

# ESUR Guidelines on Contrast Media Version 5.0

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## 1. Renal Adverse reactions

*ESUR Guidelines*

## 1.1. To avoid contrast medium induced nephrotoxicity

<b>Definition</b>		Contrast medium nephrotoxicity is a condition in which an impairment in renal function ( <i>an increase in serum creatinine by more than 25% or 44µmol/l (0.5 mg/dl)</i> ) occurs within 3 days following the intravascular administration of a contrast medium (CM) in the absence of an alternative etiology.
<b>Risk factors</b>	<b>Look for</b>	<ul style="list-style-type: none"> <li>• Raised s-creatinine levels, particularly secondary to diabetic nephropathy.</li> <li>• Dehydration</li> <li>• Congestive heart failure</li> <li>• Age over 70 years old</li> <li>• Concurrent administration of nephrotoxic drugs, e.g. non-steroid anti-inflammatory drugs.</li> </ul>
<b>In patients with risk factor(s)</b>	<b>Do</b>	<ul style="list-style-type: none"> <li>• Make sure that the patient is well hydrated [give at least 100 ml (oral (e.g. soft drinks) or intravenous (normal saline) depending on the clinical situation) per hour starting 4 hours before to 24 hours after contrast administration – in warm areas increase the fluid volume]</li> <li>• Use low- or iso-osmolar contrast media</li> <li>• Stop administration of nephrotoxic drugs for at least 24 hours.</li> <li>• Consider alternative imaging techniques, which do not require the administration of iodinated contrast media</li> </ul>
	<b>Do not</b>	<ul style="list-style-type: none"> <li>• Give high osmolar contrast media</li> <li>• Administer large doses of contrast media</li> <li>• Administer mannitol and diuretics, particularly loop-diuretics</li> <li>• Perform multiple studies with contrast media within a short period of time</li> </ul>

## 1.2. Determination of serum creatinine.

<b>At time of referral for a contrast enhanced imaging examination identify patients with increased probability of abnormal serum creatinine levels</b>	<p>The referring clinician should ask the patient for a history of:</p> <ul style="list-style-type: none"> <li>• Renal disease</li> <li>• Renal surgery</li> <li>• Proteinuria</li> <li>• Diabetes mellitus</li> <li>• Hypertension</li> <li>• Gout</li> <li>• Recent nephrotoxic drugs</li> </ul> <p>The answers should be provided to the department of Radiology with the imaging request</p>
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		Serum creatinine not older than 6 months should be provided with the imaging request, if available.
<b>Non-emergency examinations</b>	<b>Look for</b>	<ul style="list-style-type: none"> <li>• Positive answer to one or more of the above questions.</li> <li>• Known abnormal S-creatinine level at time of referral</li> <li>• Procedures requiring intraarterial contrast medium administration</li> </ul>
	<b>Action</b>	<ul style="list-style-type: none"> <li>• S-creatinine level must be measured within 7 days of the examination.</li> <li>• The Department of Radiology must be informed if the serum creatinine level is increased at least 24 hours before the scheduled examination time in order to make the necessary arrangements</li> </ul>
<b>Emergency examinations</b>		<ol style="list-style-type: none"> <li>In emergency situations serum creatinine measurement can be waived.</li> <li>If the procedure can be deferred without harm to the patient, serum creatinine should be measured.</li> </ol>
<b>In patients with abnormal serum creatinine levels</b>		<ul style="list-style-type: none"> <li>• Consider alternative imaging techniques, which do not require the administration of iodinated contrast media.</li> <li>• Stop administration of nephrotoxic drugs for at least 24 hours.</li> <li>• Make sure that the patient is well hydrated.</li> <li>• Use low- or iso-osmolar contrast media.</li> </ul>

