Review

Clinical Application of Cardiovascular Magnetic Resonance

SOPHIE MAVROGENI, F[1]. RADEMAKERS[2], DENNIS V. COKKINOS[1]

[1]Onassis Cardiac Surgery Center, Athens, Greece and [2]Gasthuisberg University Hospital, Leuven, Belgium

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Address:
Sophie Mavrogeni

50 Esperou St.,
175 61, P. Faliro,
Athens, Greece
e-mail:
soma@aias.gr

Cardiovascular magnetic resonance (CMR) is a noninvasive technique, without the use of radiation, that is able to provide almost all the information that is needed for the evaluation of cardiovascular disease. Eligible are patients who do not suffer from claustrophobia and do not have a pacemaker or a defibrillator device implanted. A magnet system consists of 3 major components:

1) The magnet, which uses niobium-titanium wire conducting with zero resistance when cooled to the temperature of liquid helium.

2) The radiofrequency (RF) coils, which generate radio waves at a frequency determined by the field strength of the magnet and by the atomic nucleus. The RF coils transmit signals and receive those emitted from the body.

3) The gradient coil, which produces small magnetic fields that vary in a programmed way and create a range of resonance signals across the field of view to allow imaging in predefined planes.

Images are derived from signals produced by protons (hydrogen nuclei). These are present in abundance in the human body, which consists mainly of water. The proton behaves like a small magnet when placed in a magnetic field. It aligns with the field and precesses with a given frequency that depends on field strength. Protons will align parallel and anti-parallel to the direction of the primary field, with a small excess of parallel protons that give rise to a net magnetization vector. This net vector can be altered by application of a secondary temporary radiofrequency pulse. Once this pulse is discontinued, the magnetization vector starts to revert to its former position, releasing a signal in the form of radio waves. This relaxation of net vector is attributable to two distinct but simultaneous processes, referred to as the longitudinal (T1) and the transverse (T2) relaxations.

A pulse sequence consists of a series of radiofrequency pulses of varying duration or strength and the application of magnetic-field gradients that are adjusted to highlight desired tissue characteristics. Basic pulse sequences used in CMR are spin-echo and gradient-echo sequences, or their faster hybrids. Spin-echo sequences are used for morphology. Flowing blood typically appears black in these sequences. Gradient-echo sequences have lower soft-tissue contrast compared to spin-echo and flowing blood is represented by high signal intensity, with turbulence showing as areas of signal void. Gradient-echo sequences are used in the assessment of valvular lesions, shunts, great vessels and ventricular function.

New hardware developed recently for CMR includes:

- multiple RF amplifiers to receive the magnetic resonance signal. When more coils and RF amplifiers are used, higher signal-to-noise ratios are produced, giving better image quality

- increase in the imaging gradient strength and speed (known as slew-rates), leading to a reduction of scan time
- increase in magnetic field strength to 3 T. Currently 1.5 T is used for CMR. Magnets at 3 T allow better image quality, shorter acquisition time and increased ability to evaluate nuclei such as phosphorus-31 and hydrogen.

CMR can measure ventricular volumes and ejection fraction noninvasively without a contrast agent. It is of great value for the evaluation of the right ventricle (ejection fraction, wall motion, tissue characterization). CMR provides 3-dimensional images of the heart, which is also feasible with 3D echocardiography. While CMR ejection fraction and volumes are more accurate and reproducible than other imaging techniques, there is a good correlation between CMR and these techniques.[1] Echocardiography is still the everyday tool for ventricular function evaluation, but there is a place for CMR, because of its high reproducibility, in order to follow individual patients with respect to changes in right and left ventricular volumes, mass and function (dilated cardiomyopathy, valvular or congenital heart disease, right ventricular dysplasia, etc.).

The main clinical applications of CMR are summarized below.

