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The emerging role of cardiovascular MRI in the evaluation of cardiovascular disorders

FAYEZ BOKHARI, MD, FRCPC; LOUIS WU, MD, FRCPC; and CHI-MING CHOW, MD, MSC, FRCPC

Cardiovascular magnetic resonance imaging (CVMRI) is a rapidly emerging field in cardiovascular medicine that has enormous potential. The first MRI examination on a human was performed on July 3rd, 1977. Although impressive at the time, it took almost 5 hours to produce 1 image and the image quality was poor when compared with the standards of today. Recent technological advances have allowed CVMRI to evolve into an imaging modality for comprehensive evaluation of patients with cardiovascular (CV) diseases. This issue of *Cardiology Rounds* focuses on how CVMRI can help to accurately diagnose various cardiovascular conditions, as well as supplement other modalities, in determining the extent of CV disease.

The machine that produces MRI images is a giant cube that measures 2 x 2 x 3 meters in size. It contains a central bore surrounded by a super-conducting magnet. MRI scanners all have the same basic design concept, although new models are rapidly shrinking in size and portable scanners are being developed. Patients are positioned on their back and slid into the central bore of the scanner where the electromagnetic field "manipulates" the molecules in the body. The human body consists mainly of hydrogen ions in the form of water (H_2O) molecules. An electromagnetic magnetic field runs inside the bore generated by the magnet and this induces resonance of the hydrogen ions, which absorb radiofrequency energy. When the radiofrequency energy is turned off, the protons return to their natural alignment and release the energy required to generate images. Static images of the constantly moving heart are acquired by a variety of ingenious cardiac and respiratory techniques. Newer methods, such as navigator pulses that monitor diaphragmatic movements, have been developed to further overcome motion artifacts.

There are 3 primary types of imaging sequences used in CV imaging:

Spin echo imaging: The blood is black and high-quality anatomic images can be produced.

Gradient echo imaging: The blood is white and high-quality cine images can be obtained that are used to identify regional myocardial function and abnormal flow patterns (Figure 1).

Velocity mapping: This is a variant of gradient echo imaging that measures flow directly, unlike Doppler techniques used in echocardiography that measure velocity rather than flow.

Recent advances in MRI techniques have increased the accuracy and widened the clinical utility of CVMRI in evaluating CV morphology, blood flow, and myocardial function. From the start, CVMRI provided excellent anatomic information, especially in patients with congenital heart disease. More recently, it has also been used to quantify global and regional cardiac function and assess valvular heart disease, cardiomyopathy, and pericardial and aortic diseases. Emerging applications for CVMRI that are being actively investigated include the assessment of coronary arteries (Figure 2), myocardial perfusion, viability, and plaque morphology.

Ventricular function assessment

There is abundant evidence linking ventricular function to patient prognosis. Current techniques, however, are not ideal. Radionuclide imaging suffers from radiation burden and low spatial resolution, while echocardiography is limited by technical issues such as acoustic windows and reproducibility.

St. Michael's Hospital
30 Bond St.,
Suite 7049, Queen Wing
Toronto, Ont. M5B 1W8
Fax: (416) 864-5941

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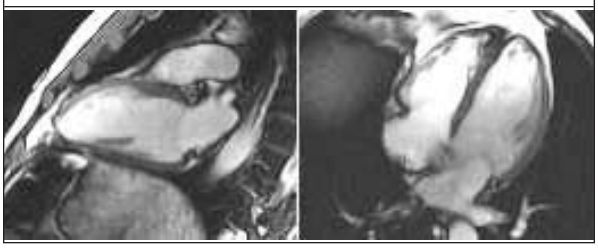
Figure 1: White blood cine-gradient echo images of 4 chamber and long axis views of the heart