### 1.3. Dialysis and contrast media administration

<b>Patients</b>	<b>Recommendations</b>
<b>On hemodialysis</b> [all contrast media can be removed by hemodialysis]	<ul style="list-style-type: none"> <li>• Avoid osmotic and fluid overload.</li> <li>• Correlation of the time of contrast medium injection with the hemodialysis session is unnecessary.</li> <li>• Extra hemodialysis session for removal of contrast medium is unnecessary.</li> </ul>
<b>With severely reduced renal function</b>	<ul style="list-style-type: none"> <li>• Please refer to ESUR guidelines to avoid contrast medium induced nephrotoxicity (hydration, use small doses of low osmolar contrast media).</li> <li>• Hemodialysis is unnecessary.</li> <li>• In MRI examinations avoid doses more than 0.3 mmol/kg BW of gadolinium-based contrast agents</li> </ul>
<b>On continuous ambulatory peritoneal dialysis (CAPD)</b> [all contrast media can be removed by peritoneal dialysis]	<p><i>Examinations using iodinated agents:</i></p> <ul style="list-style-type: none"> <li>• To protect residual renal function please refer to ESUR guidelines to avoid contrast medium induced nephrotoxicity.</li> <li>• Hydration should be considered only after careful</li> </ul>

	<p>evaluation of fluid balance state of the patient.</p> <ul style="list-style-type: none"> <li>• Hemodialysis is not recommended.</li> </ul> <p><i>Examinations using gadolinium agents:</i></p> <ul style="list-style-type: none"> <li>• To protect residual renal function use doses up to 0.3 mmol/kg BW of gadolinium-based contrast agents.</li> <li>• Hemodialysis is not recommended.</li> </ul>
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#### 1.4. Administration of contrast media to diabetics taking metformin

Serum creatinine level should be measured in every diabetic patient treated with biguanides prior to intravascular administration of contrast media. Low-osmolar contrast media should always be used in these patients.

##### **Elective studies**

a) *If the serum creatinine is normal*, the radiological examination should be performed and intake of metformin stopped from the time of the study. The use of metformin should not be resumed for 48 hrs and should only be restarted if renal function/serum creatinine remains within the normal range.

b) *If renal function is abnormal*, the metformin should be stopped and the contrast study should be delayed for 48 hrs. Metformin should only be restarted 48 hrs after contrast medium, if renal function/serum creatinine is unchanged.

##### **Emergency cases**

a) *If the serum creatinine is normal*, the study may proceed as suggested for elective patients.

b) *If the renal function is abnormal (or unknown)*, the physician should weigh the risks and benefits of contrast administration. Alternative imaging techniques should be considered. If contrast media administration is deemed necessary and the following precautions should be implemented:

- Metformin therapy should be stopped.
- The patient should be hydrated (E.g. at least 100 ml per hour of soft drinks or intravenous saline up to 24 hours after contrast medium administration – In warm areas more fluid should be given).
- Monitor renal function (serum creatinine), serum lactic acid and pH of blood.
- Look for symptoms of lactic acidosis (vomiting, somnolence, nausea, epigastric pain, anorexia, hyperpnea, lethargy, diarrhea and thirst). Blood test results indicative of lactic acidosis: pH < 7.25 and lactic acid > 5 mmol.

#### *ESUR Position Statement*

#### 1.5 The use of gadolinium-based contrast media for radiographic examinations.

<b>Legal position</b>	Gadolinium-based contrast media are not approved for X-ray examinations
<b>Uses of gadolinium-based contrast media for X-ray</b>	<ul style="list-style-type: none"> <li>• Significant renal impairment</li> </ul>

<b>examinations reported in the literature</b>	<ul style="list-style-type: none"> <li>• Prior severe generalized adverse reaction to iodinated contrast media</li> <li>• Imminent thyroid treatment with radioactive iodine</li> </ul>
<b>ESUR position</b>	<ol style="list-style-type: none"> <li>1. The use of gadolinium based contrast media for radiographic examinations is not recommended to avoid nephrotoxicity in patients with renal impairment since they are more nephrotoxic than iodinated contrast media in equivalent X-ray attenuating doses.</li> <li>2. The use of gadolinium based contrast medium in approved intravenous doses up to 0.3 mmol/kg B.W. will not give diagnostic radiographic information in most cases.</li> </ol>

## 2. Non-renal adverse reactions

### *ESUR Guidelines*

#### 2.1. Prevention of generalized contrast medium reactions

##### **A. Risk factors for reactions**

- Previous generalized contrast medium reaction, either moderate (e.g. urticaria, bronchospasm, moderate hypotension) or severe (e.g. convulsions, severe bronchospasm, pulmonary edema, cardiovascular collapse).
- Asthma.
- Allergy requiring medical treatment.

