

Review Article

Clinical Safety of Cardiovascular Magnetic Resonance: Cardiovascular Devices and Contrast Agents

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Cardiovascular magnetic resonance (CMR) is an increasingly attractive imaging modality for the evaluation of patients with cardiovascular disease. It displays important inherent safety advantages: namely its noninvasive nature and the absence of exposure to ionizing radiation, or potentially nephrotoxic iodinated contrast agents.¹⁻³ However, there are several potential hazards associated with magnetic resonance (MR) scanning of specific cardiovascular devices and implants and the utilization of gadolinium-based MR contrast agents. In light of the growing number of both MR examinations and implantable cardiac devices in routine clinical practice worldwide, the aim of this review is to familiarize the contemporary cardiologist with some important clinical issues regarding the safety of CMR.

General MR safety principles

The potential risks associated with MR scanning of cardiovascular devices arise from distinct mechanisms related to the exposure to the scanner's static main magnetic field, the gradient magnetic fields and the radiofrequency (RF) energy.^{4,5} The most commonly used static magnetic field strength for clinical MR scanning is 1.5 to 3 Tesla (T). The higher the static magnetic field of the MR system, the greater the re-

sultant forces (translational attraction and torque) on ferromagnetic or weakly ferromagnetic materials.⁶ The MR environment may be unsafe for patients with certain biomedical implants or devices, primarily because of the risk of movement or dislodgment of objects made from ferromagnetic materials (ferromagnetic objects can become projectiles when introduced into the scanner area, and could cause the patient significant injury). Furthermore, device dysfunction or damage may be caused as a result of interactions with the strong static magnetic fields. Most, but importantly not all, currently implanted cardiovascular devices are either non-ferromagnetic or weakly ferromagnetic.

During MR imaging, the localization of the signals in the body is achieved by short-term spatial variations in magnetic field strength, generated by the gradient coils and termed gradient magnetic fields. These rapidly changing magnetic fields can induce electrical currents in electrically conductive devices and may directly excite peripheral nerves.

The last, but not least, MR factor related to safety is RF energy, i.e. electromagnetic energy transmitted as an RF pulse from dedicated coils in order to excite the body nuclei. The primary biologic effects associated with exposure to RF energy are related to its thermogenic qualities and the

consequent potential tissue heating. In addition, certain metallic devices, such as leads, can act as an “antenna” and concentrate RF energy, which leads to excessive local heating. The dosimetric term used to describe the absorption of RF energy is the specific absorption rate (SAR). The SAR is the mass normalized rate at which RF power is coupled to biologic tissue and is typically expressed in Watts per kilogram. It is important to note that SAR increases with the square of magnetic field strength, which is a concern when imaging at higher field strengths (3 T or more).⁶

Before every CMR examination, all patients should undergo a thorough screening procedure for cardiovascular and other implants and devices, in the form of a questionnaire that is completed and signed by the patient and should then be thoroughly reviewed and countersigned by the MR technologist or physician. MR screening forms are available for download at several websites.

Heart valve prostheses

With respect to clinical MR procedures, there has never been a report of a patient incident or injury related to heart valve prostheses. Numerous prosthetic valves and annuloplasty rings have undergone testing for MR safety at magnetic field strengths of 1.5 and 3 T.^{4,7,8} Heating and induced currents do not appear to be problematic for these implants. Since the magnetic field-related forces exerted on prosthetic valves and annuloplasty rings are deemed minimal compared with the force exerted by the beating heart, the presence of a prosthetic heart valve or annuloplasty ring that has been formally evaluated for MR safety should not be considered a contraindication for an MR examination at 3 T or less any time after implantation.⁹ This includes the Starr-Edwards model Pre-6000 heart valve prosthesis, which was previously thought to be potentially hazardous for a patient in the MR environment. Prosthetic valves cause localized artifact, but this rarely affects image interpretation. MR examination of patients with sternal suture wires is generally considered to be safe.