Congenital heart disease

In this case, CMR is complementary to echocardiography for the evaluation of patients with congenital heart disease. Concerning coarctation, it gives an excellent overview of the aorta and best visualization of the stenotic part and collaterals. Pressure gradient can be also quantified using phase-velocity mapping. There is a special place for CMR in the evaluation of complex congenital heart diseases. Using planes aligned with cardiac chambers, lesions with complicated anatomy, such as transposition, double outlet syndrome and truncus arteriosus, can be clarified. Using consecutive transaxial images the aortic arch and pulmonary bifurcation can be easily imaged. As a consequence the technique is ideal for the diagnosis and follow-up of tetralogy of Fallot (TOF), pulmonary atresia or pulmonary artery stenosis. In TOF, the right ventricular infundibulum and hypertrophy can be assessed. CMR has also high sensitivity for the detection of atrial septal defects.[2] It is also useful for the diagnosis of anomalies of the systemic venous system, mainly in older individuals and in the follow up of past surgery (baffles, conduits, etc). Although the diagnostic value of CMR is the same as that of transesophageal echocardiography, the combination of both techniques has given the best accuracy in centers where there is documented experience in the field. Finally, CMR has the possibility to quantify shunt by measuring flow in different vessels and/or structures (aorta, pulmonary vessels, caval veins, baffles, etc.).

Valvular heart disease

Valvular stenosis or regurgitation appears as dark jets into a bright blood chamber. CMR has a special role in the evaluation of the severity of aortic or mitral regurgitation, with a diagnostic accuracy of 97%.[3] The technique, although time consuming, permits quantification of regurgitant volume and fraction and shows effect on left ventricular volumes and mass with high accuracy and reproducibility (important for follow-up in individual patients).

Pericardial disease

The normal pericardium can be visualized on anatomical (spin-echo) images as a line of low signal intensity located between the high signals of peri- and epicardial fat. Normal pericardial thickness is 2-4 mm. CMR is the best diagnostic approach for constrictive pericarditis. In these patients pericardial thickening is usually >4 mm. Depending on the severity, dilatation of hepatic veins, inferior vena cava and right atrium may coexist. Although CMR is unable to detect calcifications, and there are some forms without pericardial thickening, the diagnostic accuracy for the detection of constrictive pericarditis is 93%.[4] CMR is also useful for the detection of generalized or localized pericardial effusions and pericardial cysts. However the everyday diagnostic technique for the first evaluation of the pericardium is echocardiography because it allows easy evaluation of flow variations with respiration; with the newer magnets real time flow measurements in the left ventricular outflow tract or across the mitral valve have also become possible.

Aortic dissection

CMR has a sensitivity of 98% and specificity of 98% in the detection and evaluation of aortic aneurysm, but its use also depends on its availability outside of working hours and on the situation of the patients (hemodynamic stability). It is more accurate compared to computed tomography (sensitivity 94% and specificity

Figure 1. Aortic dissection of the descending aorta. The thrombosed pseudo-lumen is clearly seen (white arrows).

87%) and transesophageal echocardiography (sensitivity 98% and specificity 77%).[5] The big advantage of the technique is its ability to show the extension of the dissection into the aortic arch (Figure 1), the associated aortic regurgitation and intrapericardial hemorrhage. It is the technique of choice for follow up of patients with aortic dissection, postoperative complications and late complications after surgery to the aorta in sometimes symptom-free patients. Contrast aortography is no longer considered to be the diagnostic gold standard for evaluating the thoracic aorta. Multiplanar transesophageal echocardiography, spiral computed tomography (CT) and magnetic resonance imaging (MRI) have been shown to have high sensitivities and specificities for the diagnosis of aneurysms and dissections and their variants. Transesophageal echocardiography and MRI are thought to be superior to spiral CT because of their ability to evaluate the aortic valve apparatus. However, spiral CT is perhaps the easiest and most cost effective modality for screening patients with known or suspected aortic dissection.[6] Assessment of aortic elastic properties by MRI can aid early diagnosis and screening for Marfan syndrome.