##### **B. To reduce the risk of generalized contrast medium reactions**

- Use non-ionic agents.

##### **C. Premedication is recommended in high risk patients (defined in A)**

- When ionic agents are used.
- When non-ionic agents are used, opinion is divided about the value of premedication.

##### **D. Recommended premedication**

- Corticosteroids  
     Prednisolone 30 mg orally or Methylprednisolone 32 mg orally 12 and 2 hours before contrast medium.  
     Corticosteroids are not effective if given less than 6 hours before contrast medium
- Antihistamines H1 and H2 may be used in addition to corticosteroids, but opinion is divided.

##### **E. Remember for all patients**

- Have a trolley with resuscitation drugs in the examination room.
- Observe patients for 20 to 30 minutes after contrast medium injection.

**F. Extra vascular administration**

- When absorption or leakage into the circulation is possible, take the same precautions as for intravascular administration.

**2.2. Management of acute adverse reactions to contrast media.****First line emergency drugs and instruments which should be in the examination room.**

Drugs/Instruments
Oxygen
Adrenaline 1:1,000
Antihistamine H1 – suitable for injection
Atropine
β2-agonist metered dose inhaler
I.V. Fluids – normal saline or Ringers solution
Anti-convulsive drugs (diazepam)
Sphygmomanometer
One-way mouth “breather” apparatus

**Simple guidelines for first line treatment of acute reactions to contrast media*****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 intramuscularly or intravenously should be considered. Drowsiness and/or hypotension may occur.

**Profound:** Consider Adrenaline 1:1,000, 0.1-0.3 ml (0.1-0.3 mg) intramuscularly in adults, 0.01 mg/kg intramuscularly up to 0.3 max. in children. Repeat as needed.

***Bronchospasm***

1. Oxygen by mask (6-10 l/min)
2. β-2-agonist metered dose inhaler (2-3 deep inhalations)
3. Adrenaline

***Normal blood pressure***

Intramuscular: 1:1,000, 0.1-0.3 ml (0.1-0.3 mg) [use smaller dose in a patient with coronary artery disease or elderly patient]

In paediatric patients: 0.01 mg/kg up to 0.3 mg max.

***Decreased blood pressure***

Intramuscular: 1:1,000, 0.5 ml (0.5 mg), (in paediatric patients: 0.01 mg/kg intramuscularly)

***Laryngeal edema***

1. Oxygen by mask (6 – 10 l/min)
2. Intramuscular adrenaline (1:1,000), 0.5 ml (0.5 mg) for adults, repeat as needed.

### ***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

#### Vagal reaction (hypotension and bradycardia)

1. Elevate patient's legs
2. Oxygen by mask (6-10 l/min)
3. Atropine 0.6-1.0 mg intravenously, repeat if necessary after 3-5 min, to 3 mg total (0.04 mg/kg) in adults. 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: rapidly, normal saline or lactated Ringer's solution

### ***Generalized anaphylactoid reaction***

1. Call for resuscitation team
2. Suction airway as needed
3. Elevate patient's legs if hypotensive
4. Oxygen by mask (6 – 10 l/min)
5. Intramuscular adrenaline (1:1,000), 0.5 ml (0.5 mg) in adults. Repeat as needed. In paediatric patients 0.01 mg/kg to 0.3 mg (max. dose)
6. Intravenous fluids (e.g. normal saline, lactated Ringer's)
7. H1-blocker e.g. diphenhydramine 25-50 mg intravenously