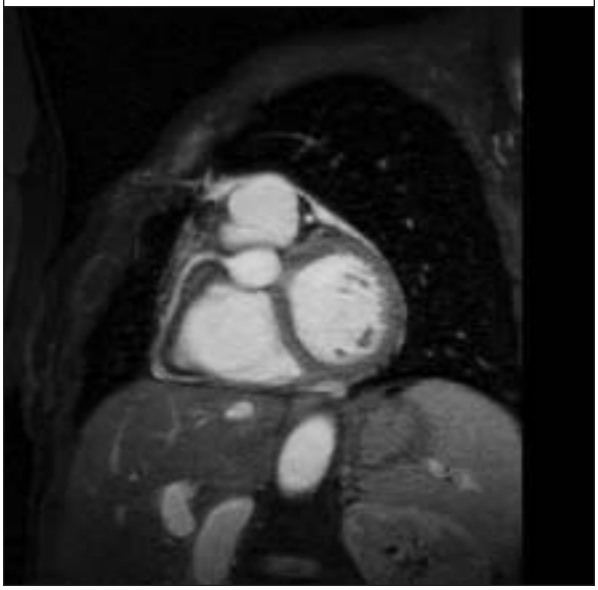
These techniques have been shown to be less accurate and reproducible than CVMRI, which is now recognized as the gold standard in evaluating ventricular function. CVMRI can produce accurate and reproducible tomographic, static, and cine images with high spatial and temporal resolution. Furthermore, it can be achieved in any desired plane without ionizing radiation and usually without contrast. Cine-gradient MRI sequences can be used to precisely measure ventricular volumes, wall motion, ejection fraction and flow across valves in one examination. Volume data can be used to construct volume-time curves to evaluate disorders such as diastolic dysfunction. The spatial resolution in cine-gradient MRI provides excellent qualitative assessment of global function with quantitative assessment of left and right ventricular ejection fraction.

Quantifying regional wall motion abnormalities objectively with noninvasive imaging methods has always been a major challenge. In CVMRI, myocardial tagging is used to quantify regional wall function objectively and with reproducibility. Specific regions of the myocardium can be tagged or labeled and tracked during systolic contraction with CVMRI. Regional wall contractile function can then be expressed by the displacement of the tagged regions from baseline.

Valvular heart disease

In patients with valvular heart disease, echocardiography and catheterization can evaluate the etiology and severity of disease, as well as the potential for surgical intervention. CVMRI can provide much of this information as well. It can define valvular morphology, grade the severity of stenosis or regurgitation, and assess cardiac structures affected by valvular dysfunction (contractile function, volumes, muscle mass, or thrombi). Evaluation of morphology has improved recently with the use of dual inversion recovery T1-weighted breath-hold imaging. The normally thin fibrous valve leaflets, which are constantly in motion, are particularly susceptible to motion artifacts. Furthermore, fibrosis and calcifications in valvular disease are characterized by MRI signal loss, making evaluation more challenging. Newer techniques, along with cine-gradient imaging, can now overcome some of these limitations. Regurgitant and stenotic jets cause signal loss or void due to turbulent flow. These are well-demonstrated in cine-gradient sequences.

