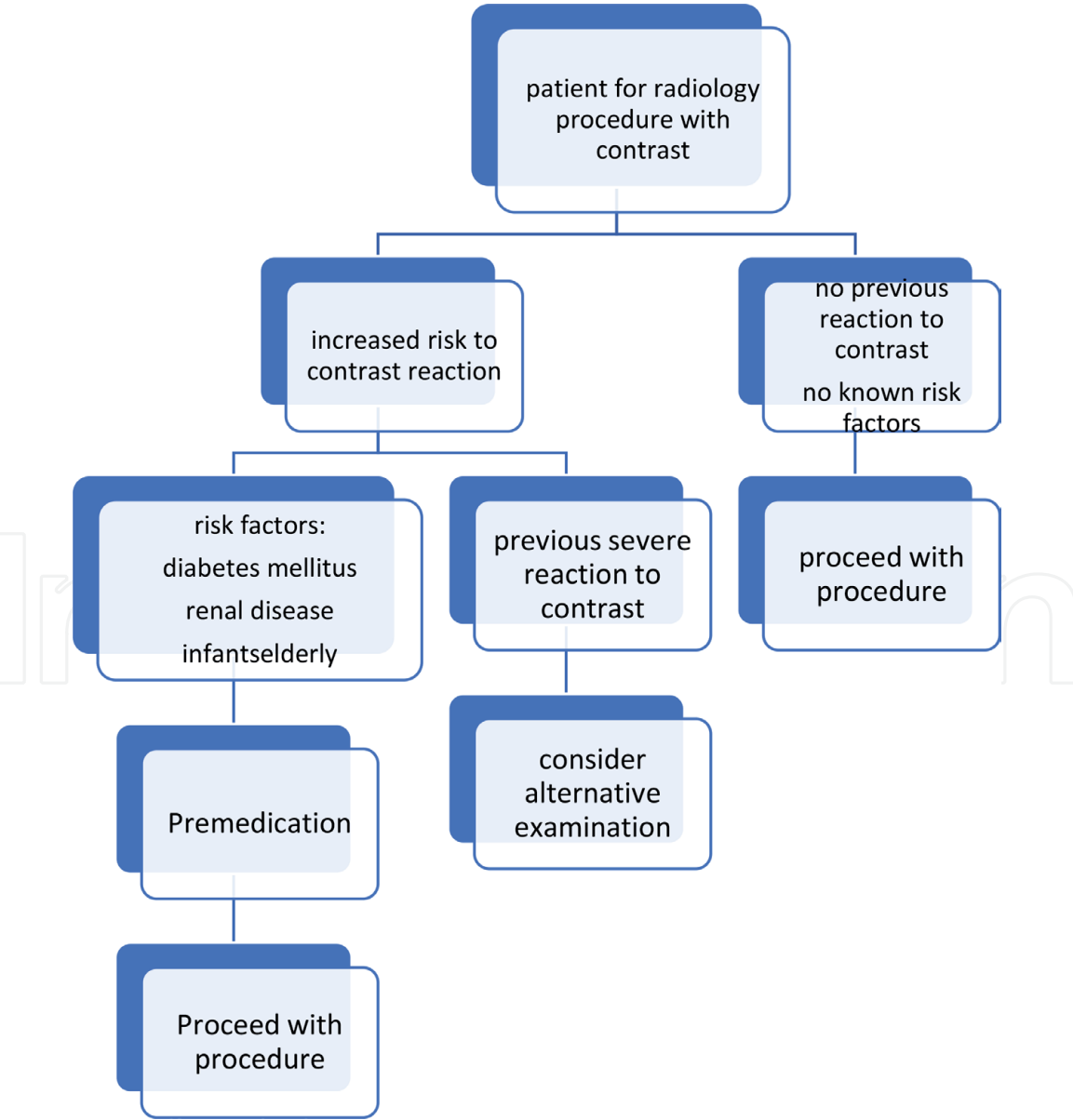


Figure 1.
Patient evaluation algorithm.

Anaphylactic reaction usually occurs within one hour of contrast administration, with majority occurring within the first 20 minutes. This is a life-threatening reaction and manifests with hypotension, bronchospasm/laryngeal oedema and circulatory collapse. Patient evaluation algorithm is as outlined in **Figure 1** above.