Coronary artery stents

Coronary artery stents have been evaluated in several *ex vivo* studies, in terms of magnetic field interactions and heating, and there do not appear to be any safety issues for these implants.^{4,7} More recent *ex vivo* studies conducted on several of the more commonly used

drug-eluting coronary stents demonstrated a lack of ferromagnetic interactions at 3 T that would pose a risk for stent migration.^{10,11} From the clinical perspective, Porto et al¹² were the first to demonstrate the safety of CMR very early (1 to 3 days) after insertion of both drug-eluting and bare metal stents. No acute thrombosis was recorded, and at 9-month clinical follow up no adverse cardiovascular events (target vessel restenosis or non-target vessel revascularization) occurred in patients treated with drug-eluting stents. Other clinical trials showed that CMR at 1.5 T can be safely performed shortly (within 1 to 14 days) after acute myocardial infarction and percutaneous revascularization with bare metal or drug-eluting stents, and is not associated with an increased risk of adverse clinical cardiac outcomes.^{13,14} Recently, it was shown that 3 T CMR is safe in the acute and chronic phase after myocardial infarction treated with primary stenting.¹⁵ In the light of published data, the recommendations are for CMR to be performed at 3 T or less any time after the implantation of a coronary stent (including drug-eluting stents).⁹ In terms of image quality, local artifact remains an issue for coronary stents, whereas the degree of in-stent stenosis cannot be assessed reliably.

Peripheral vascular stents, aortic stent grafts, and cardiac closure and occluder devices

According to the current recommendations regarding peripheral vascular stents, aortic stent grafts, and cardiac closure and occluder devices, MR examination at 3 T or less can be performed immediately after implantation for non-ferromagnetic materials, whereas for weakly ferromagnetic implants the timing of MR examination at 3 T or less should be determined on a case-by-case basis. Thus, in patients with chronic conditions in which it makes little difference whether the scan is performed at a given time or weeks later, it may be prudent to defer MR examination until about 6 weeks after device implantation.⁹

Pacemakers and implantable cardioverter-defibrillators

With regard to effects relating to clinical CMR applications, pacemakers and implantable cardioverter-defibrillators (ICDs) currently present the largest MR safety problem.¹⁶ Potential adverse interactions between pacemakers and MR include reed switch malfunction, asynchronous pacing, rapid atrial pacing, rapid ventricular pacing, induction of ventricular fibrillation, inhibition of pacing output, programming

changes, damage to the pacemaker circuitry, battery depletion, movement of the device and lead heating. In patients with ICDs, in addition to affecting pacing function, the MR environment may adversely affect tachyarrhythmia therapies. Notably, deaths associated with MR examination of patients with pacemakers/ICDs have been reported.

Recent investigations conducted using *ex vivo* techniques, laboratory animals, and patients demonstrated that certain “modern” (manufactured in year 2000 or later) pacemakers and ICDs, with features including fewer ferromagnetic components, more sophisticated circuitry, and improved electromagnetic interference rejection capabilities, are not adversely affected by MR, especially if procedures are performed under highly specific conditions.¹⁷⁻²³ More specifically, Nazarian et al²⁰ demonstrated the safety of non-cardiac and CMR imaging of patients with pacemakers and ICDs, using a protocol that incorporates device selection and programming (“asynchronous” pacing mode for pacemaker-dependent patients, disabling of magnet response and tachyarrhythmia functions) and limits the estimated whole-body averaged SAR to 2.0 W/kg. Other studies showed that CMR, as well as extrathoracic MR imaging, of non-pacemaker-dependent patients can potentially be performed safely under controlled conditions, where both MR- and pacemaker-related precautions are taken.^{21,23} It is notable that there are few current data on the performance of MR examinations of pacemaker-dependent patients, and most of the reports in the literature refer to patients with pacemakers undergoing non-cardiac MR scans.

Based on the current data, the perspective of the US Food and Drug Administration is that “a more thorough evaluation of concerns related to heating, arrhythmogenesis, and proper device function during and after MR imaging, as well as validated MR protocols, should be available before approval for labeling that endorses the use of MR imaging for pacemaker or ICD patients is obtained.”²⁴ According to the recent recommendations⁹ for the performance of MR imaging in patients with pacemakers or ICDs, the presence of a pacemaker or ICD should still be considered a strong relative contraindication for routine MR examination. Patients who have a pacemaker or ICD should not undergo an MR study if an alternative diagnostic test is available. MR examination of non-pacemaker-dependent patients is discouraged and should only be considered in cases in which there is a strong clinical indication and in which the benefits clearly outweigh the risks. With respect to pacemaker-dependent

patients and ICDs, MR examination should not be performed unless there are highly compelling circumstances and when the benefits clearly outweigh the risks. Scanning should only be performed at extremely experienced centers with expertise in MR imaging and electrophysiology, after written informed consent of the patient, under the supervision of a physician with advanced cardiovascular life support and pacemaker/ICD expertise and with the involvement of a person who has expertise in MR physics and safety.

