Minimizing Adverse Reactions to Contrast Agents

Although significant adverse reactions to iodinated contrast agents are rare, they do, justifiably, arouse concern among patients, referring physicians, and radiologists. Most reactions are mild and self-limiting, such as flushing, nausea, vomiting, pain at the injections site, pruritis, headache, and mild urticaria. They are, nevertheless, unpleasant for the patient. The very rare severe reactions, estimated to occur in 0.004 – 0.04% of patients, include life-threatening anaphylactoid reactions, cardiac dysrhythmias and arrest, and cardiovascular and pulmonary collapse. These reactions are idiosyncratic and difficult to predict since they may happen once but never again.

In contrast, nephrotoxic reactions to iodinated contrast reagents are more predictable and, with a high enough dose, would be seen in everyone. Increased levels of serum creatinine can be detected 24 hours after a contrast CT in approximately 1% of the healthy outpatient population, returning to baseline within 1-2 weeks. Nephrotoxic reactions are much more likely in patients with impaired renal function. In one study, increased levels of serum creatinine were detected in 23% of those with a baseline serum creatinine > 2 mg/dl and almost 100% of patients with serum creatinine levels > 4.5 mg/dl and diabetes. Fortunately, permanent renal damage is rare. However, contrast medium nephrotoxicity can prolong the patient’s stay in hospital and increase the risk of non-renal complications.

Is Contrast Imaging Necessary?
The best way to preclude the occurrence of adverse reactions is to avoid the use of contrast reagent. However, contrast agents play an important and sometimes essential role in many kinds of imaging. Thus, the advantages of using iodinated contrast agents for the evaluation of the patient must be weighed against the disadvantages. This is not always a simple decision. MGH radiologists may use a contrast agent unless its use is specifically contraindicated. Clinicians are given the option of specifying the whether contrast is to be used at the time of scheduling. However, if nothing is specified, the radiologist will make the decision at the time the examination is reviewed. We recommend that the use of contrast be left to the radiologist unless there is a true contra-indication.

Identifying the At-Risk Patient
The risk of a general adverse reaction is increased somewhat by several factors (see box) that should be considered before administering iodinated contrast agents. For this reason, all patients who are scheduled to receive contrast agents are asked to fill in a questionnaire to alert the radiology technologist to potential problems. The technologist will discuss any concerns with a radiologist, who will make an informed decision for that patient or contact the referring physician to discuss imaging without contrast, using an alternate contrast agent containing gadolinium, or using an alternative imaging modality.

High-risk patients include those who have experienced a previous anaphylactoid reaction to contrast agents or an anaphylactic reaction to an allergen. Although patients with asthma have a 3-fold increase in the likelihood of a contrast reaction, they are not considered to be at high risk, except for severe cases. Children have a lower frequency of contrast reactions than do adults.

Although the incidence of contrast agent nephrotoxicity is low in patients with normal renal function, it is a significant concern for those with poor renal function, diabetes, congestive heart failure, dehydration, or the concurrent use of nephrotoxic drugs.
Factors that Increase the Risk of Adverse Reactions to Iodinated Contrast Agents

A. Systemic Reactions
   - Previous adverse reaction
   - History of asthma or bronchospasm
   - History of allergy or atopy
   - Anxiety
   - Cardiac disease*
   - Medication (b-blockers)
   - Hematologic and metabolic disease (sickle cell anemia, patients with thrombotic tendency, multiple myeloma, pheochromocytoma)

B. Nephrotoxicity
   - Congestive heart failure (New York Heart Association class 3 & 4)
   - Dehydration
   - Renal disease, especially in diabetics treated with metformin (Glucophage)
   - Medications (aspirin, NSAIDs)

*Symptoms of angina or congestive heart failure with minimal exercise, severe aortic stenosis, primary pulmonary hypertension, or severe but well compensated cardiomyopathy.