4. Anaphylactic reactions to contrast media

Although contrast side effects are infrequent, the knowledge of their presentation, their relationship with pre existing conditions and their management is required to ensure optimal patient care [2, 7]. Non ionic agents are iso-osmolar or low osmolar in nature and have fewer adverse effects [8, 9].

Majority of contrast reactions occur unpredictably and severe reactions may occur even when there has been a previous uneventful examination.

Risk factors that increase the likelihood of occurrence of adverse reactions [10–12] include:

1. Previous history of allergy like reaction to contrast media.
2. Allergy to food or other drugs.
3. History of asthma.
4. Renal insufficiency.
5. Cardiac disease e.g. Congestive cardiac failure, angina.
6. Anxiety.
7. Infants and neonates.
8. Elderly, above the age of 60 years.
9. Hematological disorders: sickle cell anemia, polycythemia vera, multiple myeloma.
10. Use of drugs like beta blockers.

A detailed history should be obtained and pre medication administered prior to contrast use to reduce the risk of reaction occurrence.

Adverse reactions to contrast can be divided into organ specific and non organ specific or general reactions. They can also be classified into acute and delayed based on the timing after contrast administration.

Acute hypersensitivity reactions are those that develop within 1 hour of contrast administration and can be classified into allergic-like and physiologic [13]. Allergic-like reactions are largely dose and concentration independent. They do not require prior sensitization or Ig-E and are thus called idiosyncratic /anaphylactoid reactions. They occur via direct mast cell stimulations or via activation of complement by immune complexes [14]. These are the most frequent type of adverse reactions and may have serious, occasionally fatal, complications.

Physiologic reactions are those that are dose and concentration dependent and are thus called non idiosyncratic reactions. They are due to direct chemotoxic or osmotoxic effects of the contrast media [15].

These acute reactions can be further subclassified into 3 categories based on severity-mild, moderate and severe [11]. Mild reactions are those that are self limiting. The mild allergic-like reactions include limited urticaria, pruritus, cutaneous edema, nasal congestion while the physiologic reactions include limited nausea and vomiting, transient flushing, headache, dizziness, anxiety and vasovagal reactions that resolve spontaneously [16]. Moderate reactions are those that are progressive and more pronounced and require medical management [17, 18]. The moderate allergic-like reactions include diffuse urticaria/pruritus, diffuse erythema with normal vital signs, facial edema, throat tightness, wheezing and bronchospasms. While the moderate physiological reactions include protracted vomiting, hypertensive urgency, vasovagal reactions that require treatment and respond to it [13]. Severe reactions are those that are potentially life threatening with impending death if not managed properly [2]. The severe allergic-like reactions include diffuse edema with dyspnea, diffuse erythema with hypotension, laryngeal edema with stridor, bronchospasms with hypoxia and anaphylactic shock. The severe physiologic reactions include vasovagal reactions resistant to treatment, convulsions, arrhythmia and hypertensive emergency [13]. The end result of severe allergic like and physiologic reactions is CPA which is a medical emergency and prompt and proper management using the BLS protocol and drugs including epinephrine, vasopressors, antihistamines and inhaled B-agonists is necessary to save lives.

Contrast induced acute kidney injury and nephropathy can also occur following contrast administration [19]. Risk factors include co morbidities like diabetes mellitus, dehydration, cardiac disease, hypertension and multiple iodinated contrast media doses in less than 24 hours. Baseline serum creatinine $\pm$ glomerular filtration rate should be available before injection of contrast media in at risk patients [13]. Contrast media administration in such patients can be done with caution by: reduced dose of contrast media, hydration and use of iso-osmolar agents.

5. Management of acute contrast media reactions

Management of acute contrast begins with discontinuation of injection if not completed [13, 20]. General principals of BLS and ACLS should apply in case of cardiorespiratory arrest.

Summary of the management of contrast reactions is as outlined in **Table 3** below.

6. Premedication of at risk patients

Premedication of patients who have a higher risk of acute allergic like reactions should be considered to reduce the chance of reaction occurrence [18]. For elective premedication oral prednisolone and diphenhydramine are used. For emergency premedication I.V methyl prednisolone sodium succinate or dexamethasone sodium sulfate. I.V diphenhydramine can be used instead of steroids in emergency cases [13].

