

Requests for Imaging Using Contrast Media: What Information Must be Provided

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Abstract

A questionnaire is proposed for any imaging examination requiring contrast agent administration. Information about important risk factors is essential and drug history is also important because of possible interactions between contrast agents and other drugs. This information should be available before the appointment, so that prophylactic measures can be planned or an alternative imaging technique not requiring contrast agent administration can be advised.

1 Introduction

There are potential risks associated with the administration of contrast agents and adverse reactions may occur. In addition, contrast agents may interact with some of the drugs and clinical tests used in the management of patients (Morcos and Thomsen 2001; Morcos et al. 2001, 2005; Morcos 2005a, b; Thomsen 2006). Although most serious reactions are observed after intravascular injection, adverse effects may also develop after oral or intra-cavitary administration, because some of the contrast medium molecules may be absorbed into the circulation (Morcos 2005). Reactions to contrast agents can be divided into non-renal and renal adverse reactions. Non-renal reactions may be acute (developing within 1 h of contrast agent administration) or delayed (developing after 1 h but less than a week) (Morcos and Thomsen 2001). Some reactions, such as thyrotoxicosis and nephrogenic systemic fibrosis, may occur after 1 week and are termed very late reactions. Patients at high risk of these reactions should be identified before contrast medium administration to ensure that all necessary measures are taken to reduce the risk.

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2 Iodine-Based Contrast Media

2.1 Risk Factors for Acute Non-Renal Adverse Reactions

There is a 6-fold increase in incidence of severe reactions to both ionic and non-ionic contrast agents in patients with a history of previous severe adverse reaction to contrast agents. Asthma is also an important risk factor with a reported 6- to 10-fold increase in the risk of a severe reaction in such patients. Patients with a strong history of allergic reactions to different substances including those with a history of troublesome hay fever are also at risk (Morcos 2005a).

2.2 Risk Factors for Delayed Skin Reactions

A previous reaction to contrast medium is an important predisposing factor, increasing the risk of reaction by a factor of 1.7–3.3. A history of drug or contact allergy is a further risk factor, increasing the likelihood of a reaction by approximately a factor of two (“Late Adverse Reactions to Iodine-Based Contrast Media”). There is an increased incidence of delayed skin reactions to contrast agents in patients who have received non-ionic dimers or interleukin-2 (IL-2) (Webb et al. 2003; Morcos et al. 2005).

2.3 Risk Factors for Contrast Medium-Induced Nephropathy

Pre-existing renal impairment, indicated by serum creatinine $>130 \mu\text{mol l}^{-1}$ or preferably by an eGFR $<60 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$, calculated using the Modification of Diet in Renal Disease (MDRD) study equation (Bostom et al. 2002), is an important risk factor for contrast medium-induced nephropathy (CIN). The risk of CIN is greater if renal impairment is associated with diabetes mellitus. The degree of renal insufficiency is a major determinant of the severity of CIN (Thomsen 2006). An eGFR of $30 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$ or less markedly increases the incidence and severity of CIN (McCullough et al. 1997; Morcos et al. 1999). Other risk factors include dehydration, congestive cardiac failure, concurrent use of nephrotoxic drugs such as nonsteroidal anti-inflammatory drugs (NSAID) and aminoglycosides, hypertension, hyperuricemia, or proteinuria (McCullough et al. 1997; Morcos et al. 1999; Morcos 2004, 2005b).

Since pre-existing renal impairment is a critical risk factor for CIN, it is important to know the renal function before contrast agents are given, as precautions must be taken in patients with renal insufficiency. Measurement of serum creatinine is widely used for this purpose, but has

several limitations for accurate assessment of renal function (Morcos 2005b; Thomsen et al. 2005). eGFR is a better test when serum creatinine is abnormal, but is not perfect as all the equations used to calculate it overestimate renal function to varying degrees.

2.4 Risk Associated with Concomitant Medications

Although contrast agents are not highly active pharmacologically, interaction with other drugs may occur with possible serious consequences to the patient (“Contrast Medium-Induced Nephropathy”, “Contrast Media and Interactions with Other Drugs and Clinical Tests”). This is an important topic which should be included in a questionnaire.