Figure 2: Double oblique 3D image of a normal right coronary artery

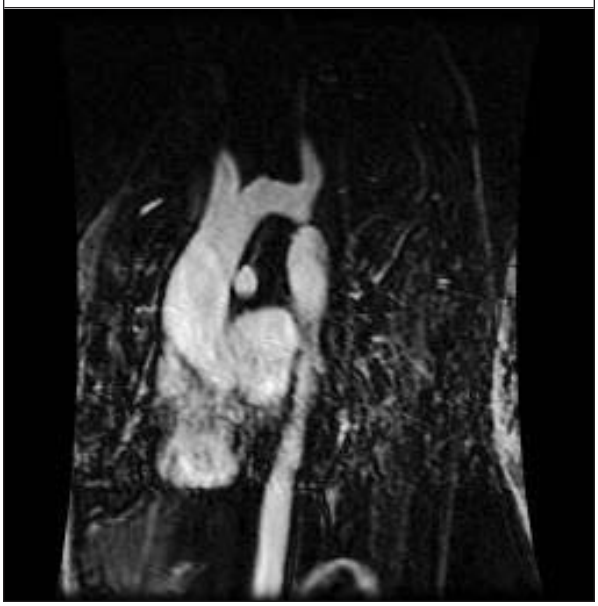


With velocity-encoding (velocity mapping) techniques, velocities and flow volumes can also be measured to provide a more objective and quantitative grading of disease. This is important for medical therapy decisions as well as timing of surgical intervention, and is particularly useful when clinical and echocardiography results are discordant or conventional assessment has failed, (eg, in the case of severe aortic stenosis when a catheter cannot be passed across the valve during invasive hemodynamic measurement). Additional information, such as ventricular volumes and function, can also be elicited during a study, thus providing all the information necessary for surgical assessment. Investigation of mechanical heart valves is also being performed, although the presence of metal still produces significant artifacts, thus limiting the clinical utility of this type of investigation for the moment.

Congenital heart disease

Literature and experience suggest that CVMRI and echocardiography are both important and complementary investigations for congenital heart disease.[1] As in other diseases, excellent morphologic assessment can be coupled with functional evaluation, including documentation of intracardiac defects or vascular anomalies. For some disease entities (eg, complex congenital anomalies, conduit evaluation, or great vessel disease), CVMRI is superior to echocardiography.[2] For example, in aortic coarctation (Figure 3), the entire aorta can be visualized in thin sections for precise measurement of diameter at appropriate levels, unhindered by the limited windows of echocardiography or the projectional imaging of conventional angiography. Furthermore, the flow mapping technique allows for a noninvasive flow comparison between the point of coarctation and the descending aorta, thus reflecting the physiologic significance of any anatomic narrowing. Intracardiac shunts can be assessed quantitatively

Figure 3: Sagittal oblique 3D S-gadolinium-enhanced image of the aorta demonstrating focal coarctation of the aorta in a juxta-ductal position



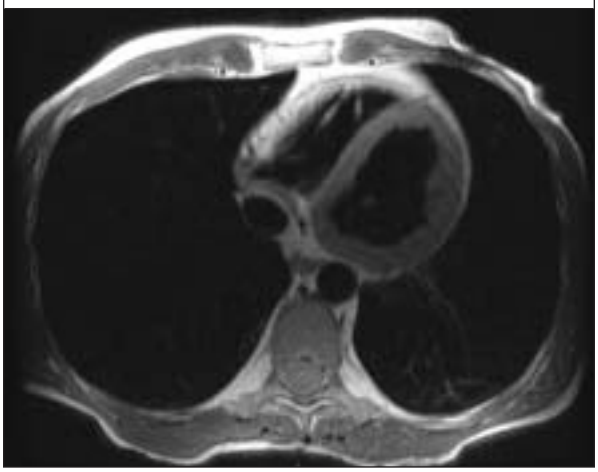
noninvasively in a similar evaluation, with measurements of the pulmonary and systemic flow for shunt ratio calculations.[3]

Cardiomyopathy

CVMRI has demonstrated its utility in evaluating cardiomyopathy. Most commonly, it is used for imaging arrhythmogenic right ventricular dysplasia (ARVD). Due to its high intrinsic tissue contrast, CVMRI is likely the most sensitive imaging tool for identifying the fatty replacement identified in ARVD (Figure 4). In addition, the morphologic and cine images allow evaluation of focal wall dyskinesis and abnormal thinning. These are the 3 primary imaging findings associated with the clinical criteria for diagnosis of ARVD.