7. Reaction rebound prevention

Intravenous corticosteroids play a role in preventing short term recurrence of an allergic like reactions. They may also be administered to patients having severe allergic like manifestations prior to transport to an emergency unit. They are however not useful in the acute treatment of any reaction.

Reaction	Monitoring	Treatment
Anaphylactoid		
Urticaria (skin rash)	Initial size with marking and follow	Mild-Usually none; if symptomatic consider diphenhydramine, 25–50 mg orally Moderate/Severe-monitor vitals and obtain IV access. Consider diphenhydramine, 25–50 mg orally intramuscularly/ intravenously; epinephrine (1:1,000), 0.1–0.3 mL subcutaneously/intramuscularly
Bronchospasm	Oxygen saturation, pulse, Blood pressure (BP)	In all forms of bronchospasms: preserve IV access, monitor vitals and oxygen saturation and give oxygen by mask 6-10 L/min Mild: Inhaled B-agonist- 2 puffs at 90mcg/puff and can be repeated up to 3 times. If response is not satisfactory, emergency response team should be contacted. Moderate Inhaled B-agonist- 2 puffs at 90mcg/puff and can be repeated up to 3 times Epinephrine (1:1000), 0.3 mL intramuscularly-this can be repeated every 5-15 minutes as needed up to 1 ml(1 mg) total; OR Epinephrine (1:10,000), 1 mL(0.1 mg) intravenously (slowly) if hypotensive; This can be repeated every few minutes as needed up to 10 ml(1 mg) total call the emergency medical team; call the emergency medical team Severe: Epinephrine (1:1000), 0.1–0.3 mL intramuscularly-this can be repeated every 5-15 minutes as needed up to 1 ml(1 mg) total; OR Epinephrine (1:10,000), 1 mL(0.1 mg) intravenously (slowly) if hypotensive; This can be repeated every few minutes as needed up to 10 ml(1 mg) total Call the emergency medical team and Inhaled B-agonist (may work synergistically). Call the emergency medical team
Facial or laryngeal edema	Oxygen saturation, pulse, BP	In all forms of laryngeal edema: preserve IV access, monitor vitals and oxygen saturation and give oxygen by mask 6-10 L/ min Call the emergency medical team if severe Epinephrine (1:1000), 0.3 mL intramuscularly-this can be repeated every 5-15 minutes as needed up to 1 ml(1 mg) total; OR Epinephrine (1:10,000), 1 mL(0.1 mg) intravenously (slowly) if hypotensive; This can be repeated every few minutes as needed up to 10 ml(1 mg) total call the emergency medical team
Hypotension(systolic BP <90 mmHg) and tachycardia (>100 bpm)	Oxygen saturation, pulse, BP	Preserve IV access, Elevate legs 60°; oxygen, 6–10 L/min; rapid intravenous fluids(1 liter of 0.9% normal saline or lactated Ringer's); epinephrine (1:10,000), 1 mL(0.1 mg) intravenously (slowly); This can be repeated every few minutes as needed up to 10 ml(1 mg) total OR Epinephrine (1:1000), 0.3 mL intramuscularly-this can be repeated every 5-15 minutes as needed up to 1 ml(1 mg) total call the emergency medical team
Hypotension(systolic BP <90 mmHg) and bradycardia (<60 bpm)	Oxygen saturation, pulse, BP	Elevate legs 60°; oxygen, 6–10 L/min; rapid intravenous fluids(1 liter of 0.9% normal saline or lactated Ringer's) If mild, no further treatment is necessary If patient remains symptomatic despite the above measures: Atropine, 0.6–1 mg intravenously (slowly); repeat to total of 2–3 mg (0.04 mg/kg) if needed; call the emergency medical team