Coronary artery disease

The approach to coronary artery disease consists of evaluation of coronary arteries and myocardial perfusion and viability.

Coronary angiography

Coronary magnetic resonance angiography (CMRA) is technically difficult because of the small size, tortuosity and complex 3D anatomy of the coronary arteries. Using 3D acquisitions, a multicenter trial showed a sensitivity of 100%, a specificity of 85% and an overall accuracy of 87% for diagnosis of coronary artery stenosis in patients with left main or 3-vessel coronary artery disease.[7] Compared to conventional coronary angiography, the sensitivity and specificity of CMRA for the detection of significant coronary stenosis vary from 63% to 90% and 71% to 92%, respectively.[8] CMRA is also excellent for detecting an anomalous origin of the coronaries[9] and the patency of bypass grafts. However, CMRA is limited for the evaluation of grafts distal to the first coronary anastomosis[10] and metallic clips can create image artifacts. CMRA is also very useful for the evaluation of coronary artery ectasia[11] and Kawasaki disease[12] (Figure 2). However, MRI of the coronaries is not yet ready for mainstream diagnostic use. The abnormal contractile response to stress and the quantification of flow reserve, studied by MRI, seem to be more physiologic and more readily available for evaluating the extent and importance of ischemic heart disease. On the other hand, left anterior descending artery flow measurement (rest/stress) with echocardiography is much easier, less time consuming and widely available.

Myocardial perfusion and viability

CMR may detect ischemia by observing wall motion, as does stress echo, but without the limitation of an acoustic window. In one study,[13] it was shown to have

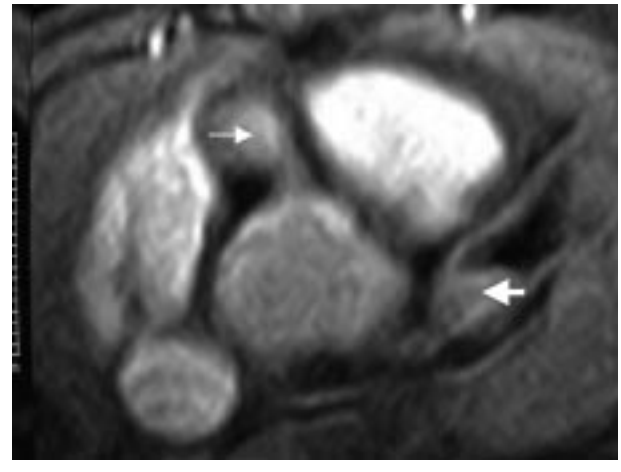

Figure 2. Kawasaki disease. Aneurysm of the right (thin arrow) and left (thick arrow) coronary artery.

a better sensitivity than dobutamine stress echocardiography. Its place, however, in daily routine remains to be proven. CMR also plays an important role in the detection of viability. After intravenous administration of a paramagnetic contrast agent, such as gadolinium chelate, perfusion can be assessed qualitatively on the first pass of the agent through the myocardium. Viability is assessed on later images (after 12 minutes or later). A defect on the initial scan represents either hypoperfused viable or infarcted myocardium. Delayed enhancement occurs in scars[14] (Figure 3). CMR has the same predictive value as positron emission tomography in the detection of viability. Its main advantage compared to nuclear techniques is the spatial resolution, which allows discrimination of subendocardial versus subepicardial perfusion abnormalities and non-transmural infarcts. This increases both sensitivity and specificity. Late enhancement is present not only in acute and chronic infarction but also in a wide range of myocardial diseases (cardiomyopathy, myocarditis, etc.) where it might have prognostic implications. Contrast-enhanced CMR and single photon emission computed tomography (SPECT) detect transmural myocardial infarcts at similar rates. However, CMR detects subendocardial infarcts that are missed by SPECT.[15] In chronic coronary artery disease, a combination of fibrosis and viable non-functional myocardium exists. Recovery of impaired left ventricular function depends on the extent of fibrosis. In a recent study,[16] ventricular contractility improved in 78% of dysfunctional segments with no hyper-enhancement compared with less than 2% of those with hyper-enhancement of more than 75% of tissue .