Other devices and implants

Safety evaluation of several hemodynamic monitoring and temporary pacing devices has been carried out. Thus, patients with pulmonary artery hemodynamic monitoring/thermodilution catheters (such as the Swan-Ganz catheter) that have conductive wires should not undergo MR examinations, whereas patients with non-ferromagnetic pulmonary artery catheters that contain no electrically conductive pathways in the catheter may undergo MR examination. In addition, scanning of patients with temporary transvenous pacing leads is not recommended. However, retained temporary epicardial pacing wires are believed to be MR safe.⁹ Hemodynamic support devices such as intra-aortic balloon pumps, left ventricular assist devices and right ventricular assist devices, due to their high ferromagnetic material content, should be considered absolute contraindications for MR examination.⁹

It should be emphasized that when doubt remains as to the MR safety of any biomedical implant and device, consulting a more detailed source of information, such as dedicated websites (www.MRIsafety.com), reference manuals, or the manufacturer’s product information when available, is mandatory.

Safety of gadolinium-based MR contrast agents

Intravenously administered contrast agents are used routinely for MR examinations. The MR contrast media contain gadolinium, a particularly powerful paramagnetic metallic element, which is bound to a chelating agent. Gadolinium-based MR contrast media have been used clinically for many years. Adverse events associated with these agents typically are minor (e.g. nausea); severe effects such as allergic reactions or tissue necrosis as a result of extravasation are rare. In addition, gadolinium-containing contrast agents are believed to be less nephrotoxic than iodinated contrast agents used in radiography.²⁵

Recently, there has been growing concern about the association of gadolinium-based MR contrast agent administration and a disorder named nephrogenic systemic fibrosis (NSF). NSF, formerly known as nephrogenic fibrosing dermopathy, is a systemic disorder characterized by widespread tissue fibrosis that involves predominantly the skin, but also affects systemic organs such as the liver, heart, lungs, esophagus, diaphragm, and skeletal muscle. It is associated with severe physical disability and death when multisystem disease supervenes and it is known to occur only in patients with renal disease—generally in those requiring dialysis. The exact cause or trigger for NSF is still obscure. Recent literature suggests that exposure to gadolinium-based contrast media is the leading suspect. The speculative mechanism is that impaired renal excretion of gadolinium prolongs the half-life and enhances the chance for dissociation of gadolinium ions from its chelate, allowing increased tissue exposure and resulting in a fibrotic reaction. Notably, among the gadolinium chelates, gadodiamide is the agent that is most commonly associated with NSF.^{26,27}

With respect to CMR safety, the association between gadolinium exposure and the development of NSF is of particular importance, since gadolinium-contrast-enhanced MR studies, such as MR angiography, myocardial perfusion imaging and delayed enhancement imaging for myocardial viability assessment, are increasingly used in a broad spectrum of cardiovascular disease. In particular, the delayed contrast-enhanced MR imaging technique currently represents the new gold standard in the identification of irreversibly damaged myocardium.²⁸⁻³⁰ Therefore, the link between gadolinium and NSF obligates CMR specialists to ensure safety regarding the use of MR contrast agents in patients with advanced renal failure. Dialysis patients are clearly at risk and should avoid gadolinium exposure at all costs. It is also prudent to avoid gadolinium administration in patients with acute kidney injury and those with stage 4 chronic kidney disease (glomerular filtration rate less than 30 mL/min). If an MR study with contrast is absolutely required, then a non-gadodiamide contrast agent using the lowest possible dosage is preferable.^{26,27}

Conclusions

The rapidly evolving role of CMR and the proliferation of cardiovascular devices and implants demand a heightened awareness on the part of the cardiology and MR community, so that they may continually re-

view and update their policies and procedures pertaining to clinical MR safety. Strict compliance with the current MR safety guidelines, and a multidisciplinary, collaborative approach to the management of safety issues related to biomedical implants and contrast agents are necessary in order to perform safe and uneventful CMR studies.

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