Reaction	Monitoring	Treatment
Cardiac arrhythmia	Oxygen saturation, pulse, BP, ECG	Follow ACLS protocols; call the emergency medical team
Hypertensive crisis (diastolic BP >120 mmHg; systolic BP >200 mmHg)	Oxygen saturation, pulse, BP, ECG	Nitroglycerine, 0.4 mg sublingually; can repeat every 5-10 minutes OR Labetalol intravenously 20 mg, administer slowly over 2 minutes. The dose can be doubled every 10 minutes. OR Lasix intravenously 20-40 mg,slowly over 2 minutes. Phentolamine, 5 mg intravenously for pheochromocytoma; Call the emergency medical team
Seizures	Oxygen saturation, pulse, BP, ECG	Observe and protect the patient Secure airway; oxygen, 6–10 L/min; Preserve IV access and give diazepam, 5 mg intramuscularly/ intravenously OR midazolam, 0.5–1 mg intravenously OR phenytoin infusion, 15–18 mg/kg at 50 mg/min; call the emergency medical team
Hypoglycemia	Oxygen saturation, pulse, BP	If patient is able to swallow orally give half a cup of fruit juice or 15 g of glucose Is the patient is unable to swallow safely, obtain IV access and give 50% dextrose, 1 ampule-25gms over 2 minutes OR 100 ml/hr. of 5% dextrose. Is patient is unable to swallow and IV access is not available give intramuscular glucagon 1 mg.
Pulmonary edema	Oxygen saturation, pulse, BP, ECG	Preserve IV access, Secure airway; oxygen, 6–10 L/min; Elevate head of the bed furosemide, 20–40 mg intravenously (slowly over 2 minutes); morphine, 1–3 mg intravenously; call the emergency medical team

Table 3.
Management of contrast reactions.

7.1 Radiology department preparedness to manage anaphylactic reactions to contrast media

The hospital administration in liaison with the heads of the radiology department and the radiology contrast committee should set up and publish an institutional policy and procedure manual on contrast media administration.

The purpose of this manual is:

- i. To ensure that administration of contrast media is done according to the protocols set up by the hospital and imaging department.
- ii. To ensure that in case of adverse reactions to contrast media, appropriate steps are taken to manage them.
- iii. To ensure that patients at risk of contrast media reactions or with prior history of such reactions receive appropriate premedication and are imaged using suitable protocols.

- iv. To ensure that patients due to receive intravenous contrast media have appropriate laboratory tests done and reviewed by the radiologist to determine their suitability for the procedure.

Guidelines for administration on intravenous contrast:

- i. Administration of intravenous contrast should be done by a trained radiology technician / nurse under the supervision of the radiologist and these staff should be competent in recognizing and managing an adverse reaction if it occurs.
- ii. Standard operating procedures on the administration of intravenous contrast media should be set up and made available to the radiology clinical staff for reference when needed.
- iii. The Radiologist should review all the imaging requests that require administration of intravenous contrast, to determine the protocol to be used which will depend on the patient's condition and clinical indication for the study.
- iv. The radiology technician and nurse attending to the patient must take a detailed history on the current clinical condition, current medications, history of allergy, asthma and prior adverse reactions to drugs and contrast media.
- v. If the patient is found to have risk factors or contraindications to administration of contrast media, then the radiologist will determine the protocol to be followed and premedication to be administered if required.
- vi. Protocols on the recognition and management of adverse reactions to contrast media should be set up and made available to all radiology clinical staff. These protocols ought to be illustrated in flow charts and placed in the various imaging sections in which intravenous contrast media is administered to facilitate proper management of these emergencies.
- vii. Close liaison between the radiology department, the emergency response team and intensive care unit must be present to ensure that the radiology department will get adequate support in case of an emergency.

7.2 Radiology department emergency trolley

All imaging sections in the radiology department must be equipped with the emergency equipment and medication required to monitor and manage a patient in cardiopulmonary arrest and more specifically a patient undergoing a severe reaction to contrast media.

Majority of the emergency equipment and medication are part of the standard crash cart/ emergency trolley; therefore, it is upon the administration of the radiology department to decide whether a dedicated contrast reaction kit is necessary. This will depend on the size of the imaging department, patient numbers and budget allocations.

The basic equipment required to monitor patients experiencing an adverse reaction to contrast media include:

- i. Devices for hemodynamic Monitoring-Pulse and blood pressure monitors.
- ii. Devices for respiratory monitoring – Pulse oximeter.

- iii. Body temperature monitor – Thermometer or adhesive pads with thermoelectric transducer.
- iv. Blood glucose monitor.
- v. Stethoscope.