Figure 3. Delayed enhancement indicative of an extensive myocardial infarction (white area shown by white arrows).

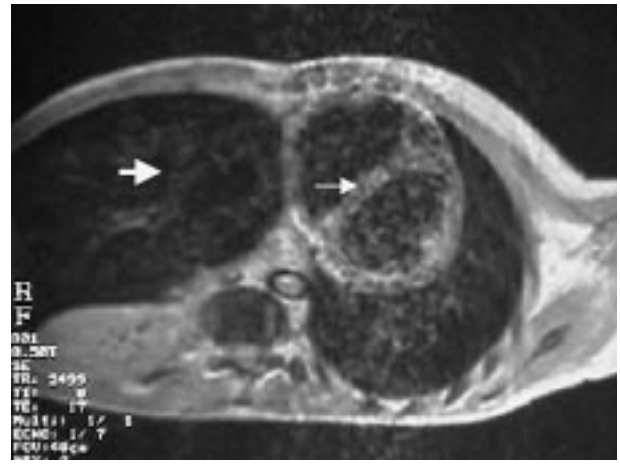

Figure 4. High iron overload in heart (thin arrow) and liver (thick arrow) in a patient with b-thalassemia.

Cardiomyopathies

CMR has a special place in the detection of arrhythmogenic right ventricle (ARVD), because of its ability for tissue characterization and wall motion study of the right ventricle. Depending on the criteria, almost 95% of ARVD cases can be identified using this technique.[17] The presence of regional dyskinetic areas is the most typical abnormality. The presence of intramyocardial fat can be more difficult to identify and is sometimes present in other diseases and even in normal individuals. CMR is also important for the assessment of patients with hypertrophic cardiomyopathy,[18] iron overload[19] (Figure 4) and the early detection of cardiomyopathy and respiratory muscle involvement in Duchenne muscular dystrophy.[20]

Masses: tumors and thrombi

CMR offers better visualization of a tumor's relation to surrounding structures and extension through cardiac and adjacent structures. There are also some possibilities for tissue characterization using T1, T2 and contrast.

Current status in Greece and future prospects

Although MRI seems to be very promising, there are still some limitations. Currently, there are not many magnets with the necessary cardiac package in Greek hospitals. The cost of the examination at the moment in this country is equal to that of a thallium scan, but approval from a medical committee is a prerequisite for performing the examination. CMR has the best spatial resolution compared to all other imaging techniques, but it is not a real time examination in most scanners. It is able to detect even subclinical changes in myocardial diseases. However, it is a time consuming technique: it takes at least one hour and a half to perform an integrated cardiac MRI study. Post-processing work, essential for the diagnosis, is also time consuming. There is a lack of expertise in the interpretation of CMR results. Stress CMR studies are not performed at the moment, due to a lack of arrangements for cardiac emergencies. Finally, although there is the possibility that the use of higher fields (3T) will permit a real time examination and an improvement in coronary angiography, this technology is not currently available in Greece.

In conclusion, CMR is a new technique that is able to provide a variety of anatomic and functional information about cardiac diseases, non-invasively and without radiation. It is likely that CMR may reduce the need for current nuclear imaging modalities in patients with coronary artery disease. It is of great value in congenital heart disease, the evaluation and follow-up of aorta pathology, arrhythmogenic right ventricular cardiomyopathy, iron overload heart disease, pericardial and tumor evaluation.

Currently, the ability of the technique to detect myocardial scar easily and reproducibly increases its diagnostic spectrum in ischemic patients, while the application of new contrast agents and the use of higher fields look more promising for coronary angiography in the near future.

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