RADIOLOGY GUIDELINE FOR THE USE OF GADOLINIUM BASED CONTRAST AGENTS

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

Currently there are more than 30 million patient administrations worldwide per year (RCR Guidance on gadolinium- based contrast agent administration to adult patients April 2019).
Gadolinium-based contrast agents (GBCAs) are remarkably safe with a low rate of adverse event for both allergic type reactions and nephrotoxicity. Severe adverse reaction rate is estimated to be 0.0025% - 0.0050% (RCR Standards for intravascular contrast administration to adult patients 3rd edition).
However, administration of GBCAs in patients with severe renal failure has been associated with the development of the rare condition of nephrogenic systemic fibrosis (RCR Standards for intravascular contrast administration to adult patients 3rd edition).
Use of GBCAs has increased in recent years and although relatively safe there are subgroups of patients for whom the administration of GBCAs carries increased risk.
In 2006, the association between the administration of GBCAs in patients with severe renal failure and development of the very rare condition, NSF came to light prompting a review of the risk classification by EMEA (European Medicines Agency) of the different agents in use in Europe. This led to restrictions on those classified as high risk in patients with impaired renal function.

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Key amendments to this guideline

Date	Amendment	Approved by:
9th Feb 24	Document reviewed with no changes	Amy Todd/Radiology Governance

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NONE OF THESE HIGH RISK AGENTS ARE USED IN WAHT MRI DEPARTMENTS FOR INTRAVASCULAR ADMINISTRATION

Recently, it has been recognised that very small amounts of at least some forms of gadolinium contrast (about 1% of the injected dose) are retained in the tissues, mostly in the bones, with tiny amounts in the brain. WAHT MRI departments **do not use any of the gadolinium products associated with this increased risk.**

Patients covered by this guideline are those for whom there is a likelihood of intravascular administration. This guideline is a consensus based document and provides information on nephrogenic systemic fibrosis (NSF) and risk to patients when administering contrast agents. It also provides the rationale for removing the current screening protocol and guidance to provide the safest environment for patients during diagnostic MRI imaging examinations, whilst still ensuring appropriate access to imaging when clinically indicated.

The potential and theoretical risks of administration of GBCAs must be weighed against the potential benefits to the patient. This document aims to provide guidance on how GBCAs can be used as safely as possible with adult patients and follows guidance provided by The Royal College of Radiologists.

Definitions

In this Guideline:

AKI - Acute Kidney Injury

PC – AKI post contrast Acute Kidney Injury

NSF - Nephrogenic systemic fibrosis

What is NSF?

Nephrogenic systemic fibrosis (NSF) is a relatively uncommon condition in which fibrous plaques develop in the dermis and, often, in deeper connective tissues. Reported cases have occurred almost exclusively in patients with severe renal disease, and almost all have been associated with prior use of gadolinium-containing MRI contrast agents. The disease is often disabling, no proven treatments exist, and it may contribute to patient demise.

Who is at risk?

Only a very small number of cases of NSF have been reported in patients with stable eGFR > 30ml/min/1.73 m2 and in all these cases the eGFR was close to 30ml/min/1.73 m2. Thus it is likely that there is no absolute threshold GFR for risk but rather a continuum, with substantially lower risk at higher GFR.

Patients with co-existing severe liver disease and renal impairment, and renal impairment of any severity in patients within one month of liver transplant (before or after), are also regarded as being at increased risk. Chronic liver disease by itself does not appear to carry any increase in risk.

Lactating patients

In the past, some recommended caution in lactating patients because of the hypothetical risk of gadolinium excretion into breast milk; however it has been shown that, for at least some gadolinium-based agents, the proportion entering the breast milk is very small (in the order of 1% of the injected dose), and very little of this is actually absorbed. Hence the risk to the child would appear negligible.

Pregnancy

Gadolinium MRI at any time during pregnancy was associated with an increased risk of a broad set of rheumatological, inflammatory, or infiltrative skin conditions and for stillbirth or neonatal death. The study may not have been able to detect rare adverse outcomes.