### 2.3 Late adverse reactions to intravascular iodinated contrast media

<b>Definition:</b>	A late adverse reaction to intravascular iodinated contrast medium is defined as a reaction which occurs 1 hour to 1 week after contrast medium injection
<b>Reactions:</b>	A variety of late symptoms (e.g. nausea, vomiting, headache, musculoskeletal pains, fever) have been described following contrast medium, but many are not related to contrast medium.  <i>Skin reactions</i> of similar type to other drug eruptions are true late adverse reactions. They are usually mild to moderate and self-limiting.
<b>Risk factors for skin reactions:</b>	<ul style="list-style-type: none"> <li>• Previous contrast medium reaction</li> <li>• Interleukin-2 treatment</li> </ul>

<b>Management:</b>	Symptomatic and similar to the management of other drug-induced skin reactions
<b>Prophylaxis:</b>	<ul style="list-style-type: none"> <li>• Generally not recommended</li> <li>• Patients who have had a previous serious late adverse reaction, can be given oral steroids (see ESUR Guidelines on prevention of generalized adverse reactions).</li> </ul>
<b>Recommendations:</b>	Tell patients who have had a previous contrast medium reaction or who are on interleukin-2 treatment that a late skin reaction is possible and that they should contact a doctor if they have a problem

### 3. Other reactions to contrast media

#### *ESUR Guidelines*

#### 3.1. Prevention and management of extravasation of contrast media.

<b>Risk factors relate to:</b>	<p>The technique</p> <ul style="list-style-type: none"> <li>• use of a power injector.</li> <li>• less optimal injection sites including lower limb and small distal veins.</li> <li>• large volume of contrast medium.</li> <li>• high osmolar contrast medium.</li> </ul> <p>The patient</p> <ul style="list-style-type: none"> <li>• unable to communicate.</li> <li>• with fragile or damaged veins.</li> <li>• with arterial insufficiency.</li> <li>• with compromised lymphatic and/or venous drainage.</li> </ul>
<b>To reduce the risk</b>	<ul style="list-style-type: none"> <li>• Intravenous technique should always be careful, preferably using plastic catheters for power injection.</li> <li>• Use low osmolar contrast medium.</li> </ul>
<b>Type of injuries</b>	<ul style="list-style-type: none"> <li>• Most injuries are minor.</li> <li>• Severe injuries include skin ulceration, soft tissue necrosis, and compartment syndrome.</li> </ul>
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• Conservative management is adequate in most cases <ul style="list-style-type: none"> <li>➢ limb elevation</li> <li>➢ apply ice packs</li> <li>➢ careful monitoring</li> </ul> </li> <li>• If a serious injury is suspected, seek the advice of a surgeon.</li> </ul>



## 3.2. Effect of iodinated contrast media on thyroid function in adults

<b>Absolute contraindication</b>	
	<ul style="list-style-type: none"> <li>Iodinated contrast media should not be given to patients with manifest hyperthyroidism</li> </ul>
<b>Development of thyrotoxicosis after iodinated contrast media</b>	
No risk	<ul style="list-style-type: none"> <li>Patients with normal thyroid function</li> </ul>
At risk	<ul style="list-style-type: none"> <li>Patients with Graves' disease</li> <li>Patients with multinodular goiter and thyroid autonomy, especially if they are elderly and/or live in areas of dietary iodine deficiency</li> </ul>
Recommendations	<ul style="list-style-type: none"> <li>Prophylaxis is generally not necessary</li> <li>Patients at risk should be closely monitored by endocrinologists after iodinated contrast medium injection</li> <li>In selected high-risk patients, prophylactic treatment may be given by an endocrinologist; this is more relevant in areas of dietary iodine deficiency</li> <li>Intravenous cholangiographic contrast media should not be given to patients at risk</li> </ul>
<b>Radioactive iodine treatment</b>	
Recommendation	<ul style="list-style-type: none"> <li>Patients undergoing therapy with radioactive iodine should not have received iodinated contrast media for at least two months before treatment</li> </ul>
<b>Isotope imaging of the thyroid</b>	
Recommendation	<ul style="list-style-type: none"> <li>Isotope imaging of the thyroid should be avoided for two months after iodinated contrast medium injection</li> </ul>