CVMRI is also useful for evaluating dilated, hypertrophic, and restrictive cardiomyopathy. With respect to follow-up imaging, CVMRI can assess chamber sizes and function with less variability and better reproducibility than 2D echocardiography (but perhaps less than 3D techniques). It can be difficult to differentiate restrictive cardiomyopathy from constrictive pericarditis using conventional diagnostic modalities such as echocardiography or invasive hemodynamic measurements. However, CVMRI can easily visualize and measure the entire pericardium and, in addition, identify abnormal inflammation or edema by gadolinium on T2-weighted images. In hypertrophic cardiomyopathy, the presence, distribution, and severity of left ventricular hypertrophy (LVH) is well-demonstrated with CVMRI. In addition, the degree of obstruction and response to therapy can be evaluated in hypertrophic obstructive cardiomyopathy.[4] Cardiomyopathies due to secondary causes can also be evaluated to greater advantage as CVMRI allows delineation of disease extent with T2-weighted and gadolinium-enhanced T1-weighted sequences. Diagnosis, response to therapy, and follow-up in cardiac sarcoidosis, amyloidosis, or hemochromatosis are less invasive than endomyocardial biopsy and may be more sensitive than echocardiography. In hemochromatosis, the deposition of iron is a specific marker that is well-identified by tailored MRI sequences.

Figure 4: Axial T1-weighted CVMRI image of the right ventricular free wall with transmural fatty replacement of the myocardium



Pericardial and aortic disease

CVMRI is invaluable in assessing the pericardium. It is capable of routinely imaging the entire pericardium as a uniform thin "dark" line on T1-weighted sequences. Along with cine-gradient imaging and gadolinium, it can also characterize various disease processes. Thus, the CVMRI can be used to differentiate uncomplicated serous fluid in pericarditis from hemorrhagic or chylous effusions, or neoplastic involvement with abnormal enhancement. Solid tissues such as thrombus and tumour can be differentiated as well as the extent of tumour involvement in the pericardium and adjacent myocardium.

Another major contribution of CVMRI involves its aforementioned role in diagnosing restrictive versus constrictive cardiomyopathy. In addition to visualizing abnormal thickening or enhancement, quantitative functional imaging with flow and volume curves can demonstrate constrictive abnormalities in diastolic ventricular filling.

A prospective comparison between established and new imaging techniques provides evidence that CVMRI and transesophageal echocardiography are preferable diagnostic tests to investigate suspected thoracic aortic dissection.[5] Unlike transesophageal echocardiography – where there is a blind spot at the aortic arch due to interposition of the bronchus between the esophagus and the aorta – the entire length of the aorta is easily investigated by CVMRI.

Coronary artery disease

CVMRI is an attractive method for evaluating patients with coronary artery disease and several reports have documented its clinical utility in evaluating ischemic heart disease. With its high spatial resolution, CVMRI can identify ischemic

areas and delineate the extent of transmural infarction. Recently, the technique of delayed enhancement with gadolinium contrast agent has been used to detect myocardial infarction. Gadolinium concentrates in necrotic tissue (acute infarction) and scar tissue (nonviable chronic infarction) because of an increased partition coefficient. There is a close correlation between signal enhancement volume and infarct size. Microvascular obstruction at the infarct core has been demonstrated in humans even after reperfusion and is a predictor of poor functional recovery and postinfarction complications.[6,7] The presence of CVMRI evidence of microvascular obstruction correlates well with a higher rate of cardiovascular events in the first 2 years after myocardial infarction. Infarct size, as determined by CVMRI, is also a major predictor of adverse cardiovascular events.[7] In addition, it has been demonstrated that reduction in the transmural extent of hyper-enhancement by contrast-enhanced CVMRI early after myocardial infarction is associated with early restoration of flow and future improvement in contractile function.[8]