2.5 Patients with Thyroid Disease

Radiographic water-soluble iodine-based contrast media solutions contain small amounts of free iodide, which may cause thyrotoxic crisis in patients with Graves’ disease or with multinodular goiter and thyroid autonomy, especially if they are elderly and living in areas of iodine deficiency. Patients at risk of thyrotoxicosis should be closely monitored by endocrinologists after iodine-based contrast medium injection. Prophylaxis is generally not necessary, but in high-risk patients, particularly those in areas of dietary iodine deficiency, prophylactic treatment may be given by an endocrinologist (“Effects of Iodine-Based Contrast Media on Thyroid Function”).

3 MRI Contrast Agents

MR contrast agents include extracellular and organ-specific agents. All current agents for intravascular use are based on gadolinium.

3.1 Non-organ-specific Extracellular MRI Contrast Agents

Most adverse reactions to extracellular agents are mild and transient. Risk factors for acute reactions include a history of allergy, bronchial asthma, or previous reaction to gadolinium-based contrast media (Niendorf et al. 1993; Shellock and Kanal 1999).

CIN is rare with doses not exceeding $0.3 \text{ mmol kg body weight}^{-1}$ (Sam et al. 2003; Thomsen 2004; Briguori et al. 2006; Ergün et al. 2006; Zhang et al. 2006). However, patients with pre-existing severe renal impairment may be

at risk of CIN after administration of extracellular nonorgan-specific gadolinium-based contrast media (Ergün et al. 2006). High doses of gadolinium agents used for X-ray procedures have a significant risk of inducing nephrotoxicity (Thomsen et al. 2002).

Nephrogenic systemic fibrosis has been reported in patients on dialysis or with a glomerular filtration below 30 ml min^{-1} , following administration of lower stability gadolinium-based contrast agents (“Nephrogenic Systemic Fibrosis and Gadolinium-Based Contrast Media”).

3.2 Organ-Specific MR Contrast Agents

The current MR organ-specific contrast agents are also gadolinium-based agents. Blood pool agents and liver-specific agents based on either iron or manganese are currently not commercially available. For the gadolinium-based blood pool agent and the liver-specific agents, the adverse reactions are the same as those seen after administration of the extracellular gadolinium-based agents (Bellin et al. 2005). Serious adverse reactions are rare. No specific risk factors have been identified for these reactions.

4 Discussion

Of all the potential adverse reactions to contrast agents, those which are most likely to have serious sequelae are severe anaphylactoid reactions and CIN. Also, patients with thyroid disease, particularly elderly patients living in regions with iodine deficiency, can be adversely affected by contrast media. In addition, it is important to be aware of the patient’s drug history as there is the possibility of interaction between contrast agents and other drugs.

It is proposed that the request for an imaging test which involves contrast agent administration should provide information about the important risk factors for the potential complications of giving the contrast agent. This information must be readily available before contrast agent administration, so that prophylactic measures can be planned, or an alternative imaging technique not requiring contrast agent administration can be advised. Some of the prophylactic measures, such as hydration or steroid prophylaxis, require time to produce the desired pharmacological effect. In emergency situations, the radiologist should try to obtain as much of this information as possible before contrast agent administration and should then, depending on the clinical problem under investigation, make a judgment of benefit against risk.

Demanding extensive information with the request is not practical and may not receive the cooperation of referring clinicians, and a questionnaire should therefore focus on

important risk factors for serious complications that are most likely to be encountered in clinical practice. The ESUR contrast agent questionnaire offers a practical approach for identifying patients at high risk of contrast agent reactions without omitting important risk factors or being excessively demanding to use routinely. It should be considered as a supplement to the standard referral for imaging examinations, and the completed questionnaire should be sent with the request to the Imaging Department for any further action. The ESUR questionnaire can be found in “ESUR Guidelines on Contrast Media Version 8.1”.

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