## 3.3. Pulmonary effects of contrast media

<b>High risk patients</b>	<b>Action</b>
History of pulmonary hypertension History of bronchial asthma Incipient cardiac failure	<ul style="list-style-type: none"> <li>Use low or iso osmolar contrast media</li> <li>Avoid large doses of contrast media</li> </ul>

## 3.4. Contrast media and Catecholamine-producing tumours (phaeochromocytoma and paraganglioma)

	<b>Tumour localisation when catecholamine-producing tumour detected bio-chemically</b>	<b>Characterisation of incidentally detected adrenal mass</b>
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Preparation		
(a) Before intravenous contrast medium (iodinated or gadolinium)	$\alpha$ and $\beta$ -adrenergic blockade with orally administered drugs under the supervision of the referring physician is advised. Further $\alpha$ -blockade with intravenous phenoxy-benzamine is not necessary.	No special preparation
(b) Before intra-arterial iodinated contrast medium	$\alpha$ and $\beta$ -adrenergic blockade with orally administered drugs and $\alpha$ -blockade with intravenous phenoxybenzamine under the supervision of the referring physician are recommended	
Type of contrast medium which should be used		
a) Iodinated agent	Non-ionic agent	Non-ionic agent
b) Gadolinium agent	Any agent (ionic or non-ionic)	Any agent (ionic or non-ionic)

### 3.5. The use of iodinated and gadolinium contrast media during pregnancy and lactation

	<b>Iodinated agents</b>	<b>Gadolinium agents</b>
<b>Pregnancy</b>	<p>a) In exceptional circumstances, when radiographic examination is essential, iodinated contrast media may be given to the pregnant female.</p> <p>b) Following administration of iodinated agents to the mother during pregnancy, thyroid function should be checked in the neonate during the first week.</p>	<p>a) When MR examination is necessary, gadolinium media may be given to the pregnant female.</p> <p>b) Following administration of gadolinium agents to the mother during pregnancy, no neonatal tests are necessary.</p>
<b>Lactation</b>	Breast feeding may be continued normally when iodinated agents are given to the mother.	Breast feeding may be continued normally when gadolinium agents are given to the mother.
<b>Pregnant or lactating</b>	No additional precautions are necessary for the foetus or neonate. Follow ESUR	No additional precautions are necessary for the foetus or neonate. Follow ESUR

<b>mother with renal impairment</b>	guidelines for contrast media administration when renal function is impaired.	guidelines for contrast media administration when renal function is impaired.
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### 3.6. Avoiding interaction between contrast media and other drugs

<b>Do</b>	Be aware of the patient's drug history. Keep proper records of the contrast medium injection (time, dose, name)	
<b>Drugs needing special attention</b>	Metformin	Refer to ESUR guidelines on Metformin
	Cyclosporine Cisplatin Aminoglycosides Non-steroid anti-inflammatory drugs	Refer to ESUR guidelines on nephrotoxicity
	$\beta$ -blocker	Refer to ESUR manuscript on prevention and management of adverse reactions
	Interleukin-2	Refer to ESUR guidelines on delayed reactions
	Hydralazine	Avoid contrast medium injection if possible
	<b>Do not</b>	Mix contrast media with other drugs in tubes or syringes Make non emergency biochemical analysis on blood or urine collected within 24 hours of contrast medium injection
<b>Isotope studies</b>	Thyroid	Refer to ESUR guidelines on thyroid function in adults
	Bone, Red blood cell labelling	Avoid contrast medium injection for at least 24 hours before the isotope study

### 3.7. Safety of ultrasound contrast media

<b>Statement:</b>	<ul style="list-style-type: none"> <li>• Ultrasound contrast media are generally safe</li> </ul>
<b>Type and severity of reactions:</b>	<ul style="list-style-type: none"> <li>• The majority of reactions are minor (e.g. headache, nausea, sensation of heat, altered taste) and self-resolving.</li> <li>• Allergy-like reactions occur rarely.</li> </ul>
<b>To reduce the risk:</b>	<ul style="list-style-type: none"> <li>• Check for intolerance of any of the components of the contrast agent</li> <li>• Use the lowest level of acoustic output and shortest scanning time to allow a diagnostic examination.</li> </ul>
<b>Treatment:</b>	<ul style="list-style-type: none"> <li>• If a serious event occurs - refer to ESUR guidelines on management of adverse reactions to contrast media.</li> </ul>