Myocardial viability

The identification of viable myocardium is useful in predicting which patient will have improved survival and increased left ventricular function after revascularization. Noninvasive methods, such as the thallium rest and redistribution nuclear test or the low-dose dobutamine stress echocardiogram, have proven clinical utility for assessing viability, but each has limitations that may reduce diagnostic accuracy. Ventricular wall motion cannot be used to quantify myocardial salvage after myocardial infarction because necrotic, stunned, and hibernating myocardium all present with impaired contractile function. Several promising CVMRI techniques[9-12] have been used to assess viability in recent years. Gadolinium-enhanced CVMRI can be used to distinguish between reversible (viable) and irreversible (nonviable) myocardial ischemic injury, regardless of the extent of regional wall motion or the age of the infarct. Delayed hyper-enhancement (by 3 to 15 minutes) in contrast CVMRI is associated with nonviability, while the absence of hyper-enhancement indicates viability, regardless of resting contractile function and correlates well with radionuclide and echocardiographic determination of viability.[13] In one study,[9] the likelihood of functional improvement in regions without hyper-enhancement (viable) was 86% for segments with at least severe hypokinesis, and 100% for segments with akinesis or dyskinesis.

Coronary artery assessment

As magnetic resonance angiography (MRA) has supplanted conventional angiography in larger vessels, significant effort has been made in improving sequences for coronary artery imaging. These include non-contrast enhanced "white blood" gradient echo, as well as gadolinium-enhanced coronary MRA sequences. Early confidence in identifying origins and proximal coronary arteries has made MRA an excellent noninvasive method for documenting coronary anomalies. In fact, several reports suggest that it should be the preferred test in cases of misclassification, when there is an inability to classify anomalous vessels by conventional angiography,[3,14] or in cases with associated cardiac anomalies.

Coronary MRA can also be used to assess the patency of bypass grafts and evaluate in-stent restenosis after successful percutaneous coronary intervention (PCI). At present, in-stent restenosis is usually detected invasively with conventional catheter angiography. Several investigators have reported on the utility of phase-contrast CVMRI coronary flow reserve to identify flow-limiting (>70%) stenosis in patients with recurrent chest pain after PCI. The sensitivity and specificity of CVMRI coronary artery flow reserve <2.0 were 100% and 89%, respectively for identification of >70% restenosis. It also can be used to assess functional restenosis in borderline 50% lesions.[15] Manning et al reported 90% and 92% sensitivity and specificity, respectively, for detection of >50% narrowing using coronary angiography as a gold standard.[16] The exclusion or confirmation of coronary artery disease is an important future application as part of the complete noninvasive CVMRI package. This particular aspect also has tremendous potential as hardware and software continue to advance.

Spontaneous rupture of atherosclerotic plaque with subsequent thrombosis is the most frequent cause of acute coronary events and the determination of plaque composition and morphology may determine whether a plaque rupture is likely. Intravascular CVMRI can detect different plaque components (lipid, collagen, fibrin, and calcium) and may be used to clinically assess plaque stability.[17,18]

Myocardial perfusion and ischemia detection

Contrast-enhanced CVMRI can be used for detecting and assessing the extent of coronary ischemia. In addition, it can be used to assess the effect of revascularization on myocardial perfusion.[19] There are approximately six million nuclear perfusion studies performed worldwide annually and all involve exposure to ionizing radiation. A safer technique would be medically welcome, provided it can maintain the same diagnostic accuracy. Perfusion stress MRI is fast and simple. It involves a baseline first-pass perfusion study using gadolinium as a contrast agent and a repeat study during adenosine or dobutamine stress. Areas of reduced perfusion show up as dark areas surrounded by normally enhanced areas. Substantial progress has also been made in the field of contrast echocardiography for assessing myocardial

Table 1: Contraindications for CVMRI

Absolute contraindications

- Cardiac pacemakers or implantable cardioverter defibrillators (ICDs)
- Coronary stents or IVC filters implanted within 6 weeks
- Occular implants

Relative contraindications

- Prosthetic heart valves
- Coronary stents or IVC filters implanted more than 6 weeks
- Aneurysm clips in particular neurosurgical clips
- Carotid vascular clips
- Metallic foreign objects (eg, bullets)
- Severe obesity (eg, over 300 lbs, depends on specific MRI model)
- Claustrophobia
- Cochlear implants
- Dental implants
- Pregnancy

perfusion. The diagnostic and clinical utility of these exciting new techniques is being actively investigated.