Gadolinium-enhanced MRI was associated with a higher risk of stillbirth or neonatal death and a broad set of rheumatological, inflammatory, or infiltrative skin conditions.
Current recommendations are to forgo use of gadolinium enhanced MRI at any point during pregnancy, unless absolutely essential, and to carefully consider use of non-enhanced MRI in the first trimester

Identifying patients at increased risk

April 2019 RCR guidance states:

High volumes of GBCAs are nephrotoxic and in the presence of renal impairment there is a potential for post contrast-induced acute kidney injury.

However the guidance does '*not recommend contraindicating the use of GBCAs in patients with renal impairment because in some cases there are no alternatives, although the dose should be limited to the minimum consistent with the investigation being carried out.'*

Advice for all patients is

- Not to use large volumes >30mls
- Use a low risk GBCA and
- If a medium risk GBCA is necessary (liver imaging), a single lowest dose can be used (a dose not exceeding 0.1mmol/kg)
- Not to administer a repeat dose for at least 7 days without radiologist discussion and with consideration of total dose over the 7 days. In most cases the overall contrast volume will be less than 20ml. In-patient studies can require repeat IV contrast (if initial imaging is not diagnostic) and the risk of repeat contrast is still considered low.
- Avoid administering GBCAs in AKI whilst creatinine is still rising.

All GBCAs are administered by radiographers against a PGD with the exception of Magnevist which is injected directly into the joint space by a radiologist prior to MRI scan.

PGDs for Doterem and Primovist allow a maximum dose of 10mls & Gadovist 15mls.

GBCAs used in WAHT imaging departments	Risk Classification	Dose according to PGD / maximum dose permitted PGD
Gadoterate meglumine - Dotarem	Low	0.2ml / patient body weight – maximum of 10mls
Gadobutrol – Gadovist Gadovist is used in MRI cardiac scans under the supervision of a radiologist or cardiologist with dose based on weight. This may on occasion exceed >20mls but <30 mls	Low	0.1ml / patient body weight - maximum of 15mls
Gadoxetate disodium - Primovist	Medium	0.1ml / patient body weight - maximum of 10mls
Gadopentate Dimeglumine - Magnevist	High	Used only by radiologists for joint injections 10-12mls (Other adverse reactions seen with IV injections of gadolinium chelates have not been reported with Magnevist 2mmol/l due to the low dose and topical administration. No signs of intoxication secondary to overdose have been reported. Gd

		retention has not been identified for intra-articular administration.

Using the GBCAs in the table above in conjunction with the maximum doses permitted, radiology already follow the guidance for patients identified with any of the risk factors in that <30mls of GBCA are administered .

If a repeat dose is required then this should be discussed with the radiologist who will take into account the total amount administered over the 7 day period and whether the patient should have a renal function test first. For in-patient studies, where renal function is regularly monitored, the risk of repeat contrast is likely to be low especially if eGFR is more than 30.

Formal Assessment of Kidney Function if advised by the radiologist for a repeat dose within 7 days

If one or more of the below risk factors for kidney disease are present, an eGFR is required prior to administration of gadolinium: referrers will be prompted to answer these questions on ICE referral.

If an eGFR is required – then the following timescale apply:

- <3 months for outpatients
- <7 days for inpatients

Risk factors:

- Known history of kidney disease or dialysis
- Age > 65 years
- History of diabetes
- Liver transplant (within previous month) or transplant list

eGFR Measurement Reliability

Situations where eGFR measurement is an unreliable marker of GFR include:

- AKI (Acute Kidney Injury) (note that serum creatinine may not stabilize until 7-10 days after an acute insult),
- Peri-operative liver transplant patients
- Patients with “hepato-renal syndrome”
- Patients with chronic liver disease where eGFR may overestimate true GFR

References:

Royal College of Radiologists (RCR)	Guidance on gadolinium- based contrast agent administration to adult patients April 2019
‘Association Between MRI Exposure During Pregnancy and Fetal and Childhood Outcomes’	(JAMA September 6, 2016 Volume 316, Number 9 953 Joel G. Ray,MD, MSc, FRCPC; Marian J. Vermeulen, BScN, MHSc;

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