### 3.8. Safety of MR extra-cellular contrast media

Safety	Generally safe; low incidence of adverse event
Adverse events	Similar type to those seen after iodinated contrast media
Management	See ESUR guidelines on Management
Prophylaxis	If there has been a previous hypersensitivity-like reaction to gadolinium based compounds, consider an alternative modality or premedication (see ESUR guidelines on prophylaxis)
Contrast medium induced nephropathy	May occur – see ESUR guidelines on nephrotoxicity
Dialysis	See ESUR Guidelines on dialysis
S-creatinine Hydration	No special precautions are recommended
Pregnancy and Lactation	See ESUR guidelines on pregnancy and lactation
Interaction	See ESUR guidelines on interaction
Radiography	Not approved for this use

### 3.9. Safety of liver specific MR contrast media

<b>Types of adverse reactions</b>	Similar to reactions observed with other types of contrast media such as nausea, vomiting, urticaria, rash, generalized anaphylactoid reactions. Back pain may also occur with superparamagnetic iron oxides. Serious life threatening reactions are rare
<b>Patients &lt; 18 years old</b>	Safety has not yet been established
<b>Contraindications</b>	<p>Iron oxides</p> <p>Known allergy or hypersensitivity to parenteral iron or dextran</p> <p>Manganese based contrast media</p> <p>Known allergy to the preparation,</p> <p>Pregnancy,</p> <p>Lactation,</p> <p>Severe liver impairment,</p> <p>Gadolinium based contrast media</p> <p>Known allergy to the preparation</p>
<b>Cautions</b>	<p>Iron oxides</p> <p>In patients with hemosiderosis or hemochromatosis: iron-overload may be aggravated.</p> <p>Manganese based contrast media</p> <p>Liver impairment and heart failure</p> <p>Gadolinium based contrast media</p> <ul style="list-style-type: none"> <li>• Agent with high hepatocyte uptake: Liver and renal failure</li> <li>• Agent with low hepatocyte uptake: Renal failure</li> </ul>

### 3.10. Safety of Barium contrast media

		<b>Recommended action</b>
<b>Contraindications</b>	Integrity of gut wall compromised	Use iodinated water-soluble contrast media In neonates and patients at risk of leakage into mediastinum and/or lungs use low- or isoosmolar contrast media

	Previous allergic reactions to barium products	Use iodinated water-soluble contrast media and be prepared to treat a reaction
<b>Cautions</b>	Bowel strictures	Use only small amounts
	Extensive colitis	Avoid barium enemas
<b>Complications</b>	Reduced bowel motility	Encourage fluid intake
	Venous intravasation	<ul style="list-style-type: none"> <li>• Early identification and careful observation</li> <li>• Antibiotics and intravenous fluids</li> <li>• Emergency treatment may be needed</li> </ul>
	Aspiration	<ul style="list-style-type: none"> <li>• Bronchoscopic removal for large amounts</li> <li>• Chest physiotherapy</li> <li>• Antibiotics</li> </ul>

### *ESUR Statement*

#### 3.11. Effects of iodinated contrast media on blood and endothelium

The clinically important adverse effect of iodinated contrast media on blood and endothelium is thrombosis. It is recognized that:

- All contrast media have anticoagulant properties, especially ionic agents.
- High osmolar ionic contrast media may induce thrombosis due to endothelial damage, particularly in phlebographic procedures.
- Drugs and interventional devices that decrease the risk of thromboembolic complications during interventional procedures minimize the importance of the effects of contrast media.

#### Guidelines

- Meticulous angiographic technique is mandatory and is the most important factor in reducing thromboembolic complications.
- Low- or isoosmolar contrast media should be used for diagnostic and interventional angiographic procedures including phlebography.

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