Detection of LV contractile dysfunction induced during exercise or dobutamine stress echocardiography has proven clinical utility, but wall motion visualization by transthoracic echocardiography can be difficult in patients with poor acoustic windows, large body habitus, obstructive pulmonary disease, or prior cardiac surgery. While obese patients and conduction abnormalities can affect the diagnostic accuracy in stress nuclear imaging, cine-gradient echo CVMRI is an attractive alternative that can be used to assess LV contraction and diagnose inducible myocardial ischemia. The diagnostic accuracy of dobutamine/ atropine/adenosine CVMRI stress testing has been shown to be comparable to dobutamine stress echocardiography[20] and radionuclide scintigraphy.[21,22] In one study, the sensitivity and specificity for detecting a >50% luminal diameter narrowing were 83% and 83%, respectively, which are similar to other noninvasive tests.[23]

Conclusion

CVMRI is safe and has several advantages, including high intrinsic tissue contrast between blood pool and cardiovascular structures. This provides excellent edge definition of the different cardiac layers and consequently, contrast agents are not routinely required in CVMRI. When employed, gadolinium has an extremely safe profile and can be administered to patients with renal failure since it is essentially non-nephrotoxic. A potential advantage that CVMRI possesses over echocardiography is its ability to be more quantitative and objective in nature, with higher image resolution and <5% inter-study variability. This allows for enrollment of a smaller number of patients in research studies to achieve statistical significance. In addition, CVMRI allows more accurate and reproducible serial quantitative assessments of disease severity in patient follow-up. However, the clinical use of CVMRI is influenced by the already widespread, lower cost, and more portable echocardiography. Consequently, the current clinical role of CVMRI is to complement the information obtained by echocardiography.

Drawbacks and limitations to CVMRI include the high set-up costs, its limited availability, as well as the lengthy imaging times (total scan time ranges from 40 to 90 minutes, depending on the indication). The most essential and basic requirement for imaging is the ability to perform proper ECG gating; however, many cardiac patients are prone to dysrhythmias (eg, atrial fibrillation, frequent premature atrial or ventricular contractions) and this can be a challenging and sometimes insurmountable obstacle.

In addition, many patients cannot undergo CVMRI exams due to various absolute and relative contraindications (Table 1). There are potential hazards and artifacts due to the ferromagnetic and non-ferromagnetic metals used in CVMRI. The relative contraindication of these materials depends on the degree and location of ferromagnetic objects. Currently, there is no known biological hazard to humans from exposure to the magnetic fields of clinical CVMRI, although pregnant women do not routinely undergo CVMRI because of the potential risk to the fetus. It is important to communicate with the CVMRI lab regarding various potential contraindications when requesting an examination for your patient.

In conclusion, CVMRI is recognized as an established modality for the comprehensive evaluation of cardiac morphology and function. Its safety profile, excellent image quality, reproducibility, and clinical utility compares favourably with other widely accepted noninvasive and invasive diagnostic modalities. However, CVMRI is still in the early phase of its clinical application and adoption into everyday clinical practice and its widespread clinical use is limited by many factors (eg, portability, high set-up costs, limited availability, and perhaps the false perception of poor patient tolerance to this procedure). Making a meaningful judgment about the cost-effectiveness of CVMRI requires further research to examine the actual patterns of use and its effects on clinical outcomes. Specialty training has barely begun and there will be a shortage of expertise for some time to come. Fortunately, the new American College of Cardiology Training Symposium Guidelines recommend training in CVMRI for all cardiology trainees in North America. When coupled with close collaboration between cardiologists, radiologists, and cardiac surgeons, the potential contribution of CVMRI to patient clinical care and research is limitless.

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