Equipment and supplies for managing patients in an acute adverse reaction include:

- i. Oxygen supply from a wall unit or oxygen cylinder.
- ii. Devices to supply the supplemental oxygen e.g. nasal cannula, simple face mask, face mask with oxygen reservoirs (non-rebreather mask). The latter is preferred as it is able to deliver a large dose of approximately 95–100% oxygen at a flow rate of 10-15 ml/min. Another device is a bag mask device which uses positive pressure ventilation with a face mask or advanced airway to administer a high concentration of oxygen to the patient. These devices must be available in adult and pediatric sizes.
- iii. Suction device used to clear the airway of secretions to enable the patient to breathe. A patent airway is required for effective cardiopulmonary resuscitation in case of cardiopulmonary arrest in the case of severe contrast media reactions. The suction device may be wall mounted or mobile and used in conjunction with suction tubing/ catheters.

Basic medication required in case of a contrast media reactions include:

- i. Epinephrine
 - Emergency trolley / crash carts in hospital setting are usually equipped in 1 mg in 10 ml of epinephrine for intravenous administration (1:10000).
 - Epinephrine 1 mg in 1 ml vial is used for intramuscular injection.
 - Epinephrine autoinjectors in pediatric, and adult doses can also be used if available.
- ii. Oral and intravenous antihistamines.
- iii. Inhaled or nebulized B2 agonists.
- iv. Normal saline intravenous fluid in 500 ml and 1 liter bags/ bottles.
- v. Atropine 1 mg in 10 ml for intravenous administration.

Additional medication and supplies include:

- i. Emergency drugs – these include the standard emergency medications which are part of standard crash cart/ emergency trolley.
- ii. Supplies that form part of the standard emergency trolley like various sizes of intravenous cannulas, needles, syringes and intravenous giving sets.
- iii. Advanced cardiovascular life support equipment including:

- Advanced airway adjuncts e.g. endotracheal tube.
- Suction catheters.
- Automated external defibrillator.

In view that cardiopulmonary arrest and adverse reactions to contrast media in the radiology department are rare, it is imperative that periodic stock checks are done to ensure the equipment and medications stocked for the management of these emergencies are within the recommended validity period.

7.3 Hospital emergency response team

When faced with a severe reaction to contrast media in which the patient's condition warrants implementation of basic life support and advanced cardiac life support protocols, it is imperative that the hospital emergency response team be alerted to assist in initiation of these lifesaving protocols.

Modern radiology departments are fitted with an emergency bell that alerts the emergency response team to respond to an emergency in each imaging section. All radiology staff must be made aware of the location of these bells to activate them when needed.

In the event that such a system is not in place, the phone number of an internal/external emergency response unit should be clearly posted in each imaging section.

7.4 Training

Despite the rare occurrence of contrast media reactions, they may carry substantial morbidity and mortality and thus require immediate intervention by the attending staff. These staff must therefore be equipped with the knowledge and skills to initiate effective cardiopulmonary resuscitation in order to manage these emergencies as they await the arrival of the emergency response team.

All clinical staff should receive life support training upon employment and thereafter attend at least three yearly refresher course as recommended by the American heart association.

Continuous medical education on contrast media reactions and their management should be held frequently to ensure these vital knowledge and skills are up to date.

Advanced radiology life support TM is a course that uses concepts from basic life support and advanced cardiac life support to radiology clinical staff on recognizing and managing life threatening emergencies occurring in the imaging department.

This training covers:

- Types of contrast media used in imaging.
- Recognition of the signs and symptoms of contrast media reactions.
- Risk factors of contrast induced nephropathy and approach to administration of contrast media in renal insufficiency.
- Safety of Gadolinium based contrast agents and nephrogenic systemic fibrosis.
- Airway management in emergencies.
- Safe management of sedated patients in the imaging department.

Advanced radiology life support™ has been successful in United states of America and Canada in training of radiologists, radiology technicians and nurses in the management of contrast media reactions and cardiopulmonary arrest in the radiology department. Accreditation is by the Mayo clinic of medicine and Science.

This training is available online in form interactive videos, therefore imaging departments should allocate a budget for purchase of this training for each of its clinical staff members.

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