Immediate Adverse Reactions to CT Contrast Agents

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Self limited without evidence of progression</td>
</tr>
<tr>
<td></td>
<td>Hives, nasal stuffiness, itching, headache, shaking, dizziness</td>
</tr>
<tr>
<td></td>
<td><em>Not necessarily due to contrast but reported as adverse event:</em> Nausea and vomiting</td>
</tr>
<tr>
<td>Moderate</td>
<td>Clinical findings require treatment and careful observation for progression</td>
</tr>
<tr>
<td></td>
<td>Tachycardia, bradycardia, hypertension, hypotension, dyspnea, bronchospasm, wheezing, laryngeal edema, pronounced cutaneous reaction</td>
</tr>
<tr>
<td>Severe</td>
<td>Severe, life threatening symptoms, usually requires hospitalization</td>
</tr>
<tr>
<td></td>
<td>Laryngeal edema, convulsions, profound hypertension, unresponsiveness</td>
</tr>
</tbody>
</table>

Pre-medication Recommendations

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pre-Medication Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Adverse</td>
<td>Prednisone, 50 mg PO at 13 hr, 7 hr, and 1 hr before scan</td>
</tr>
<tr>
<td>Reaction*</td>
<td>Diphenhydramine (Benadryl), 50 mg PO, 1 hr before scan</td>
</tr>
<tr>
<td>Nephrotoxicity</td>
<td>If creatinine level &gt; 2 mg/dl, consult radiologist</td>
</tr>
<tr>
<td></td>
<td>Discontinue metformin before and for 48 hrs after scan (diabetics)</td>
</tr>
<tr>
<td></td>
<td>Hydrate well (all patients)</td>
</tr>
</tbody>
</table>

*Patients with history of severe reaction should not receive CT contrast agents. Contact radiologist to discuss alternate imaging options.

Minimizing Contrast Agent Reactions and Nephrotoxicity

MGH radiologists routinely use non-ionic iodinated contrast agents, which have about one fifth the incidence rate of general adverse reactions (around 3%) compared to the older ionic agents. For patients that are at high risk of an anaphylactoid reaction, pretreatment (prednisone 50 mg PO at 13, 7, and 1 hr before, and diphenhydramine (Benadryl) 50 mg, 1 hr before) decreases the chance that a reaction will occur. In cases in which the use of iodinated contrast agent is deemed the best option, despite a severe risk of an anaphylactoid reaction, the presence of an anesthesiologist to monitor the patient is required.

In order to minimize nephrotoxicity, all adult patients scheduled to receive an iodinated contrast agent must have had a recent test to measure serum creatinine. If one is not available or if there is any reason to think that there might have been a recent change, blood will be drawn before the imaging procedure and the serum creatinine level measured. If the level is 2 mg/dl or more, the radiology technologist must consult a radiologist before proceeding with the study.

Hydration lowers the risk of renal failure and is especially important in patients who have mild renal...
insufficiency, diabetes, or multiple myeloma. Patients should be encouraged to drink plenty of clear fluids both before and after the procedure. In those patients unable to take oral fluids, hydration is ensured through IV saline infusion. N-acetyl-cysteine is routinely used to reduce the chance of nephrotoxicity in cases of mild renal insufficiency. Other prophylactic drugs are available but these are only suitable for inpatient use.

Diabetic patients who are taking metformin (Glucophage) are at an increased risk for lactic acidosis if they suffer nephrotoxicity after contrast administration. For this reason, they must discontinue the drug at the time of the procedure until at least 48 hours afterwards and after it has been confirmed that the serum creatinine level remains within the normal range.

Further Information
MGH radiologists welcome all questions regarding the use of contrast agents and the choice of imaging modality. Please contact a radiologist in the appropriate Division of the Department.

For general questions about web-based Radiology scheduling, call 617-726-0304

For general questions about Radiology Services, call 617-724-4902

Scheduling and Reporting
CT imaging with contrast can be performed at Mass General West Imaging in Waltham, Mass General Imaging in Chelsea or the main MGH campus and can be ordered online via the Radiology Order Entry (ROE) system http://mghroe/ or by calling 4-XRAY (617-724-9729). Results are made available to physicians online within 24-48 hours.

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References


Tippins, RB, Torres, WE, Baumgartner, BR and Baumgarten, DA. (2000) Are screening serum creatinine levels necessary prior to outpatient CT examinations? Radiology 216: 481-4


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